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KEMENTERIAN KESIHATAN
MINISTRY OF HEALTH

GUIDELINE ON GOOD STORAGE AND DISTRIBUTION PRACTICE

FOR MEDICINAL PRODUCTS

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PREFACE

The Department of Pharmaceutical Services has the pleasure to present all of you this 2nd edition of the Guideline on Good Storage and Distribution Practice for Medicinal Products (GSDP) for your reference. This guideline shall supersede the Guideline on Good Storage Practice (GSP) for Medicinal and Health Products- 1st Edition 2010 and the Guideline on Cold Chain Management- 1st Edition 2009.

In the rapidly evolving field of pharmaceuticals, ensuring the safety, efficacy, and integrity of medicinal products is of paramount importance. Proper storage and distribution of medicinal products are essential to preserving their quality and hence safeguarding public health.

This guideline is produced with reference to the World Health Organization GSDP guideline, Pharmaceutical Inspection Co-operation Scheme (PIC/S) Guide to good distribution practice for medicinal products and other recognized publications/standards to establish best practices and quality standards for the manufacture, storage and distribution of medicinal products. The GSDP guideline serve as a guide for manufacturers, importers, wholesalers, logistic providers, retailers, health care providers and other relevant stakeholders involved, whether directly or indirectly in the pharmaceutical supply chain, promoting consistency and supporting compliance to regulatory requirements.

As the pharmaceutical landscape continues to evolve, it is imperative for stakeholders to remain vigilant and adapt to emerging challenges. This includes staying updated with the latest revisions and advancements in manufacture, storage and distribution practices and developing your own Standard Operating Procedure using the principles laid out in this guideline. By embracing innovation, leveraging technological solutions, and fostering a culture of continuous improvement, stakeholders can ensure that medicinal products reach patients in optimal condition, free from compromise.

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1. Introduction

This Good Storage and Distribution Practice for Medicinal Products (GSDP) guideline is intended for those involved in the manufacture, storage, transportation and distribution of medicinal products. Medicinal products may be subjected to various risks at different stages in the supply chain, for example during purchasing, manufacturing, storage, repackaging, transportation and distribution. It is essential to prevent substandard and falsified products from entering the supply chain as they pose a significant threat to public health and safety.

Good storage and distribution practice is an important part of the overall quality assurance system in order to protect the public health by ensuring that patients receive the medications they need in a safe and effective manner.

The primary objective of GSDP is to ensure that all relevant stakeholders involved in the manufacture, storage and distribution of medicinal products, do so in a manner that maintains the quality, safety and efficacy of the medicinal products throughout their lifecycle. This includes considerations for factors such as temperature control, hygiene, documentation, traceability, and risk management. By implementing and complying with this guideline, stakeholders contribute to the preservation of product integrity and patient safety.

This guideline should be adapted to meet individual stakeholder's needs where applicable. Every activity in the manufacture, storage and distribution of medicinal products should be carried out according to the principles of GSDP as applicable and other relevant guidelines including but not limited to:

- Guidance for Reporting of Medicinal Product Defects in Ministry of Health Facilities April 2021
- Guidance for Medicinal Product Quarantine and Recall in Ministry of Health Facilities May 2021

- Guidance for Medicinal Product Defect, Quarantine and Recall For Licensed Manufacturers/ Licensed Wholesalers/ Licensed Importers/ Product licence holder in Brunei Darussalam February 2022
- Guidance for Reporting of Medicinal Product Defect, Quarantine And Recall In Non-Ministry Of Health Facilities July 2022
- Guideline on Health Care Waste Management, October 2019
- Brunei Darussalam Pharmacovigilance Guidelines: Part 2 - Guideline for Licensed Manufacturers, Licensed Wholesalers, Licensed Importers, Product licence holder/import licence holder/import licence holders, June 2018

2. Quality Management

- The system for quality management should encompass the organizational structure, processes and activities required to maintain the integrity and quality of the product delivered during manufacture, storage and transportation.

- The quality system should incorporate good storage and distribution practices and principles of quality risk management and management review.

- All stakeholders involved should maintain a quality system setting out responsibilities, processes and risk management procedures in relation to their activities. The quality system is the responsibility of the organization's management particularly the senior management and requires their leadership and active participation to ensure that an effective quality system is established, implemented and maintained.

- The management should ensure that all parts of the quality system are adequately resourced with competent personnel and suitable premises and equipment.

- The size, structure and complexity of the organization's activities should be taken into consideration when developing or modifying the quality system.

- Designated responsible person(s) should be appointed by the management, who should have clearly specified authority and responsibility for ensuring that a quality system is implemented and maintained.

- All quality system related activities should be fully documented in a quality manual and its effectiveness monitored. A change control procedure should be implemented to ensure that all changes to the operation are fully evaluated in terms of impact on product quality and traceability.

- The quality system should ensure that:
  - Medicinal products are appropriately manufactured, procured, supplied, stored, imported, distributed throughout their shelf life in compliance with the requirements of good storage and distribution practice and the relevant legislations
  - Management and all personnel's responsibilities are clearly specified in job description
  - Operations are clearly specified in written procedures
  - Products are delivered to the correct recipients within a satisfactory time period
  - All risks are identified and the necessary controls are implemented
  - A procedure for self-inspection and quality audit is available
  - A quality risk management system is in place
  - A system for managing returns, complaints, reporting adverse reactions and recalls is in place
  - Deviations from established procedures are documented and investigated
  - Appropriate corrective and preventive actions (CAPA) are conducted to correct any deficiencies and prevent them in line with the principles of quality risk management

3. Quality Risk Management

- A systematic process for the assessment, control, communication and review of risks to the quality of medicinal products should be in place. The evaluation of the risk should be based on scientific knowledge, experience with the process and ultimately links to the protection of the patient. The level of effort, formality and documentation of the process should be reflective of the level of the risk to the product.

- Risk assessments should be carried out by competent personnel and should be reviewed and approved systemically by the relevant personnel.

4. Management Review

- There should be a formal process for reviewing the quality system periodically. The review should include:
  - Review of the quality system objectives
  - Assessment of performance indicators to monitor the effectiveness of processes within the quality system such as recalls, returns, complaints, self-assessment procedures and external assessments such as inspection
  - Regulations and quality issues that may impact the quality management system
  - Identification of opportunities for improvement
  - Follow-up on suggestions from previous management review meetings

- The outcome of each management review should be documented in a timely manner and communicated effectively to the relevant personnel.

- It is imperative that management provides adequate resources and maintains oversight of good storage and distribution practice compliance.

5. Personnel

- A designated responsible person within the organization, with appropriate qualification and training, should be appointed by the organization with the following responsibilities which include but are not limited to:
  - ensuring that a quality management system is implemented and maintained
  - focusing on the management of authorised activities and the accuracy and quality of records
  - ensuring that initial and continuous training programs are implemented and maintained
  - coordinating and promptly performing any recall operations for medicinal products
  - ensuring that relevant customer complaints are dealt with effectively
  - ensuring that suppliers and customers are approved
  - approving any subcontracted activities which may impact on GSDP
  - ensuring that self-inspections are performed at appropriate regular intervals following a prearranged program and necessary corrective measures are put in place
  - keeping appropriate records of any delegated duties
  - deciding on the final disposition of returned, rejected, recalled or falsified products;
  - approving any returns to saleable stock
  - ensuring that any additional requirements imposed on certain products by national legislation are adhered to

- There should be an adequate number of competent personnel to carry out all the various activities.

- Personnel should have clear written job descriptions with no gaps or unexplained overlaps in the responsibilities and updated as appropriate.

- Designated responsible person(s) for out of hours contact (e.g., emergencies and/or recall) should be appointed. Designated responsible person(s) may delegate duties but not responsibilities.

- Personnel should have appropriate educational qualification, experience and training relative to the activities undertaken.

- Personnel dealing with hazardous products (such as highly active materials, radioactive materials, narcotics and other hazardous, environmentally sensitive and/or dangerous pharmaceutical products, as well as products presenting special risks of abuse, fire or explosion) should be given specific training.

- Personnel should receive initial and continuous training in accordance with a written training program. The training should cover the requirements of Good Storage Practice and Good distribution Practice, as well as on-the-job training. Other topics should be included, such as product security, product identification and the detection of falsified products. The effectiveness of the training should be periodically assessed and staff training records, attendance and assessment should be kept at all times.

- Personnel should have the authority and resources needed to carry out their duties and to follow the quality systems, as well as to identify and correct deviations from the established procedures.

- Safety procedures should be in place relating to all relevant personnel and property, environmental protection and product integrity.

- Appropriate procedures relating to personnel hygiene, relevant to the activities to be carried out, should be established and observed. Personnel should maintain good health and hygiene practices to prevent contamination of medical products. They should report any illness or condition that may pose a risk to the products or patients.

- Personnel handling products should wear garments suitable for the activities that they perform. Personnel should wear appropriate Personal Protective Equipment (PPE), such as gloves and masks, when handling hazardous pharmaceutical products, including products containing materials that are highly active, toxic, infectious or sensitizing. The PPE should be regularly inspected, maintained, and replaced when necessary.

- Procedures must be put in place to ensure only relevant personnel have access to medicinal products to minimize the possibility of such products coming into the possession of unauthorized persons or entities.

- Codes of practice and procedures should be in place to prevent and address situations where persons involved in the storage and distribution of medicinal products are suspected of, or found to be implicated in, any activities relating to the misappropriation, tampering, diversion or falsification of any product.

- Personnel should carry out their duties free from external influences such as commercial, political, financial and personal interests, or other pressures or conflict of interest that may have an adverse effect on the quality of service provided or on the integrity of medicinal products.

6. Premises

- Premises for keeping bulk pharmaceuticals should be located in a suitable and accessible area. It must have enough space for operation such as receiving bay, stock storage and for the movement of goods and personnel. The receiving bay should not be obstructed by parked vehicles.

- The premise should be well designed and well maintained, with working lights and air-conditioning system. Pest and natural calamity prevention such as flooding or leaking must be routinely carried out.

- Premise should be properly labelled and access should be controlled and preferably recorded.

- Sufficient security system should be provided. Unauthorised access to all areas of the authorised premises should be prevented. Prevention measures may include CCTV or alarm system and appropriate access control. Visitors should be accompanied by authorised personnel.

- Premise must be equipped with appropriate environmental control systems (e.g., temperature, humidity) and these systems must be regularly maintained to ensure products are stored according to the manufacturer's storage requirements.

- An initial temperature mapping exercise should be carried out on the storage area before use, under representative conditions. Temperature monitoring equipment should be located according to the results of the mapping exercise, ensuring that monitoring devices

are positioned in the areas that experience the extremes of fluctuations. The mapping exercise should be repeated for significant changes according to the results of a risk assessment exercise. For small premises of a few square meters which are at room temperature, an assessment of potential risks should be conducted and temperature monitors placed accordingly.

- Designated area should be available for products pending a decision as to their disposition or products that have been removed from saleable stock. They should be segregated physically and if applicable, their status reflected on an equivalent electronic system. This applies to falsified medicinal products, expired products, recalled products, rejected products and medicinal products not authorised for the internal market. The appropriate degree of security should be applied in these areas to ensure that such items remain separate from saleable stock. These areas should be clearly identified through clear labels, signage, or other markings to prevent confusion and ensure proper segregation.

- Appropriate controls and measures should be in place to cater for items that required special conditions such as cold-chain items, light sensitive items, flammable items and radioactive materials.

- System must be in place to record the movement of goods in and out of the premise.

- Premise must be kept clean free from litter and dust. Cleaning programme, instructions and records should be in place.

- Toilets, washing, rest and food preparation areas must be separated from the main storage area. Avoid the presence of pipes above the storage area.

- Eating, drinking and smoking must be prohibited in all storage area.

- Premises should be designed and equipped so as to afford protection against the entry of insects, rodents or other animals. A preventive pest control programme should be in place. Appropriate pest control records should be maintained.

7. Equipment

- Equipment used in the premise must be suitable for the purpose they are used for. They must be professionally installed and configured/calibrated for use. Preventative maintenance of equipment should be routinely carried out.

- Thermo hygrometers used to control or to monitor the environment where the medicinal products are stored should be calibrated at defined intervals based on a risk and reliability assessment.

- Appropriate alarm systems should be in place to provide alerts when there are excursions from predefined storage conditions. Alarm levels should be appropriately set and alarms should be regularly tested to ensure adequate functionality.

- IT equipment for managing stock of pharmaceuticals should only be used by authorised personnel and it should be password locked.

- Electronics transactions of goods must have an audit-trail that include the name of personnel handling the record.

- Computers and IT equipment must have antivirus software updated and documents and records backed up regularly.

- During equipment failure, equipment repair, maintenance and calibration operations, procedures should be in place to ensure the quality and integrity of medicinal products are maintained and/or not compromised.

- Adequate records of repair, maintenance and calibration activities for key equipment should be made and the results should be retained. Key equipment would include for example equipment used in manufacturing and assembly, cold stores, monitored intruder alarm and access control systems, refrigerators, thermo hygrometers, or other temperature and humidity recording devices, air handling units and any equipment used throughout the supply chain.

8. Activities and Operation

- All activities and operations should be conducted in accordance with national legislation and associated guidelines.

- Storage and distribution of medicinal products should be done by persons authorized to do so, in accordance with national legislation.

- Activities and operations should be performed in accordance with documented procedures.

- Storage and retrieval systems and operations should comply with current guidelines.

8.1 Receipt

- Medicinal products should be procured from appropriately authorized suppliers. The suppliers themselves should have the appropriate import/wholesale/manufacturer's licence for supplying the product in question. Qualification and approval of suppliers should be performed prior to procurement of any medicinal products. This should be controlled by a procedure and the results documented and periodically reviewed using a risk-based approach.

- Deliveries should be examined for damage, seal intactness, signs of tampering, labelling, completeness of order and other related aspects (e.g., availability of a certificate of analysis, where applicable), at the time of receiving.

- Medicinal products requiring special handling, storage or security measures should be prioritised and once appropriate checks have been conducted, they should be immediately transferred to appropriate storage facilities.

- Containers and consignments that do not meet acceptance criteria at the time of receipt should be labelled, kept separated and investigated. This includes suspected substandard and falsified medicinal products.

8.2 Storage

- Medicinal products requiring specific storage conditions, or controlled access (e.g., narcotics), should be processed without delay and stored in accordance with their requirements.

- Appropriate controls should be implemented to prevent contamination, spillage, breakage and/or mix-ups during storage.

- Medicinal products should not be stored directly on the floor.

8.3 Repackaging and relabeling

- Repackaging and relabeling of materials and products are not allowed without authorization from relevant parties e.g., product owner and national regulatory authority. Where repackaging and relabeling are required, these activities should only be performed by entities appropriately authorized to do so and in compliance with GMP.

- Procedures should be in place for the controlled disposal of original packaging, to prevent re-use thereof.

8.4 Distribution and Transport

- Medicinal products should be transported in accordance with the conditions stated on the labels and described by the manufacturer. The risk to the quality of the medicinal product during transport and distribution should be eliminated or minimized to an acceptable level.

- Product, batch and container identity should be maintained at all times.

- All labels should remain legible.

- Distribution records should be sufficiently detailed to allow for a recall when required.

- Drivers of vehicles should be identified and present appropriate documentation to demonstrate that they are authorized to transport medicinal products.

- Vehicles should be suitable for their purpose, with sufficient space and appropriately equipped to protect medicinal products.

- The design and use of vehicles and equipment must aim to minimize the risk of errors and permit effective cleaning and/or maintenance, to avoid contamination, build-up of dust or dirt and/or any adverse effect on the quality of the products.

- Where feasible, consideration should be given to adding technology, such as global positioning system (GPS) and/or electronic tracking devices to enhance the security and traceability of vehicles with products.

- Where possible, dedicated vehicles and equipment should be used for medicinal products. Where non-dedicated vehicles and equipment are used, procedures should be in place to ensure that the quality of the medicinal products will not be compromised. Defective vehicles and equipment should not be used. These should either be labelled as such or removed from service.

- There should be procedures in place for the operation and maintenance of all vehicles and equipment.

- Equipment and materials used for the cleaning of vehicles should not become a source of contamination or have an adverse effect on product quality.

- Vehicles used for transportation of medicinal products should be qualified, where applicable, to demonstrate their capability to maintain the required transport conditions. There should be a maintenance programme for the cooling system.

- Appropriate environmental conditions should be maintained and monitored. Instruments used for monitoring conditions, for example, temperature and humidity, within vehicles and containers should be calibrated at regular intervals.

- Transporting of rejected, recalled and returned products, as well as those suspected as being substandard and falsified, should be securely packaged, clearly labelled and accompanied by the appropriate supporting documentation.

- Measures should be in place to prevent unauthorized persons from entering and/or tampering with vehicles and/or equipment, as well as to prevent the theft or misappropriation thereof.

- Shipment containers should have no adverse effect on the quality of the medicinal products and should offer adequate protection to materials and these products. Containers should be labelled indicating, for example, handling and storage conditions, precautions, contents and source, and safety symbols, as appropriate.

- Special care should be taken when using dry ice and liquid nitrogen in shipment containers, owing to safety issues and possible adverse effects on the quality of medicinal products.

- Written procedures should be available for the handling of damaged and/ or broken shipment containers. Particular attention should be paid to those containing potentially toxic and hazardous products.

8.5 Dispatch

- There should be documented, detailed procedures for the dispatch of products.

- Medicinal products should only be sold and/or distributed to persons or entities that are authorized to acquire such products in accordance with the applicable national legislation. Supplier shall conduct due diligence to check and periodically recheck the status of their client prior to supply of the medicinal products e.g. valid poisons licence, wholesaler's licence etc.

- Dispatch and transportation should be undertaken only after the receipt of a valid order, which should be documented.

- Records for the dispatch of products should be prepared and should include information such as, but not limited to:

    - date of dispatch;
    - complete business name and address (no acronyms), type of entity responsible for the transportation, telephone number, names of contact persons;
    - status of the addressee (e.g., retail pharmacy, hospital or community clinic);
    - a description of the products, including, for example, name, dosage form and strength (if applicable);
    - quantity of the products, i.e., number of containers and quantity per container (if applicable);
    - applicable transport and storage conditions;
    - a unique number to allow identification of the delivery order; and
    - assigned batch number and expiry date (where not possible at dispatch, this information should at least be kept at receipt, to facilitate traceability).

Records of dispatch should contain sufficient information to enable traceability of the product. Such records should facilitate the recall of a batch of a product, if necessary, as well as the investigation of potentially substandard and falsified medicinal products.

- Vehicles and containers should be loaded carefully and systematically on a last-in/first-out (LIFO) basis, to save time when unloading, to prevent physical damage and to reduce security risks. Extra care should be taken during loading and unloading of cartons, to avoid damage.

- Medicinal products should not be supplied or received after their expiry date, or so close to the expiry date that this date is likely to be reached before the products are used by the consumer.

- Medicinal products and shipment containers should be secured in order to prevent or to provide evidence of unauthorized access. Vehicles and operators should be provided with additional security where necessary, to prevent theft and other misappropriation of products during transportation.

- Medicinal products should be stored and transported in accordance with procedures such that:
  - the identity of the product is not lost
  - the product does not contaminate and is not contaminated by other products
  - adequate precautions are taken against spillage, breakage, misappropriation and theft
  - appropriate environmental conditions are maintained, for example, using cold-chain for heat sensitive products

- Written procedures should be in place for investigating and dealing with any failure to comply with storage requirements, for example, temperature deviations. If a deviation has been noticed during transportation, by the person or entity responsible for transportation, this should be reported to the supplier, distributor and recipient. In cases where the recipient notices the deviation, it should be reported to the distributor.

- Transportation of products containing hazardous substances or narcotics and other dependence-producing substances, should be transported in safe, suitably designed, secured containers and vehicles. In addition, the requirements of applicable international agreements and national legislation should be met.

- Spillages should be cleaned up as soon as possible, in order to prevent possible contamination, cross-contamination and hazards. Written procedures should be in place for the handling of such occurrences.

- Damage to containers and any other event or problem that occurs during transit must be recorded and reported to the relevant department, entity or authority and investigated.

- Products in transit must be accompanied by the appropriate documentation.

9. Stock control and rotation

- All pharmaceutical products kept must have a record of transactions either on paper or in electronic format. These records must be updated immediately after each transaction (e.g., entries, issues, losses, adjustments). The records should be kept for a minimum of 3 years from the date of last entry.

- Periodic stock reconciliation must be performed to check for discrepancy of the actual stock balance and the recorded stock balance.

- Pharmaceutical products must be arranged and issued according to the FEFO (First Expiry First Out) principle.

- Quarantined or recalled stock must be removed immediately and kept in assigned area for quarantined or recalled stock while waiting for further instruction.

- Expired stock must be removed immediately and kept in assigned area for expired stock or returned them to the pharmacy or store where it was issued from.

- Stock intended for destruction should be appropriately identified, held separately and handled in accordance with a written procedure. Records of all destroyed medicinal products should be retained for a defined period.

- Discrepancy in stock amount should be handled immediately to prevent further loses or abuses.

- Follow manufacturer's advice for additional storage information, e.g., keep upright, do not stack on top of each other.

- Cold chain items may be subjected to additional storage requirement.

- Special considerations for controlled drug and psychotropic drug:

    - Controlled drug and psychotropic drug have additional storage requirements.

    - These drugs must be kept locked in a control drug cabinet, a safe box or a strong room and access restricted to only authorised personnel.

    - All transactions must be recorded according to legal requirements specific for these drugs.

    - A separate register or separate part of the register for entries must be made in respect of each controlled/psychotropic drug.

    - All registers and books kept shall be preserved for a period of 3 years from the date on which the last entry therein is made.

10. Documentation

- Documentation should include all specifications of the medicinal products and Certificate of Analysis (applicable mainly to Import/Product Licence Holder), standard operating procedures, instruction protocols, contract and records whether in paper or electronic form. Documents should be readily available for audit purposes.

- Documents should be appropriately designed, completed, reviewed, authorized, distributed and kept as required.

- Written procedures/Standard Operating Procedures should be in place and followed for all activities/processes relating to storage and distribution of medicinal products.

- Documents should be laid out systematically and be easy to complete, review and check. The title, scope, objective and purpose of each document should be clear.

- All documents should be completed, signed and dated as required by authorized person(s) and should not be changed without the necessary authorization.

- Documentation should be prepared and maintained for a minimum of 3 years or in accordance with the national legislation.

  Records should be accurate, legible, traceable, attributable and unambiguous. Electronic data should be backed-up in accordance with written procedures. Records should be maintained for the back-up and restoration of data.

- Procedures for the identification, collection, indexing, retrieval, storage, maintenance, disposal of and access to all applicable documentation should be followed.

- Documents should be reviewed regularly and kept up-to-date. When a document has been revised, a system should exist to prevent inadvertent use of the superseded version.

- All records should be stored and retained using facilities that prevent unauthorized access, modification, damage, deterioration and/or loss of documentation during the entire life-cycle of the record. Records must be readily retrievable.

- Comprehensive records should be maintained for all receipts, storage, issues and distribution. The records should include, for example:
  - date (e.g., receipt or dispatch, as appropriate);
  - name and description of the product;
  - quantity received, or supplied;
  - name and address of the supplier and customer;
  - batch number(s);
  - expiry date;
  - suitability of the supplier;
  - qualification of suppliers; and
  - customer qualification.

- All containers should be clearly labelled with at least the name of the medicinal product, batch number, expiry date or retest date, and the specified storage conditions.

11. Outsourced activities

- Any outsourced activities relating to the storage and distribution of a medicinal products that is delegated to another person or party should be performed by the appropriately authorized parties, in accordance with national legislation and the terms of a written contract.

- A written contract between the contract giver and the contract acceptor must be in place that clearly establishes the roles and responsibilities of each party, including compliance with this GSDP guideline.

- The contract giver is responsible for ensuring that the contract acceptor has the competence and adequate premises and equipment, procedures, knowledge and experience, and competent personnel to successfully carry out the work required, and that the principles and guidelines of GSDP are followed. This can be done through a combination of assessment and audits.

- An assessment of the contract acceptor should be performed before commencement of, and whenever there has been a change to, the outsourced activities. Any contract acceptor should be audited periodically by the contract giver. The requirement for audit and the frequency for audit should be defined based on risk depending on the nature of the outsourced activities. Audits by the contract giver should be permitted at any time.

- The contract acceptor should not pass to a third party any of the work entrusted to him under the contract without the contract giver's prior evaluation and approval of the arrangements.

- The contract acceptor must refrain from any activity that could adversely affect the quality of the product(s) handled for the contract giver, and must forward any information that can influence the quality of the product(s) to the contract giver in accordance with the requirements of the contract.

12. Complaints

- There should be a written procedure for the handling of complaints. In the case of a complaint about the quality of a medicinal product or its packaging, the original manufacturer and/or product licence holder/import licence holder should be informed as soon as possible.

- Where required, the information should be shared with the Authority and a recall initiated where appropriate.

- All complaints should be recorded and appropriately investigated. The root cause should be identified, and the impact (e.g., on other batches or products) risk-assessed. Appropriate Corrective and Preventive Actions (CAPAs) should be taken.

- A distinction should be made between complaints about a medicinal product or its packaging and those relating to distribution.

- The relevant information, such as the results of the investigation of the complaint, should be shared with the relevant entities.

- Medicinal product quality problems and suspected cases of substandard or falsified products identified should be reported to the Authority/product licence holder/import licence holder and handled according to relevant authorized procedures.

- There should be written procedures for handling all reports of adverse reactions arising from the use of the medicinal product. The system and procedures in place must be adequate for receipt, investigation and reporting of adverse reactions to the national regulatory authority within the stipulated timelines.

- Relevant stakeholders shall refer to the appropriate guidance below on how to handle product complaints:
  - Guidance For Reporting of Medicinal Product Defects in Ministry of Health Facilities April 2021
  - Guidance For Medicinal Product Quarantine and Recall in Ministry of Health Facilities May 2021

  - Guidance For Medicinal Product Defect, Quarantine and Recall for Licensed Manufacturers/ Licensed Wholesalers/ Licensed Importers/ Product licence holder in Brunei Darussalam February 2022
  - Guidance For Reporting of Medicinal Product Defect, Quarantine and Recall in Non-Ministry Of Health Facilities July 2022

- Relevant stakeholders shall refer to the appropriate guidance below on how to handle adverse reactions:

  - Brunei Darussalam Pharmacovigilance Guidelines: Part 2 - Guideline for Licensed Manufacturers, Licensed Wholesalers, Licensed Importers, Product licence holder, June 2018

13. Returned goods.

- Returned medicinal products should be handled in accordance with authorized procedures.

- All returned medicinal products should be placed in quarantine upon receipt. The status of the goods should be clear and properly segregated. Precautions should be taken to prevent access and distribution until a decision has been taken with regard to their disposition. The particular storage conditions applicable to the medicinal products should be maintained until their disposition.

- Medicinal products returned should be destroyed unless it is certain that their quality is satisfactory, after they have been critically assessed in accordance with a written and authorized procedure.

- The nature of the medicinal product, any special storage conditions it requires, its condition and history and the time lapse since it was issued, should all be considered in this assessment. Where any doubt arises over the quality of the medicinal product, it should not be considered suitable for reissue or reuse. Any action taken should be appropriately recorded.

- When handling returned goods, the following considerations at least should be taken:
  - a risk-based process should be followed when deciding on the fate of the returned goods. This should include, but not be limited to, the nature of the product, storage conditions, condition of the product history, time-lapse since distribution and the manner and condition of transport while being returned
  - the terms and conditions of the agreement between the parties and

- examination of the returned goods, with decisions taken by suitably qualified, experienced and authorized persons

- Where returned goods are rejected, authorized procedures should be followed for further action such as its disposal including safe transport.

- Destruction of products should be done in accordance with international, national and/or local requirements regarding disposal of such products, and with due consideration to the protection of the environment.

- Stolen products that have been recovered cannot be returned to saleable stock and sold to customers.

- Records of all returned, rejected and destroyed medicinal products shall be preserved for a period of 3 years.

14. Recalls

- There should be a written procedure, in compliance with national requirements, to effectively and promptly recall medicinal products.

- In the event of a product recall, all customers to whom the product has been distributed shall be informed with the appropriate degree of urgency and clear actionable instructions.

- The effectiveness of the procedure should be checked at least annually and updated as necessary.

- The original manufacturer and/or product licence holder/import licence holder or other relevant contract party, should be informed in the event of a recall.

- Information on a recall should be shared with the appropriate national regulatory authority.

- All recalled products should be secure, segregated, transported and stored under appropriate conditions. These should be clearly labelled as recalled products. The particular storage conditions applicable to the product should be maintained where possible.

- All customers and competent authorities of all countries to which a given medicinal product may have been distributed should be informed promptly of the product recall where appropriate.

- All records, including distribution records, should be readily accessible to the designated person(s) responsible for recalls. These records should contain sufficient information on products supplied to customers (e.g., name, address, contact detail, batch numbers, quantities and safety features – including exported products).

- The progress of a recall process should be recorded and a final report issued, which includes a reconciliation between delivered and recovered quantities of medicinal products. The final report should be submitted to the relevant Authority.

15. Substandard and Falsified Products (SF)

- Companies must make every effort to ensure that the medicinal products they deal with are genuine and meet the quality standards by purchasing from only reputable source.

- Companies must take all necessary measures to mitigate substandard and falsified medicinal products. Procedures must be in place to assist in identifying and handling medicinal products that are suspected to be substandard and/or falsified.

- Where such medicinal products are identified, the product/import licence holder and the Authority should be informed immediately and the sale and distribution of a suspected counterfeit product should be suspended immediately.

- Designated areas should be available to store SF medicinal product in a secure, segregated area and clearly identified to prevent further distribution or sale. Access should be controlled.

- Records should be maintained reflecting the investigations and action taken, such as disposal of the product. SF products should not re-enter the market.

16. Self-Inspection

- Self-inspections should be conducted to monitor the implementation and compliance with all aspects of GSDP, the regulations and other relevant guidelines as well as to propose appropriate corrective measures.

- A self-inspection programme should be conducted on a periodic basis by competent and knowledgeable personnel who are impartial.

- All self-inspections should be recorded. Reports should contain all observations made during the inspection and shared to the management and relevant personnel. For any deficiencies observed, their cause should be determined and the necessary CAPA should be taken and followed up.

17. Inspection of storage and distribution facilities

- The Authority will inspect storage and distribution facilities at regular intervals, either scheduled and/or unannounced, to ensure compliance with current legislation and good storage and distribution practices.

- Inspections should cover personnel, premises and equipment, stock handling and inventory management, disposal procedures, documentation, handling of product complaints, reporting adverse reactions, recalls and other related aspects as contained in this guideline.

- The inspected entity must submit a Corrective and Preventive Action (CAPA) plan for any non-compliances listed in the inspection report to the Authority within the period specified in the report for review.

- Inspections should be closed with a conclusion of compliance only if the Authority is satisfied with the CAPA plan submitted by the inspected entity.

- Auditees should refer to **Annex A**- **Key areas for pharmaceutical inspection**, for some information on preparing for the inspection by the Authority

18. Cold chain Management

Most cold chain products are either unstable chemical entity or sensitive biological substances that progressively lose their potency and ability to protect or treat the recipient against the targeted disease. Cold chain products are more heat-sensitive after reconstitution, but some are highly sensitive to extreme cold and will lose their entire potency if frozen. There are others that can sustain freezing without incurring damage. This loss of potency is much faster when the cold chain product is exposed to temperatures outside the recommended storage condition. Once potency is lost, returning the cold chain product to correct storage condition cannot restore it. Hence, storage of cold chain products at the recommended temperature range is vitally important to retain full potency up to the moment of administration.

All losses of potency are cumulative each time a cold chain product is exposed to incorrect temperature or strong light, whereby its potency will reduce. If the item has already been exposed previously, consecutive exposure no matter how small will increase damage to the item. Ultimately, due to cumulative damage, the cold chain product may be destroyed, with

all its potency lost. Therefore, it is important to know the correct storage conditions for each cold chain product, and to ensure that it is always stored at the recommended conditions.

Cold chain management is a system of storing and transporting products with pre-determined conditions supported by stability data, at recommended temperatures from the point of manufacture to the point of use. Drug products which are particularly temperature-sensitive must be kept refrigerated or frozen and handled with appropriate care to avoid the product's exposure to temperatures outside the recommended storage conditions, compromising the safety and effectiveness of the product.

Examples of cold chain or temperature sensitive products mentioned in this guideline are vaccines, pharmaceuticals, and biological products which must always be kept refrigerated or frozen and handled with appropriate care throughout the supply chain.

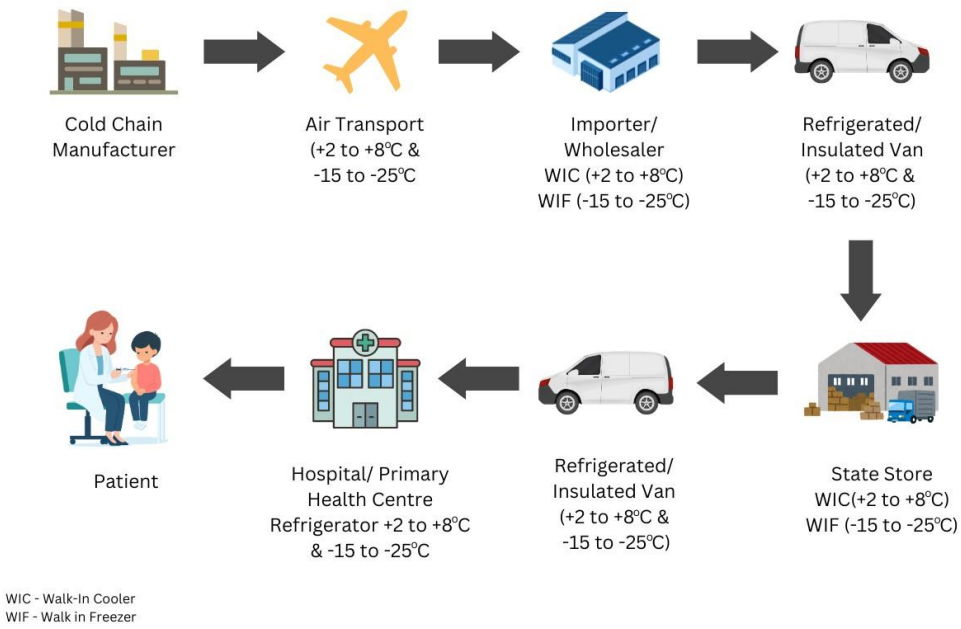

Figure 1. Cold Chain System (Sourced from: Immunization handbook for Medical Officers, WHO)

18.1 Cold chain equipment

Cold chain equipment is designed to maintain the recommended temperatures for cold chain products to preserve their quality during storage and transportation from the manufacturing site to the point of use. Cold chain equipment (electrical and non-electrical) may consist of equipment as summarized in Figure 2.

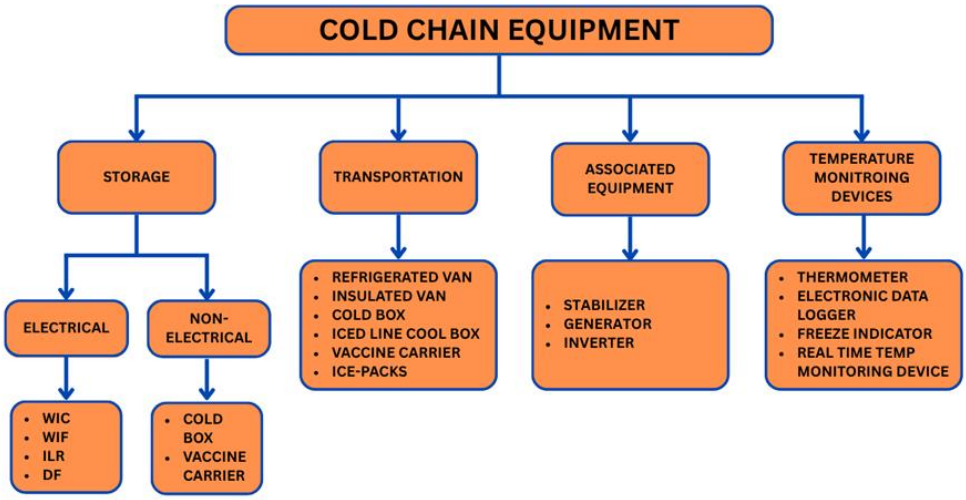

Figure 2. Overview of cold chain equipment (Sourced from: Immunization handbook for Medical Officers, WHO)

Glossary

WIC – walk-in cooler; WIF – walk-in freezer; ILR – ice-lined refrigerator; DF – deep freezer

18.1.1 Pharmaceutical refrigerators and freezers

Pharmaceutical refrigerators and freezers should:

- Always maintain temperature condition between +2^{o}C and +8^{o}C, and at least between -15 ^{o}C and -25 ^{o}C respectively regardless of the ambient temperature
- Be large enough to hold maximum stock required – recommended 70% of total volume of the chamber
- Be well maintained

- Be equipped with alarms
- When combined, be a two-door unit with separate freezer compartment and door
- Allow for adequate air distribution and orderly storage within the chamber. Storage practices and loading configurations should not lead to the obstruction of air distribution
- Fill the bottom of the refrigerator with cool water packs as this help maintain the temperature range, especially when there is a power failure
- Hold in only small quantities of cool water packs at any one time when put with frozen cold chain products in the same freezer. Adding large quantity of cool water packs at one time can raise the temperature to a level that endangers the cold chain product
- Always keep a calibrated thermometer in the middle part of the main compartment of the refrigerator or freezer
- Have sensors for continuous monitoring and alarms located at points representing the temperature extremes
- Have main power connected to a voltage regulator or stabiliser to safeguard the equipment from voltage fluctuations by providing a constant voltage
- Have a standby generator set with adequate fuel or a UPS (Uninterrupted power supply) unit and regularly checked at predetermined interval for correct operation to provide standby power supply

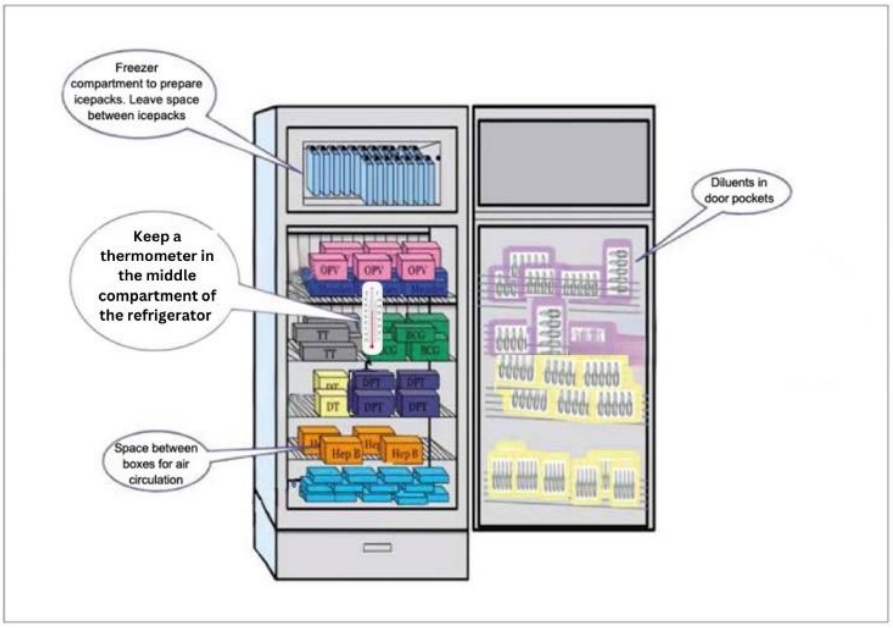

Figure 3: Recommended storage arrangement of cold chain items in a pharmaceutical refrigerator (Sourced from: Immunization handbook for Medical Officers, WHO)

18.1.2 Walk-in-Coolers (WIC)/Cold room, Walk-in-Freezer (WIF) and Ultra-Low temperature freezer

Walk-in-Coolers (WIC)/Cold room, Walk-in-Freezer (WIF) and Ultra-Low temperature freezer should:

- Be temperature controlled to maintain temperatures between +2^{o}C and +8^{o}C for WIC,

  -15 ^{o}C and -25 ^{o}C for WIF and -90 ^{o}C and -60 ^{o}C for Ultra-Low temperature storage using calibrated monitoring devices with continuous temperature recorder
- Have temperature mapping conducted to determine hot and cold spots where specific areas identified and marked for each cold chain product type.

For instance, do not place cold chain items such as DPT, hepatitis B vaccines and insulin in the direct airflow from the cooling machinery, where they may become frozen

- Allow free circulation of cool air between boxes
- Sensors of the recording thermometer and mercury thermometer should not be fitted in the airflow from the evaporator
- Have sensors for continuous monitoring and alarms located at the points representing the temperature extremes (hot and cold spots)
- Fitted with an alarm system to give alert regarding temperature excursion/deviation
- Have main power connected to a voltage regulator or stabiliser to safeguard the equipment from voltage fluctuations by providing a constant voltage
- Have a standby generator set with adequate fuel or a UPS (Uninterrupted power supply) unit and regularly checked at predetermined interval for correct operation to provide standby power supply.
- Ensure that it has restricted entry to keep cold chain products safe and secure
- Allow unpacking, sorting, and packaging of cold chain products into cold boxes inside the cold room. It is important not to leave packed cold chain products with ice packs in the cold room as freezing may occur.

18.1.3 Cold boxes and vaccine carriers

Cold boxes and vaccine carriers should:

- Be an insulated container that can be lined with ice-packs to keep cold chain products within recommended temperatures during transportation and emergency storage of cold chain products/ice packs for a short period of time
- Be able to maintain temperatures between +2°C and +8°C during storage and transportation of the cold chain products
- Be securely labelled with warning statements (example, 'Perishable Drug Product', 'Do not freeze' etc.)
- Be properly maintained

<u>Packing cold boxes and vaccine carriers:</u>

- Place temperature protection components (e.g., ice/water blankets, water/gel packs, phase change materials, insulated packaging, etc.) at the bottom and sides of the cold box
- Use cardboard cartons or polythene bags to provide a barrier between the temperature protection components and the cold chain product.
- Never place freeze-sensitive medicines and vaccines directly in contact with temperature protection components.
- Keep a thermometer or data logger in the cold box
- Place temperature protection components above the cold chain products or as specified by the validated process
- Securely close the lid of the cold box
- Refer to **Annex B** for information on ice packs

Figure 4. Packing a cold box (Sourced from: Immunization handbook for Medical Officers, WHO) - ***For illustration purposes***

18.1.4 Refrigerated or Insulated vehicle

Refrigerated or Insulated vehicle should:

- be used to transport cold chain products in bulk
- be able to maintain temperature range as per specific requirements of the cold chain products e.g., +2^{o}C to +8^{o}C and -15 ^{o}C to -25 ^{o}C
- have the refrigeration system started to get the required temperature before loading in refrigerated vehicle
- be cool and dry for boxes to be loaded
- be loaded in a minimum possible time
- have the doors closed immediately after loading and start for destination immediately

18.2 Storage Temperature

- All cold chain products should be stored according to conditions stated on the product label usually refrigerated between +2^{o}C and +8^{o}C or kept frozen at -10 ^{o}C or lower, or at least between -25 ^{o}C and -15 ^{o}C or ultra-low temperature (ULT) at -90 ^{o}C to -60 ^{o}C. When specified on the product label, controls for light should be in place.

- Temperatures should be controlled and monitored using calibrated monitoring devices.

- Alarm systems should be installed to give alert regarding temperature excursion/deviation.

- Records of temperatures and alarms, where applicable, should be maintained in a comprehensive logbook. Monitoring is conducted at points presenting the extremes of temperature range based on temperature mapping within the immediate storage area.

- An independent temperature monitoring probe or data logger, an electronic device that continuously records the temperature of refrigerators is recommended. A designated individual should be appointed to verify the temperature and humidity records on a periodic basis. The records should be documented and easily retrievable upon request. A key benefit of using a probe or data logger device is its ability to indicate how long a temperature excursion lasted, should one occur. These devices must also be calibrated at least once a year, following the manufacturer's guidelines. Premises without continuous temperature and relative humidity monitoring must ensure manual recording is conducted at least twice per day

- Written procedures should be available describing the actions taken in the event of temperature excursions outside the labelled storage conditions. All excursions outside the labelled storage conditions must be appropriately investigated and the disposition of the stock in question must be evidence-based.

18.3 Maintenance of Cold Chain Equipment

18.3.1 Pharmaceutical refrigerators and freezers

- To ensure minimal equipment breakdown at all times, all repairs must be responded to and repaired as soon as possible such as gas changing, filter replacement, replacement of compressor and topping up gas/refrigerant, chemical cleaning of system when oil traces are found and modification in the system. In general, the authorized vendor should be consulted for the maintenance of the equipment.

- Ideally routine preventative maintenance of equipment should be performed on a daily, weekly, and monthly basis. A logbook should be made available to record the maintenance and repairs undertaken. The table below shows some of the routine maintenance activities to be performed on the equipment.

Frequency	Task
Daily	• Outside surface of equipment neat and clean • Equipment is level • Recording temperature at least twice daily
Weekly	• Formal review and signature on the temperature logbook • Clean the rubber/gasket with a light soapy cloth and allow to dry • Check rubber seal (Gasket) of the lid/door. It should fit tightly. To check the gasket/rubber seal, following test may be conducted, which is called the "Paper Test" <u>Paper Test</u> • Place a piece of paper in between the lid/door and close it • After closing the door, try to pull the paper • If the paper doesn't come out easily, it indicates that the rubber/gasket is working properly
Monthly	• <u>For freezer</u>-Defrosting the equipment when frost thickness on the inner wall is more than 5mm. Never try to use heat source to speed up defrosting or remove the ice with knife or ice pack, since doing so can permanently damage the freezer • Clean the inside of the refrigerator and door seal with a cloth • Allow cleaned parts to dry completely and allow temperature in the main section to fall to +8^{o}C or lower before returning cold chain products into the refrigerator

Note: Manufacturer's manual should also be referred for guidance on the maintenance of equipment

The table below shows the preventative maintenance tasks of the exterior and interior part of the equipment.

Exterior	Interior
1. Exterior is clean and dry 2. Equipment is levelled and firmly placed on the floor 3. Placed at least 10cm away from walls 4. Away from direct sunlight 5. Room is well ventilated 6. Equipment opened only when necessary 7. Lid is closing correctly without any gaps 8. Lid seal is clean	1. There is no frost in the deep freezer 2. Thickness of frost formation in deep freezer is less than 5mm thickness 3. Baskets are used and all cold chain products are neatly placed with space for air circulation. Do not use solid walled containers e.g. Schaffer box 4. Cold chain products are not touching the wall/bottom of the refrigerator 5. A working thermometer/probe is placed with the cold chain products in the middle of the refrigerator

18.3.2 Cold boxes and vaccine carriers

Maintain Vaccine Carrier/ Cold Box by:

- Cleaning and drying after every use
- Examining inside and outside surface for cracks
- Checking that rubber seal around lid is not broken
- Adjusting the tension on the latches (if provided) so that the lid closes tightly.
- Not keeping the lid locked when not in use
- Protecting all cold chain carriers from direct sunlight, otherwise the plastic body may get warped or cracked.
- Not leaving the lid open once packed
- Never dropping or sitting on the vaccine carrier/cold box

18.4 Transportation and products in transit

- The transport process and containers should prevent damage and maintain the integrity and quality of the cold chain products. For example, ampoules exposed to physical stress could develop hairline cracks.

- Written procedures for the transportation of cold chain products should be established. Such procedures should consider the nature of the cold chain products, local conditions, and any seasonal variation experienced, and describe any special handling precautions. These procedures should be verified to ensure that appropriate conditions are maintained under worst case scenarios.

- Where controlled storage conditions (example, temperature, relative humidity, light, etc.) are required during transit, the necessary controls must be in place.

- Within a transportation container, the packaging configuration, which provides the primary means of environmental control for the cold chain product, should ensure that the cold chain product remains within the acceptable temperature range.

- Refrigerated vehicles/ transportation containers should be mapped and monitored if they provide the primary means for environmental control. However, this is not necessary if a qualified insulated container is used as the primary means of environmental control.

- Temperature and humidity monitoring devices should be calibrated at predetermined intervals.

- Transportation practices by carriers, including any storage and/or transportation activities performed by sub-contractors, should be periodically verified, or audited by

reviewing documentation. A record of the review or audit should be kept, and any discrepancies should be investigated.

18.5 Containers and Container labelling

- Any controlled transport and/or storage conditions as well as warning statements (example, 'Perishable Drug Product', 'Do not freeze') should be clearly stated on the label applied to transportation containers. This label should be securely affixed and indelible. The transportation documents should clearly state that these products must be transferred to the specified storage temperature immediately upon receipt.

- When cold packs are placed in cold chain containers used to transport cold chain products:
  - The type, size and number of cold packs should correspond to the transportation duration and temperature needed
  - The location of the packs should ensure the product is maintained within the recommended storage conditions
  - Ice packs should be conditioned prior to final packing by allowing them to 'sweat' until water droplets appear on their surface before putting them in the container
  - Adequate barrier materials should be used to avoid direct contact of the packs with the products especially vaccines that must not be frozen.

- When dry ice is placed in containers used to transport cold chain products, in addition to safety issues, it must be ensured that the dry ice or its vapours does not have an adverse effect on the cold chain product or its primary package.

- Use cold chain monitors (CCM) or temperature data loggers to follow the cold chain products throughout the journey from the beginning of the journey to the end user. The freeze indicator can also be used to monitor cold chain products that lose their potency if frozen.

- If temperature excursions outside the labelled storage conditions occur, product disposition must be evaluated and documented. Corrective action should be implemented where necessary and documented. Clear directions should be provided to the recipient for the evaluation or disposition of CCM/indicators and products.

18.6 Receiving

- Where controlled storage conditions (example temperature, relative humidity, light etc.) are required during transit, the recipient should examine the shipment upon reception following written procedures.

- Products should be promptly transferred to the appropriate environmentally controlled storage area. It is important to note that cold chain products packed with ice should not be placed in the cold room or refrigerators as freezing might occur.

- The subsequent checking for signs of tampering, damage and non-compliance with cold chain storage condition, as well as physically verifying the label description, and product quantity, against the relevant information in the purchase order should be carried out under the storage conditions as recommended on the product label unless otherwise justified.

18.7 Documentation

- When commercial carriers are used, all pertinent conditions should be specified in written contract between the distributor, importer, or wholesaler, and the third party. All contract acceptors should comply with the requirements in this guideline as applicable.

- Distributors, importers, and wholesalers should maintain transportation records of inbound and outbound shipments, including monitoring records where applicable for a minimum period of three years.

- Keep all completed temperature record sheets in a file or safe place for future reference.

- Records of investigations and actions taken in the event of excursions outside the labelled storage conditions are kept for a minimum of one year after the expiration date of the cold chain product.

18.8 Cold chain breaks and emergencies

Preparation for a cold chain emergency

- Prepare an emergency plan to ensure maintenance of the cold chain for each storage point and during transportation before a break happens. Any interruption to the normal functioning of refrigerators and freezers due to power failure or mechanical failure must be considered an emergency. However, the risks can be minimised if emergencies are anticipated and backup plans are prepared in advance.

Important points to remember in preparation for any cold chain emergency:

- Keep appropriate number of ice packs at the bottom of the refrigerator.
- In the event of power failure, know the duration at which the refrigerator can keep cold chain products at the safe temperature without opening it. This can be done so by monitoring the temperature at specific intervals. E.g. Every 15 mins.
- Keep the minimum number of ice packs available for use in cold boxes required to store cold chain products during a break.
- Keep suitable cold boxes available in case cold chain products must be moved.
- Know the person responsible for the cold chain storage area in case the break in cold chain occurs outside working hours.
- Know the location of the nearest suitable refrigerators/ freezers to be used if cold chain products must be moved, and the name and telephone number of the contact person if it is another building or institution.
- Know the duration at which the cold box can keep cold chain products at a safe temperature (below +8^{o}C) without changing the ice packs and without opening it.
- Know the location of fuel for generator, if available, in case urgently needed.

<u>During a cold chain emergency</u>:

A cold chain product is in danger, and unless action is taken QUICKLY there is a risk of damage or complete loss of the cold chain stock. In the event of an undetermined power failure or equipment failure, activate your local procedures for handling cold chain emergencies.

Important points to remember during any cold chain emergency:

- Keep all refrigerators, freezers, cold rooms, freezer rooms and cold boxes CLOSED as long as possible. Only open when essential, and work as quickly as possible.

- To prevent break in cold chain, cold chain products should be TRANSFERRED from the refrigerator/freezer to a cold box with adequate icepacks or the next working refrigerator/freezer. Upon resumption of power supply, do not return the products to the refrigerator/freezer until proper storage temperatures are restored (i.e., +2^{o}C and +8^{o}C). Remember that some cold chain products are much more sensitive to heat than others. Give them priority when making alternative storage arrangements in an emergency.
- Temperature records associated with the cold chain product must accompany the product if it is moved to another refrigerator or freezer or to a cold box, even if temporarily.
- Monitor the duration of the break in cold chain by recording the date, time and temperature during the whole duration of the power outage.
- There should be established procedures for investigating and reporting cold chain emergencies.

19. List of references:

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Annex A

Key areas for GSDP inspection	
Personnel • Organizational Chart • Name & Designation of Personnel • Job Description • Qualification • Training Programme / Records **Premise and Equipment** • Layout Plan / Floor Area • Security • Warehouse / Store • Equipment • Storage of controlled drugs/psychotropics/cytotoxic products/blood products • Pest Control Management • Cleaning/Sanitation • Ventilation equipment • Lighting • Backup power/generator • Fire protection • Validation and Calibration of equipment • Temperature mapping • Temperature and humidity monitoring • Suitability of transport **Stock handling/Stock control** • Storage conditions • Stock rotation and expiry dates • Inventory management • Stock handling and movement (receiving procedures, appropriate checks, dispatch procedures) • Record keeping and documentation • Control on rejected, returned, expired stock • Monitoring of condition • Quarantine • Disposal	**Documentation** • Standard Operating Procedure (SOP) • Site Master File/Company Profile • Documentation system, backup and access • Receiving and distribution records, invoices and delivery orders • Record retention and available for inspection • Reviewed date and whether up to date • Outsourced activities and contracts **Product complaints, reporting adverse reactions and recalls** • SOP / System for Investigation • Establishment of Level of Recall • Records **Self-inspection** • Procedure - plan, frequency, scope • Reports/Records **Cold chain products** • Cold chain equipment • Storage condition • Maintenance of cold chain equipment • Transportation and products in transit • Containers and container labelling • Receiving and incoming checks • Procedure to handle cold chain emergencies. Eg power failure, break in cold chain • Monitoring records • Labels/means to identify cold chain products • Alarm system for temperature excursion • Backup generator/plan • Packing procedure and records, and independent check • Qualified/validated containers for transport • Delivery procedure

Annex B

Ice Packs

Ice packs are plastic containers filled with water, hard frozen when kept in the freezer, placed inside cold boxes and vaccine carriers to improve and maintain the holdover time.

It is recommended that about 20-25 ice packs (8-10kg of ice) and 35-40 ice packs (12-14kg of ice) can be frozen in one day in small and large deep freezers, respectively. Standard ice packs used for cold boxes and vaccine carriers are of 0.4 litre capacity or as specified by the validated process.

Important points to consider when using ice packs:

- Check and ensure the ice packs doesn't leak
- Clean the outer surface of ice packs with dry cloth before putting into the freezer
- Keep ice packs horizontally (not flat) in a criss-cross manner in the deep freezer (brick layered pattern). Refer to Figure 5
- Keep a gap/breathing space between ice packs for freezing to be faster and uniform
- Ensure use of conditioned ice packs when storing/transporting cold chain products

Figure 5: Keep ice packs horizontally (not flat) in a criss-cross manner in the deep freezer (brick layered pattern)

(Sourced from: Immunization handbook for Medical Officers, WHO)

Conditioning of ice packs

Ice packs when taken out of the freezer is at temperatures of about -20 °C. They need to be kept at room temperature for a period of time to allow the ice core of the ice pack to rise to 0 °C / 'sweat' until water droplets appear on their surface before putting them in the container. This will take up to one hour at +20 °C and rather less at higher temperatures. This process is called "conditioning".

- Conditioning of ice packs prevents freezing of cold chain products during transportation
- Freeze-sensitive medicines and vaccines can be damaged if they come in direct contact with ice packs
- When required for use, take all the ice packs that you need from the freezer and close the door. Lay these out on a table leaving a 5 cm space all around each ice pack
- Lay out ice packs preferably in single rows but never in more than 2 rows
- Wait until there is a small amount of liquid water inside the ice packs
- Shake one of ice packs every few minutes. The ice is conditioned as soon as it begins to move about slightly inside its container

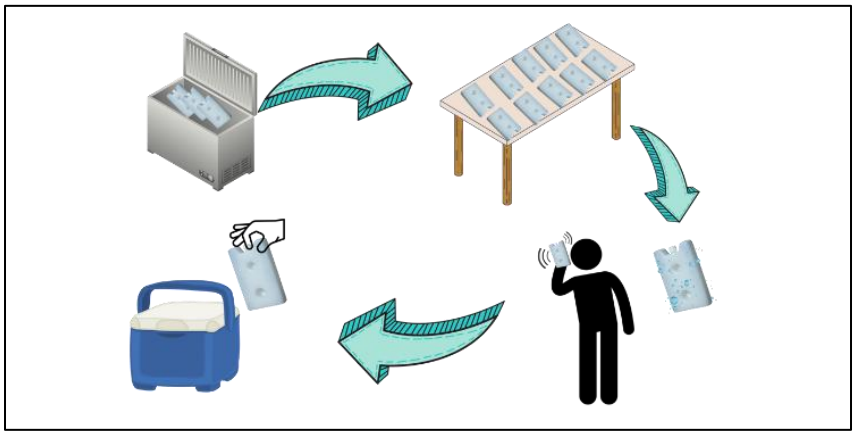

Figure 6: Conditioning the ice packs (Sourced from: Immunization handbook for Medical Officers, WHO)