



Temperature Control
Best Practices
FINAL document

OBJECTIVE

CAPDM's objective in developing a Best Practices document is to provide its Members in the pharmacy supply chain with guidelines to achieve proper and effective temperature control management.

BACKGROUND

Maintaining the safety and efficacy of the supply chain for pharmaceutical and non-prescription products continues to be the focus of the Canadian Association for Pharmacy Distribution Management (CAPDM). Ultimately, it is the responsibility of various trading partners to ensure the integrity of the products within the Canadian pharmacy supply chain (in order for patients and consumers to receive quality products). This document provides guidance for a consistent approach in proper and effective temperature control management throughout the pharmacy supply chain. It applies to manufacturers, distributors, self-distributing retailers, third party logistics providers (3PLs) and transportation providers.

Manufacturers, distributors, self-distributing retailers and 3PLs are responsible for the appropriate handling, storage and distribution of drugs according to C.02.015 of the Food and Drug Regulations. It is understood that every activity in the distribution of drugs should be carried out in accordance with the Food and Drug Act, the principles of Good Manufacturing Practices (GMP), good storage and good distribution practices, and the Guidelines for Temperature Control of Drug Products during Storage and Transportation (Guide-0069).

Temperature is one of the most important parameters to control within the pharmacy supply chain. Drugs must be stored, handled and transported according to pre-determined conditions (e.g. temperature) as supported by stability data (see Appendix for temperature ranges).

The CAPDM Board of Directors supported the idea of creating a Temperature Control Committee in January 2005. The Committee is comprised of Member representatives from the pharmacy supply chain, including distributors, self-distributing retailers, 3PLs and manufacturers. The Committee, through a task group, included a select number of transportation providers (e.g. courier, specialty, line haul and LTL carriers) as they are integral to the pharmacy supply chain.

The CAPDM Temperature Control Committee identified that maintaining proper temperature control in the pharmacy supply chain as a significant issue for industry trading partners. The Committee determined that a good approach to the issue would be to develop a **Best Practices** document.

The Best Practices are not intended to cover every conceivable situation; however, the Temperature Control Committee attempted to cover the most critical steps and procedures within the pharmacy supply chain. Distributors, self-distributing retailers, 3PLs, manufacturers and transportation providers are responsible for interpreting and applying these Best Practices in accordance with their own existing Standard Operating Procedures (SOP).

The recommended Best Practices are subdivided into the following categories:

1. Manufacturer
2. 3PL (Third Party Logistics Provider)
3. Transportation Provider
4. Distributor/Self-distributing Retailer

The Best Practices are as follows:

1. Manufacturer **Best Practices**

RECEIPT & STORAGE

Manufacturers receive large volume shipments of pharmaceutical and non-prescription products from domestic and global suppliers into their warehouse. Employees involved in the receipt, storage and distribution of such products should receive ongoing GMP and SOP training and be periodically assessed. Inbound shipping conditions should be approved by the Quality Department in advance of shipment, and these conditions should be specified in supplier quality agreements. Where required, temperature monitors should be included alongside the product. Upon receipt of product shipment, the inbound shipping conditions, modality of transportation and vendor (among other things) should be verified against the supplier quality agreement and the product should be placed under Quality HOLD pending disposition by the Quality Department.

Within the warehouse, Best Practices in receipt, handling and storage should be documented in the SOP and include the following:

- a) Pre-shipment notification should be issued by the shipper to support the prompt transfer of products to the appropriate storage environment upon receipt.
- b) Temperature monitors are retrieved and processed; the locations of such should be clearly indicated on the shipper's documentation.
- c) Temperatures outside of product labelled storage conditions are evaluated by the Quality Department and a release decision is made based on the available stability data.
- d) Shipping and storage temperature excursions should be fully documented, a root cause identified and actions put in place to prevent reoccurrence.
- e) Products should be stored in accordance with the conditions as indicated on the product label.
- f) Products should not be stored in areas that are unsuitable.

Within a pharmaceutical and non-prescription warehouse, Best Practices for mapping and monitoring of these facilities shall include:

Temperature Mapping of Product Storage Locations:

- a) Mapping should be performed during seasonal extremes and mimic potential storage capacity levels (e.g. empty and full states, where applicable).
- b) Data collection should be simultaneous, and use appropriately specialized, sensitive and calibrated equipment.
- c) Mapping should be repeated periodically and after any significant modifications are made to the storage environment as required in the change control process.
- d) Mapping results should be assessed to determine if thermostat settings are appropriate and temperature-monitoring probes are appropriately located.
- e) The mapping protocol should be robust enough to identify hot and cold areas.

Calibration, Monitoring and Design of Coolers, Freezers and Warehouse HVAC systems:

- a) Calibration requirements, alarm set point values and methodology for alarm set point challenges should be included in a SOP.
- b) Coolers and freezers should be equipped with alarms that will alert the manufacturer and the alarm company of temperature excursions.
- c) Monitoring probes should be designed based on the type of product(s) within the storage environment and should be continuous.
- d) Pre- and post-calibration readings should be recorded. Product impact should be assessed if significant adjustments are required during calibration.
- e) The Quality Department should review calibration and temperature monitoring records. Records must be retrievable and provide evidence of compliance.
- f) Computer-based temperature monitoring systems should be appropriately validated.
- g) Preventative maintenance programs should be in place to ensure that environmental systems are operating as designed.
- h) Contingency plans are in place to mitigate the risk to product in the event of a systems failure. This may include backup compressors, generators and provisions for alternate storage locations that have been qualified for that purpose.

PICK/PACK PRACTICES

The nature of the product is vital in making packaging and shipping choices. Packaging should be selected by taking into consideration: Modality; transport times (keeping in mind potential delays); expected temperature exposures; product stability; quantity of product; multiple orientations; and the location of temperature monitors.

When designing protective packaging, standardized components should be selected where possible and specifications documented, including size of box, thickness and density of Styrofoam or insulating material, number of ice/refrigerated gel/warm packs and any preconditioning requirements. A protocol should be written and approved prior to the execution of the qualification testing. Qualification should be planned to test typical worst-case conditions including summer and winter temperatures and longest transit times. Worse-case conditions should be determined through field testing. When new packaging materials or configurations are introduced, re-qualification should take place. The results and conclusions of the qualification testing should be documented, retained and available for inspection.

Within the storage facility, picking and packing practices should be documented in a SOP and includes the following:

- a) Examination and approval of qualified packaging components before use.
- b) Packaging materials should be pre-conditioned before use and in accordance with SOPs.
- c) Cold chain products should be picked and packed as close to shipping time as practical.
- d) Containers should be labelled with special handling requirements that are visible on packaging/shipping container.
- e) The manufacturer should use the appropriate qualified packaging based on the shipping lane profile.

SHIPPING

Carriers and modality of transportation should be selected with care.

Storage facility shipping practices should be documented in a SOP and includes the following:

- a) Products should be shipped within the acceptable temperature range and in accordance with the nature of the product.
- b) Profiling of shipping lanes should be conducted, taking into consideration seasonal variations, geography, climate, modality and service level.
- c) Preferred transportation providers should be identified and appropriate agreements should be signed, with periodic assessment based on a supplier quality management program.
- d) Transportation providers should also be evaluated against key performance indicators (KPI) such as those described in CAPDM's green (position) paper titled "CAPDM's Carriers: Lead Times, Measurements & Controls".
- e) A mechanism for logging, tracking and correcting transportation-related complaints should be in place.
- f) Handling of temperature excursions for cold chain products should be given an appropriate degree of urgency.
- g) The Quality and Logistics and Operations departments should collaborate to determine the most appropriate shipping strategy.
- h) All necessary bills of lading, labels, etc. should be clearly marked with any special handling requirements and provided to the transportation provider.
- i) Transportation of Dangerous Goods (TDG), temperature control and special delivery conditions should be prominently labelled.

Temperature monitors can play an important role in the pharmaceutical and non-prescription supply chain. Manufacturers should determine if a monitor should be used, based on applicable factors that may include the following:

- a) direct shipment
- b) shipping duration
- c) level of qualification of the shipping package
- d) robustness of qualification
- e) level of transporter management and confidence in provider
- f) modality of transportation
- g) risk of delay or service interruption
- h) shipment value
- i) season
- j) geography
- k) availability of product stability data

Manufacturers should apply labels to indicate temperature monitor location and indicate on the bill of lading that temperature monitors are included with the shipment (i.e. proof of temperature required). Ease of use of temperature monitors should be considered during selection; use of pass/fail or easily interpreted monitors is generally preferred. If temperature data loggers are used, the manufacturer should provide the mechanism for the return and reading of data loggers.

RETURNED GOODS/UNSALEABLES

These Best Practices apply to returns of product that have not left the facility of a distributor, self-distributing retailer or 3PL, after receipt of the products. Examples include, but are not limited to; over-shipments, mis-shipments, and damaged products.

- a) If the product is to be returned, the manufacturer should select a transportation provider, provide temperature monitoring devices (where required) and arrange for pick-up of the returned product at the facility of the distributor, self-distributing retailer or 3PL.
- b) If requested, the distributor, self-distributing retailer or 3PL should provide information to support redistribution of the product by the manufacturer, such as temperature records.
- c) Upon receipt at the manufacturer, the returned product should be processed in accordance with the manufacturer's inspection procedures and all product eligible to be placed back into saleable inventory should be subject to a quality assessment.

The manufacturer's return policy governs how returns from other facilities such as hospitals, health care facilities, pharmacies and other types of retail stores should be managed.

PRODUCT INFORMATION

Manufacturers should conduct stability studies on temperature excursions that might occur during the distribution of their products.

Manufacturers should provide, where available, temperature range, time exposure limits for cold and hot conditions, allowable temperature excursion levels and simple instructions that outline the intended use. The manufacturer should complete special handling and storage requirements on a product information form. The manufacturer should group products with like profiles based on compatibility and appropriateness. Manufacturers should update product information promptly.

A distributor, self-distributing retailer and 3PL should contact the manufacturer in the event of an excursion outside of the allowable temperature range.

FILING & RECORD KEEPING

A filing system should be maintained and should include the following documents related to temperature control:

- a) Shipping records
- b) Receiving records
- c) Qualification data/protocol
- d) Mapping records
- e) Employee training records
- f) Monitoring records
- g) Shipping lane temperature profiles records
- h) Housekeeping/maintenance records (coolers, freezers)
- i) Letters from Distributors/Self-distributing Retailers/3PLs
- j) Temperature control data spreadsheet
- k) Contracts – Distributors/Self-Distributing Retailers/3PLs and Transportation Providers

TRADING PARTNER RELATIONSHIPS

Contracts should be established between individual manufacturers, distributors, self-distributing retailers, 3PLs and transportation providers. Periodic assessment and/or random auditing of the contractual obligations should be conducted by the manufacturer to ensure temperature control compliance by all trading partners.

A central repository for product data should be considered by industry (e.g. ECCnet).

2. 3PL (Third Party Logistics Provider) **Best Practices**

BACKGROUND

For the purposes of this Best Practices document a 3PL is defined as an outsourced provider that manages all or a significant part of an organization's logistics requirements and performs transportation, locating and sometimes product consolidation activities. While a 3PL is held to the same GMP standards and requirements as a manufacturer, the fundamental difference is that a 3PL does not take title to the pharmaceutical and non-prescription products that it stores and distributes. The 3PL provider must adhere to GMP guidelines and can maintain an Establishment License with Health Canada as an Importer / Distributor, however since they do not own the product, the ultimate liability lies with the owner of the products, which is typically a manufacturer, distributor or self-distributing retailer that is utilizing the 3PL's services. 3PLs should maintain their own set of Standard Operating Procedures (SOPs), however, these SOP's must be reviewed, amended, and/or accepted by the Quality Assurance designated authority of the owner of the product for whom the 3PL is providing services.

RECEIPT & STORAGE

3PLs receive large volume shipments of pharmaceutical and non-prescription drugs from domestic and global suppliers into their warehouse. Employees involved in the receipt, storage and distribution of products should receive ongoing GMP training, as well as being trained on specific client-approved SOP's and be periodically assessed.

The supplier should notify the 3PL of incoming temperature controlled products as the transportation provider may not necessarily be aware they have received such product at the time of delivery. The transportation provider should notify the supplier or inform the 3PL of any delivery delays prior to the delivery.

Inbound shipping conditions should be approved by the Quality department in advance of shipment in accordance with supplier quality agreements. Where required, temperature monitors are included alongside the product. The 3PL should carry out a receiving inspection against the approved instructions by the owner of the product, such as; upon receipt temperature requirements should be noted, and the material moved immediately to the appropriate storage area to meet the required conditions. Packaging conditions, quantity and integrity should be checked prior to accepting the products. Temperature monitors/data loggers should be removed from the shipment and prepared for shipment to the client QA, or as outlined in a pre-described client approved SOP. The product should be placed under Quality HOLD pending disposition by the Quality Department for products shipped from foreign sites. Domestically produced material may be received directly into saleable goods.

Within the warehouse, best practices in receipt, handling and storage should be documented in a SOP and include the following:

- a) Pre-shipment notification should be issued by the shipper to support the prompt transfer of products to the appropriate storage environment upon receipt.
- b) Temperature monitors are retrieved and processed; the locations of such should be clearly indicated on the shipper's documentation.
- c) Temperatures outside of product labelled storage conditions are reported to the Quality department of the owner of the products. The owner of the products, based on the available stability data, then makes a release decision.
- d) Shipping and storage temperature excursions should be fully documented, a root cause identified and actions put in place to prevent reoccurrence.
- e) Products should be stored in accordance with the conditions as indicated on the product label.
- f) Products should not be stored in areas that are unsuitable.

Within a 3PL warehouse storing pharmaceutical and non-prescription products, best practices for mapping and monitoring of these facilities should include:

Temperature Mapping of Product Storage Locations:

- a) Mapping should be performed during seasonal extremes and mimic potential storage capacity levels (e.g. empty and full states, where applicable).
- b) Data collection should be simultaneous, and use appropriately specialized, sensitive and calibrated equipment.
- c) Mapping should be repeated periodically and after significant modifications are made to the storage environment as required in the change control process.
- d) Mapping results should be assessed to determine if thermostat settings are appropriate and temperature-monitoring probes are appropriately located.
- e) The mapping protocol should be robust enough to identify hot and cold areas.

Calibration, Monitoring and Design of Coolers, Freezers and Warehouse HVAC systems:

- a) Calibration requirements, alarm set point values and methodology for alarm set point challenges should be included in a SOP.
- b) Coolers and freezers should be equipped with alarms that will alert the 3PLs and the alarm company of temperature excursions.
- c) Monitoring probes should be designed based on the type of product(s) within the storage environment and should be continuous.
- d) Pre- and post-calibration readings should be recorded. If significant adjustments are required during calibration, notification should be made to the QA of the owner of the product so product impact can be assessed.
- e) The Quality department should review calibration and temperature monitoring records. Records should be retrievable and provide evidence of compliance.
- f) Computer-based temperature monitoring systems should be appropriately validated.
- g) Preventative maintenance programs should be in place to ensure that environmental systems are operating as designed.
- h) Contingency plans should be in place to mitigate the risk to product in the event of a systems failure; this may include backup compressors, generators and provisions for alternate storage locations that have been qualified for that purpose.

PICK/PACK PRACTICES

The nature of the product is vital in making packaging and shipping choices. Packaging should be selected taking into consideration: modality, transport times (keeping in mind potential delays), expected temperature exposures, product stability, quantity of product, multiple orientations and the location of monitors.

When designing protective packaging, standardized components should be selected where possible and specifications documented including size of box, thickness and density of Styrofoam or insulating material, number of ice/refrigerated gel/warm packs and any preconditioning requirements. A protocol should be written and approved by the QA department or designate of the owner of the products prior to the execution of the qualification testing. The 3PL may assist in the qualification testing process once approved. Qualification should be planned to test typical worst case conditions including summer and winter temperatures and longest transit times. Worst case conditions should be determined through field testing. When new packaging materials or configurations are introduced, re-qualification should take place.

In all cases the 3PL provider should adhere to the packaging standards, and requirements set out by the owner of the products.

Within the storage facility, picking and packing practices should be documented in a SOP, which has been approved by the QA department or designate of the owner of the products, and includes the following:

- a) Examination and approval of qualified packaging components before use.
- b) Packaging materials should be pre-conditioned before use, and in accordance with SOPs.
- c) Cold chain products should be picked and packed as close to shipping time as practical.
- d) Containers should be labelled with special handling requirements that are visible on packaging/shipping container.
- e) The 3PL should use the appropriate qualified and approved packaging based on the shipping lane profile.

SHIPPING

Carriers and modalities should be selected with care.

Within the storage facility shipping practices should be documented in a SOP that has been reviewed and accepted by designated QA for the owner of the products, and includes the following:

- a) Products should be shipped within the acceptable temperature range and in accordance with the nature of the product.
- b) Profiling of shipping lanes should be conducted, taking into consideration seasonal variations, geography, climate, modality and service level.
- c) Preferred transportation providers should be identified and appropriate agreements should be signed, with periodic assessment based on a supplier quality management program.
- d) Transportation providers should also be evaluated against key performance indicators (KPI) such as those described in CAPDM's green (position) paper titled "CAPDM's Carriers: Lead Times, Measurements & Controls".
- e) A mechanism for logging, tracking and correcting transportation-related complaints should be in place.
- f) Handling of temperature excursions for cold chain products should be given an appropriate degree of urgency.
- g) The Quality designate of the owner of the products, and Logistics and Operations departments should collaborate to determine the most appropriate shipping strategy.
- h) All necessary bills of lading, labels, etc. should be clearly marked with any special handling requirements and provided to the transportation provider.
- i) Transportation of Dangerous Goods (TDG), temperature control and special delivery conditions should be prominently labelled.

Temperature monitors can play an important role in the pharmaceutical and non-prescription supply chain. Manufacturers should determine if a monitor should be used, based on applicable factors that may include the following:

- a) direct shipment
- b) shipping duration
- c) level of qualification of the shipping package
- d) robustness of qualification
- e) level of transporter management and confidence in provider
- f) modality of transportation
- g) risk of delay or service interruption
- h) shipment value
- i) season
- j) geography
- k) availability of product stability data

The 3PL should apply labels to indicate temperature monitor location and indicate on the bill of lading that temperature monitors are included with the shipment (i.e. proof of temperature required). Ease of use of temperature monitors should be considered during selection; use of pass/fail or easily interpreted monitors is generally preferred. If temperature data loggers are used, the 3PL on behalf of the owner of the products should provide the mechanism for the return and reading of data loggers.

RETURNED GOODS/UNSALEABLES

These best practices apply to returns of product that have not left the facility of a distributor or self-distributing retailer, after receipt of the products. Examples include, but are not limited to; over-shipments, mis-shipments, and damaged products.

- a) If product is to be returned, the owner of the product should inform the 3PL of their wishes to have temperature control conditions for the return of the products. The 3PL should select a transportation provider, provide approved temperature-monitoring devices (where required) and arrange for pick-up of the returned product at the facility of the distributor or self-distributing retailer.
- b) If requested, the distributor or self-distributing retailer should provide information to support redistribution of the product by the owner of the product, such as temperature records.
- c) Upon receipt at the 3PL the returned product should be processed as per procedures approved by QA department or designate of the owner of the products, and all product eligible to be placed back into saleable inventory should be subject to a quality assessment.

The 3PL should follow the owner of the products' return policy governing how returns from other facilities such as hospitals, health care facilities, pharmacies and other types of retail stores should be managed.

PRODUCT INFORMATION

The 3PL should request manufacturers to provide (where available) temperature range, time exposure limits for cold and hot conditions, allowable temperature excursion levels and simple instructions that outline the intended use (i.e. assist with product distribution).

The 3PL should request manufacturers to complete special handling and storage requirements on a product information form.

The 3PL should request manufacturers to group products with like profiles based on compatibility and appropriateness.

The 3PL should ask their manufacturers to update product information promptly.

FILING & RECORD KEEPING

A filing system should be maintained and should include the following documents related to temperature control:

- a) Shipping records
- b) Receiving records
- c) Qualification data/protocol
- d) Mapping records
- e) Employee training records
- f) Monitoring records
- g) Shipping lane temperature profiles records
- h) Housekeeping/maintenance records (coolers, freezers)
- i) Letters from Distributors/Self-distributing Retailers/3PLs
- j) Temperature control data spreadsheet
- k) Contracts – Distributors/Self-Distributing Retailers/3PLs and Transportation Providers

TRADING PARTNER RELATIONSHIPS

Contracts should be established between individual manufacturers, distributors, self-distributing retailers, 3PL's and transportation providers. Periodic assessment and/or random auditing of the contractual obligations should be conducted by the manufacturer to ensure temperature control compliance by all trading partners.

A central repository for product data should be considered by industry (e.g. ECCnet).

3. Transportation Provider Best Practices

TRANSPORTATION PROVIDER SELECTION CRITERIA

Transportation provider selection should be based on the temperature control requirements for each shipment. Transportation providers should be evaluated prior to use to determine their capabilities and whether they meet the requirements of the shipment. Additional supplier management is required when the transportation provider is contracted to provide the primary method of temperature control. Use of protective/qualified packaging or a robust stability profile may mitigate the risks associated with using a transport provider that does not specifically control transport temperature. Shipping decisions can also be influenced by multiple factors, including season, transit time, modality, destination, etc.

TRANSPORTATION PROVIDER AS PRIMARY METHOD OF CONTROLLING TEMPERATURE

Deliverables

- a) Transportation providers should maintain temperature records, and any related documents, for a minimum period of six (6) years from date of shipment.
- b) Transportation providers should provide evidence of the ambient temperature while the shipment was in their possession or control. This would include sub-contractors and other agents. The transportation provider's responsibility begins the moment that the transportation provider takes physical possession from the shipper and ends when the delivery is made to the consignee.
- c) Temperature records for a given shipment should be available to the shipper within a reasonable amount of time after the shipment has been delivered.

Knowledge Required

Transportation providers should be familiar with Good Manufacturing Practices (GMPs), Good Distribution Practices (GDPs), and the Health Canada Guidelines for Temperature Control of Drug Products During Storage and Transportation (Guide -0069).

QMS (Quality Management System)

- a) Transportation providers should have quality systems in place, which include procedures that outline how temperature control is managed, how temperature excursions are handled and how employees are trained to control temperature-sensitive freight.
- b) Transportation providers should identify a delegate that is responsible for maintaining the quality system and investigating temperature excursion events.
- c) Transportation providers should promptly contact the shipper if product has been exposed to temperature excursions outside the acceptable range.
- d) If transportation providers are providing the primary means of temperature control, a Quality Agreement should also be in place. The agreement should include (but not be limited to) provisions for temperature control services, temperature monitoring, standard operating procedures, business continuity, security, sanitation, data retention, excursion management, communication, right to audit, use of subcontractors and pest control. These contractual obligations should also be extended to any sub-contractor or agent.

Qualification

- a) Delivery/Transportation units (trailers, rail-cars, etc.) should have a temperature monitoring system independent from the reefer.
- b) Delivery/Transportation units should be mapped (by unit).
- c) Delivery/Transportation units should be qualified (by unit).
- d) Temperature monitors should be placed in locations susceptible to temperature excursions, as identified during mapping.
- e) Temperature monitors should be calibrated (as per monitor vendor specifications).
- f) Thermo-units should be calibrated and have established preventative maintenance plans that support operational effectiveness.
- g) Delivery/Transportation units should be equipped with an alarm system that notifies the driver and/or central dispatch in the event of a temperature excursion.
- h) Delivery/Transportation units should have the capability for remote access to allow for gathering of temperature data, location, etc., as close to real time as possible. Event monitoring is also, suggested.
- i) The transportation provider facilities should be mapped, temperature monitored, RH (relative humidity) monitored, and qualified. If product is always direct-drive, or not removed from primary pick-up vehicle, these requirements are not needed.
- j) Transportation providers should have appropriate pest controls, security and storage conditions in place.
- k) If a product is to be removed from the primary pick-up vehicle, the product should be stored within the specified handling requirements (e.g. temperature, relative humidity, light).

Business Continuity

Transportation provider should have continuity plans in place to mitigate the risk to product in the event of a systems failure (e.g. power failures, weather related delays, mechanical problems, etc.).

Provider Expectations

All necessary transportation provider bills of lading, labels, etc., should be clearly marked and communicated to the transportation provider, including prominent labelling that clearly indicates the service requested (i.e. proof of temperature required, Transportation of Dangerous Goods (TDG)).

Ongoing Evaluation

Transportation provider should also be evaluated against key performance indicators on a periodic basis, including but not limited to; on-time service, service complaints, damages, temperature excursions, etc.

TRANSPORTATION PROVIDER IS NOT PRIMARY METHOD OF CONTROLLING TEMPERATURE

- a) Transportation providers should have applicable SOPs and/or other governance documents that support their ability to carry out their responsibilities.
- b) Shipper must ensure that the packaging provides sufficient product protection during the entire expected transportation process.
- c) All necessary transportation provider's bills of lading, labels, etc., should be clearly and prominently marked and communicated to the transportation provider (e.g. Transportation of Dangerous Goods (TDG), temperature control, special delivery conditions, etc.).
- d) Transportation providers should have business continuity plans in place.
- e) Transportation providers should be evaluated against key performance indicators on a periodic basis, including but not limited to: on-time service; service complaints; damages; etc.
- f) Transportation providers should have appropriate pest controls, security and storage conditions in place.

TRADING PARTNER RELATIONSHIPS

- a) Contracts should be in place between the Transport Provider and the Shipper specifying pertinent conditions of transport as well as other requirements and customary terms and conditions.
- b) Compliance with the terms of the agreement(s) should be periodically assessed by the consignee. This may occur through documentation review or periodic quality audits of the transportation provider.

4. Distributor/Self-distributing Retailer **Best Practices**

RECEIVING

The receiving distribution centre should inquire if temperature sensitive products are included in the shipment at the time of accepting the appointment for delivery.

The distributor/self-distributing retailer should request that a manufacturer apply labels to indicate location of temperature monitors and indicate on the bill of lading that temperature monitors are included in the shipment.

The distributor/self-distributing retailer should ask the manufacturer to provide instructions for reading and disposition of temperature monitors.

Upon receipt, if there are any questions concerning product integrity, the distributor or self-distributing retailer should place product under Quality HOLD pending disposition and contact the manufacturer, as appropriate.

Incoming shipments should be checked for ice packs/warm packs and temperature monitors where applicable, and any concerns or issues should be investigated and documented in co-operation with the manufacturer. The receiver should notify the manufacturer as soon as practical of any discrepancies in the shipment, including but not limited to, over/under shipments and incorrect product.

Cold chain products should be received in a walk-in cooler or refrigerator, if possible. Otherwise, the products should be transferred into the appropriate storage area as quickly as possible after receiving. Inventories should not be stored in areas that are unsuitable.

A courier lane to facilitate receipt of courier shipments should be available.

PUT AWAY/STORAGE

Within a distribution centre, Best Practices for mapping and monitoring of these facilities should include:

Temperature Mapping of Product Storage Locations:

- a) Mapping should be performed during seasonal extremes and mimic potential storage capacity levels (e.g. empty and full states, where applicable).
- b) Data collection should be simultaneous and use appropriately specialized, sensitive and calibrated equipment.
- c) Mapping should be repeated periodically and/or after significant modifications are made to the storage environment as required in the change control process.
- d) Mapping results should be assessed to determine if thermostat settings are appropriate and temperature-monitoring probes are appropriately located.
- e) The mapping protocol should be robust enough to identify hot and cold areas.

Calibration, Monitoring and Design of Coolers, Freezers and Warehouse HVAC systems:

- a) Calibration requirements, alarm set point values and methodology for alarm set point challenge should be included in a SOP.
- b) Coolers and freezers should be equipped with alarms that will alert the distributor/self-distributing retailer and the alarm company of temperature excursions.
- c) Monitoring probes should be designed based on the type of product(s) within the storage environment and should be continuous.
- d) Pre- and post-calibration readings should be recorded. Product impact should be assessed if significant adjustments are required during calibration.
- e) The Quality Department should review calibration and temperature monitoring records. Records must be retrievable and provide evidence of compliance.
- f) Computer-based temperature monitoring systems should be appropriately validated.
- g) Preventative maintenance programs should be in place to ensure that environmental systems are operating as designed.
- h) Contingency plans should be in place to mitigate the risk to product in the event of a systems failure. This may include backup compressors, generators and provisions for alternate storage locations that have been qualified for that purpose.

PICK/PACK PRACTICES

The nature of the product is vital in making packaging and shipping choices. Packaging should be selected by taking into consideration: modality; transport times (keeping in mind potential delays); expected temperature exposures; product stability; quantity of product; multiple orientations; and freeze and/or temperature indicator location.

When designing protective packaging, standardized components should be selected where possible and specifications documented, including size of box, thickness and density of Styrofoam or insulating material, number of ice/refrigerated gel/warm packs and any preconditioning requirements. A protocol should be written and approved prior to the execution of the qualification testing. Qualification should be planned to test typical worst-case conditions including summer and winter temperatures and longest transit times. Worse-case conditions should be determined through field testing. When new packaging materials or configurations are introduced, re-qualification should take place. The results and conclusions of the qualification testing should be documented, retained and available for inspection.

Within the storage facility, picking and packing practices should be documented in a SOP and includes the following:

- a) Examination and approval of qualified packaging components before use.
- b) Packaging materials should be pre-conditioned before use and in accordance with SOPs.
- c) Cold chain products should be picked and packed as close to shipping time as practical.
- d) Containers should be labelled with special handling requirements that are visible on packaging/shipping container.
- e) The distributor/self-distributing retailer should use the appropriate qualified packaging based on the shipping lane profile.

SHIPPING

It is estimated that the majority of shipments sent out by distributors/self-distributing retailers are in transit less than 24 hours. Many products typically stored at ambient (room temperature) conditions may not require special handling or shipping conditions.

The distributor/self-distributing retailer should request from the manufacturer information indicating the following:

- a) Products requiring special packaging/handling.
- b) Products that can be exposed to freezing (below 0° C) or hot conditions.
- c) Products that have temperature range limitations, allowable time limits and acceptable temperature excursion data, where available.

Distributor/self-distributing retailer should monitor shipments as needed and based on the information provided by the manufacturer. Distributor/self-distributing retailer should include a temperature monitor in shipments of controlled temperature products or use qualified packaging or other shipping methods to ensure that the quality of the products is maintained. Ease of use for temperature monitors should be considered. Use of pass/fail or easily interpreted monitors is preferred by the distributor/self-distributing retailer.

Annual seasonal route profiling should be performed by the distributor/self-distributing retailer to estimate worst-case scenarios. Data should be evaluated against the qualification parameters used to qualify the packaging.

Distributors/self-distributing retailers should apply labels to indicate temperature monitor location and indicate on the bill of lading that temperature monitors are included with the shipment (i.e. proof of temperature required). Instructions for reading and disposition of temperature monitors should be provided to the end receiver. Ease of use of temperature monitors should be considered; use of pass/fail or easily interpreted monitors is generally preferred. If temperature data loggers are used, the distributors/self-distributing retailers should provide the mechanism for the return and reading of data loggers.

Distributors/self-distributing retailers should evaluate the transportation provider against key performance indicators on a periodic basis, including but not limited to; on-time service; service complaints; damages; temperature excursions; etc. Transportation providers should be selected based on consideration of information gathered during seasonal profiling, special shipping conditions (e.g. temperature controlled vehicles), use of qualified packaging and other factors.

RETURNED GOODS/UNSALEABLES

Products should be returned by the same shipping methodology that they were shipped to maintain product integrity. The shipping time from the pharmacy back to the distributor/self-distributing retailer should be evaluated by Quality Assurance/Quality Control Department, as part of the decision to release the product back to stock.

The following Best Practices apply to return of product that has not left the facility of a distributor/self-distributing retailer, after receipt from the manufacturer. Examples include, but are not limited to; over-shipments; mis-shipments; and damage products.

- a) The distributor/self-distributing retailer should hold the product at the labelled storage temperature.
- b) The distributor/self-distributing retailer should contact the manufacturer to agree upon a process for disposition of the products (e.g. return, destroy, redirect and keep).
- c) If requested, the distributor/self-distributing retailer should provide information to support redistribution of the product by the manufacturer, such as temperature records.
- d) Returned products and unsaleable products should be clearly identified by the distributor/self-distributing retailer, and include all required documentation.

Refer to CAPDM's Best Practices for Returned Goods/Unsaleables for additional guidance on returned products and unsaleable products.

FILING & RECORD KEEPING

A filing system should be maintained and should include the following documents related to temperature control:

- a) Proof of Delivery (POD)
- b) Shipping records
- c) Receiving records
- d) Qualification data/protocol
- e) Mapping records
- f) Employee training records
- g) Monitoring records
- h) Shipping lane temperature profiles records
- i) Housekeeping/maintenance records (coolers, freezers)
- j) Letters from Manufacturers
- k) Temperature control data spreadsheet
- l) Contracts – Manufacturers/Transportation Providers

PRODUCT INFORMATION

The distributor/self-distributing retailer should request manufacturers to provide (where available) temperature range, time exposure limits for cold and hot conditions, allowable temperature excursion levels and simple instructions that outline the intended use (i.e. assist with product distribution).

The distributor/self-distributing retailer should request manufacturers to complete special handling and storage requirements on a product information form.

The distributor/self-distributing retailer should request manufacturers to group products with like profiles based on compatibility and appropriateness.

The distributor/self-distributing retailer should ask their manufacturers to update product information promptly.

TRADING PARTNER RELATIONSHIPS

Contracts should be established between individual manufacturers, distributors/self-distributing retailers and transportation providers. Periodic assessment and/or random auditing of the contractual obligations should be conducted to ensure temperature control compliance by all trading partners.

A central repository for new product data should be considered by the industry (e.g. ECCnet).

APPENDIX

Temperature Ranges*

Frozen	(-10 to -25 degrees Celsius)
Refrigerated	(2 to 8 degrees Celsius)
Cool	(8 to 15 degrees Celsius)
Controlled Room Temperature	(20 to 25 degrees Celsius)
Room Temperature	(15 to 30 degrees Celsius)
Excessive Heat	(>40 degrees Celsius)

* see USP for full definitions

GLOSSARY

Calibration- Determination of the accuracy of an instrument, usually by measurement of its variation from a standard, to ascertain necessary correction factors.

Data loggers- An electronic device that records the temperature to which product has been exposed along a journey. This information is then downloaded into a main computer system.

Distributor- Defined as a wholesaler in federal government regulations and guidelines.

ECCnet- The GS1 Canada data repository for information (product e-Catalog).

Ice Packs- A device that absorbs heat energy.

Manufacturer- A business engaged in the manufacturing of product (including fabricator and importer as defined in the GMPs)

Modalities- All types of transportation such as; road, rail, air and ocean.

Monitors- Chemical or electronic devices that provide alarm or other form of notification when specific temperatures have been reached or exceeded.

POD (Proof of Delivery)- A receipt showing date, place of delivery to consignee, as well as the signature of the person receiving the shipment.

Profiling- A process that when completed, indicates the temperature ranges that products have been exposed to during the shipping process.

Promptly- With little or no delay (whichever is reasonably practical under the circumstances).

Qualified Packaging- The establishment of documented evidence through pre-determined studies that are designed to evaluate packaging and challenge the components, systems, sub-systems and processes for the transportation of the product, in order to provide a high degree of assurance that the packaging of the product will maintain the desired temperature and other environmental conditions for the product under the conditions tested.

Quality Agreement- A written contract that specifies the responsibilities of a named supplier or service provider for implementing the GMPs and other technical arrangements relating to the material, products or services supplied to the company.

Reefers- A refrigeration/heating unit on a tractor trailer designed to maintain a specified temperature range.

Refrigerated Gel Pack- A device that is pre-conditioned and able to maintain a temperature of 2°C to 8°C.

Self-Distributing Retailer- Defined as a wholesaler in federal government regulations and guidelines.

Shipping lanes- A route that an order takes when traveling from one point to another.

SOP – Standard Operating Procedure: A written document that describes in detail how a procedure should be done within a company’s operations.

Stability data- Evidence establishing the period of time during which a product in the container in which it is sold will meet the manufacturer’s specifications for that product.

3PL– Third Party Logistics Provider: An outsourced provider that manages all or a significant part of an organization's logistics requirements and performs transportation, locating and sometimes product consolidation activities.

Transportation Provider-A company that takes possession of a product and transports it from one point to another.

Warm Packs- A device that emits heat energy.

This document represents suggested industry best practices as determined by CAPDM based on input from CAPDM members. The best practices provide voluntary guidelines and procedures on the subject matter of this document. CAPDM encourages its members to consider these best practices and adopt them into their everyday operations, where appropriate. Each member is however responsible for using his or her own judgment. In no event will CAPDM or its directors, employees, agents or advisors be liable for any direct, indirect, special or consequential damages resulting from the use of this information by any member or third party.
