Good Distribution Practices (GDP’s) & Pharma Supply Chain Mgt

Migration from GMPs into the Pharma Supply Chain Regulations overview – PDA March 1st, 2011

Dave Ulrich – Abbott Pharma Dist QA
Major Transformational Trends for the Pharma Supply Chain

1. From GMP to GDPs
   - Quality systems expanded from mfg’ing into both 1) the Pharma Mfg’ing supply chain (including Clinicals) and 2) the Commercial Dist supply chain
   - Stand alone GDPs are “new” (used to be a subset of GMPs)

2. GxPs specific to pharma (and device) supply chain
   - World wide >35 GDPs (WHO and FDA/EU)
   - All are similar, but some have specifics (Argentina, Brazil, etc)

3. Initial Focus was “cold chain”, now expanded to GS1, anticounterfeit and diversion, “normal channel/trade (licensed trade partner), quality agreements and data sharing (to include LSP and TSP)

4. Pedigree (ePedigree) and serialization
   - Turkey, S. Korea, Argentina, etc

5. Increased regulatory focus – standard audit items
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• Australia – Draft Code of Good Wholesaling Practice (partner w/FDA on audits)
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• Pakistan – Drug Act of 1976
• Brazil- Resolution –RDC No. 234
• Health Canada- 0069 Guidelines for: Temp control of Drug Products during Storage and Trans.
• Irish Medicines Board (IMB)
• Japan – Biological Pharma revision H15.5.15 (rPAL)
• UK- MHRA - GDP Risk Assessment Strategy
• UK - MHRA - Updated Policy on returns of non-defective refrigerated (2-8c) medicinal products
• UK - MHRA- Cold Chain Distribution
• UK - MHRA - Guidance on preventing breaches in the cold chain for medicinal products
• ISRAEL – The Status of Current GDP Regulations in Israel (adopt EU &/or WHO)
• Malaysia - National Pharmaceutical Control Bureau Ministry of Health Malaysia (NPCB) – Guidelines on Good Distribution Practice (GDP)
• UAE Circular No. 246-2011
• Argentina: “Regulating the Cold Chain of Medicines” (Ley 26492)
• FDA – Standardized Numerical Identifier
Good Distribution Practices (GDP’s)

The purpose of the Good Distribution Practice guidelines are to ensure the proper distribution of medicinal products in all stages of the distribution/supply chain. Since October 2005 when the World Health Organization’s (WHO) was adopted by the WHO Expert Committee on Specifications for Pharmaceutical Preparations, the guidelines have been sent for comments and revised a number of times by the Expert Committee.

In the European Union, the principles and guidelines for GMP are stated in directive 92/23/EEC. It says that wholesalers must comply with the principles and guidelines of Good Distribution Practice. Compliance of these guidelines is mandatory within the European Economic Area.

In the United States, the U.S. FDA specifically covers good distribution practices under its Good Manufacturing Practices in sections 21 CFR 211.142 and 21 CFR 211.150.
Good Distribution Practices (GDP)

Three main components of GDPs

- Good Cold Chain Practices (GCCPs)
- Good Import Practices (GIPs)
- Distribution Control Systems (DCS)

FD&C Act
- GMPs
- GLPs
- GCPs
- Now GDP

GDPs started with a focus on Cold Chain
Now migrated to holistic supply chain quality systems
Good Distribution Practices (GDP) – Regulation & Drivers

- C-TPAT, TSA (CCFS/CCSP)
- Rules of Origin (COO), 10+2 (ocean transport), Trusted importer program
- ISA – Importer Self Assessment

- RF TT, ISS Qualification, “Import/Export” Issues, returns, restock, Reverse Logistics Complaint mgt, Quality Agreements

- FEI rule Changes
eDLRS and GS1

- Beyond Our Borders, FDA Green lane, Import optimization (AOCC), RF enabled info Flow and “supplier supplier” information, Lacey Amendment, etc.

- Good Cold Chain Practices (GCCPs)

- Good Import Practices (GIPs)

- Distribution Control Systems (DCS)

- GS1 (GTIN, GLN), Track and Trace, Authentication, ePedigree, Serialization & Dist. Control

- Dingle Bill (HR 759), Buyer- Matheson (HR 5839), Bennet Bill (SB 3690)
- FDA SNI Sec. 913-505D(b)(2)
- FDA UDI
- CA SB 1307 (track & trace)
- Many other country regs
Updated and Newly Issued Regulations and Guidelines

Expanded focus on regulatory AND Standards-based Guidance

Regulatory Guidances
- Argentina
- Australia
- Austria
- Brazil
- Canada
- China
- Czech Republic
- EU
- EMA
- Egypt
- FDA
- ICH
- India (IPPO)
- Ireland
- Italy
- Malaysia
- Mexico
- MHRA
- Romania
- Saudi Arabia
- Singapore
- S. Africa
- S. Korea
- UAE
- Venezuela
- WHO

Recently Issued/Updated

Process
PDA Technical Support
No 39 Revised 2007
No 46 Issued 2009

Standards
USP <1079>
IATA PCR, Ch. 17,
2009
AFF et SFSP*

New PDA guidance coming out

IATA Labeling Standard

* Guide Pratique: Chaine du froid de medicament
WHO- Draft GDP’s

Model requirements for the storage and transport of time and temperature sensitive pharmaceutical products

Version 2b

SEND YOUR COMMENTS TO
Dr Umit Kartalolu by email: kartalolu@who.int
or
by fax: +41 22 791 4384

Revision history:
- Version 1a: Issued 01.10.2009
- Version 2: Issued 01.06.2010
- Version 2a: Issued 05.05.2010
- Version 3a: Issued 11.05.2010

Author(s): N/A
Date: November 5, 2010
Web Link: http://www.who.int/immunization_standards/model_requirements_v2b.pdf
Summary:

• Guideline to set out the principal requirements for the safe storage and distribution of time temperature-sensitive pharmaceutical products (TSPP).

• Balanced overview of the major aspects of good storage distribution practice for TTSPPs.

• Reference requirements from GMP, GSP and GDP guidelines.

• Listed requirements should be directly applicable to all countries (less developed as well as industrialized world).

• Guideline contains regulations on the following points:
  • Quality management, organization and personnel
  • Premises and storage areas
  • Transport vehicles, external packaging and labeling
  • Distribution and shipping practice, documentation
  • Repackaging and relabeling
  • Complaints, recalls and returned products
  • Imports and contracting

Of Note:

WHO - Draft GDP’s
FDA to partner with EU RA THIS Year
draft joint GDPs
Step towards ICH
(just like Q7A)
Europe – Guidelines on GDP’s

<table>
<thead>
<tr>
<th>Summary:</th>
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</thead>
<tbody>
<tr>
<td>• Level of quality should be maintained (wholesalers must comply with principles and guidelines on GDP’s)</td>
</tr>
<tr>
<td>• Personnel (a management representative should be appointed in each distribution point).</td>
</tr>
<tr>
<td>• Documentation (must be made available on request of competent authorities, written procedures in place and records).</td>
</tr>
<tr>
<td>• Specific temperature storage conditions (areas should be equipped with temperature recorders to record temperature).</td>
</tr>
<tr>
<td>• Deliveries (to authorized wholesalers or authorized persons only).</td>
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<tr>
<td>• Transport of temperature controlled products (must be transported by appropriately specialized means).</td>
</tr>
<tr>
<td>• Returns of non-defective medicinal products (special attention must be given to temperature controlled products. Advice should be sought from the holder of the marketing authorization or the QP of the manufacturer of the product.)</td>
</tr>
<tr>
<td>• Records of returns and FIFO</td>
</tr>
<tr>
<td>• Emergency plan for urgent recalls (procedure should be described in writing)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Of Note:</th>
</tr>
</thead>
</table>
| Author(s): | • IPEC-EUROPE: Dr. Mathias Brenken, Reiner Gellrich, Dr. Andreas Lekebusch, George Mansveld, Dr. Frank Milek, Dr. Alexander Schoch, Dr. Najib Sehat, Allan Whiston  
• IPEC-USA: (see document for list) |
<p>| Date: | • 2006 |</p>
<table>
<thead>
<tr>
<th>Summary:</th>
<th>Standard GDP’s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Of Note:</td>
<td>This guide provides additional explanatory notes to:</td>
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<tr>
<td></td>
<td>“GOOD TRADE AND DISTRIBUTION PRACTICES FOR PHARMACEUTICAL STARTING MATERIALS” [1]</td>
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What triggered this?

Melamine, Heparin, ethylene glycol

Economically motivated Adulteration
<table>
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<tbody>
<tr>
<td>3.2 Measures should be in place to prevent unauthorized persons from entering the premises.</td>
<td>Self-explanatory</td>
</tr>
<tr>
<td>3.3 Premises should be designed and equipped so as to afford maximum protection against the entry of insects, rodents or other animals.</td>
<td>Extract from IPEC IQC GMP Guide 2006 [2], chapter 6.4.4.</td>
</tr>
<tr>
<td>3.4 Suitable supporting facilities and utilities (such as air control, lighting and ventilation) should be in place and appropriate to the activities performed.</td>
<td>Self-explanatory</td>
</tr>
<tr>
<td>3.5 There should normally be a separate sampling area for pharmaceutical starting materials in a controlled environment. If sampling is performed in the storage area, it should be conducted in such a way to prevent contamination or cross-contamination. Adequate cleaning procedures should be in place for the sampling area.</td>
<td>Self-explanatory</td>
</tr>
</tbody>
</table>

4. Warehousing and Storage

GSP is applicable in all circumstances in which and all areas where materials are stored.

GSP – Good Storage Practice [3]

4.1 There should be authorized procedures describing the activities relating to the receipt, storage and distribution of materials.

Written procedures should describe receipt of the excipient; its storage and further dispatch.

Some considerations (that may not be applicable in all situations) are:
- Receipt: visual inspection of the container (packaged or bulk) integrity, confirmation of material identity from the label against documentation, evidence of infestation;
- Storage: cleanliness of excipient storage area, accuracy of the inventory;


as amended by


Official Journal L – 33, 08/02/2003, p. 10 – 49


Author(s): • N/A

Date: • 2004

Europe – Consolidated directive 2001/83/EC

<table>
<thead>
<tr>
<th>Summary:</th>
<th>Wholesale Distribution of Medicinal Products must comply with GDP established by the Commission:</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>• Principle</td>
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<td></td>
<td>• Personnel</td>
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<td></td>
<td>• Documentation</td>
</tr>
<tr>
<td></td>
<td>• Premises and equipment</td>
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<tr>
<td></td>
<td>• Deliveries to customers</td>
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<tr>
<td></td>
<td>• Self inspections</td>
</tr>
<tr>
<td></td>
<td>• Provision of Information to Member States in relation to wholesale activities</td>
</tr>
</tbody>
</table>

| Of Note: | “The level of quality [of medicinal products] should be maintained throughout the distribution network”. |
|          | “A tracing system should enable any faulty product to be found” |
|          | “There should be an effective recall procedures”. |

"The level of quality [of medicinal products] should be maintained throughout the distribution network".

"A tracing system should enable any faulty product to be found"

"There should be an effective recall procedures".
European Medicines Agency (EMA)
“The QP declaration template”

Author(s): European Medicines Agency
Date: December 2010

Template for the Qualified Person’s declaration concerning GMP compliance of the active substance used as starting material and verification of its supply chain “The QP declaration template”

Draft

| Adoption by CHMP for release for consultation | 5 December 2010 |
| Adoption by CHMP for release for consultation | 16 December 2010 |
| End of consultation (deadline for comments) | 30 April 2011 |

Comments should be provided using the template. The completed comments form should be sent to QPQ@ema.europa.eu

Keywords: Qualified Person; Active Substance; Starting Material; good Manufacturing Practice; Supply Chain
### Summary:

- “The active substance supply chain of each of the active substance manufacturing sites listed in Part A has been established and documented”
- There exists a documented risk assessment for all sites in the supply chain of the active substance
- Documents are available for inspection

### Of Note:

- QP vs
- RP
Chapter 17 Air Transport Logistics for Temperature-Sensitive Healthcare Products

17.1 Overview

Over the past decade, the growth of healthcare manufacturing has largely gone from *intra-plant* to *international*. The pharmaceutical industry is experiencing unparalleled change and challenge... globalization, treatment and pricing economics, government controls and ever-advancing technology. It is not uncommon for a drug to go from active pharmaceutical ingredient to finished product in multiple steps, through multiple countries. As a result, the requirements for packaging, storing, transporting and distributing them have, like the drugs and treatments themselves, become more sophisticated and the ability to maintain precise temperature control, more critical. Transport of healthcare products may include bulk reagents, intermediates or finished product. The packages can range in size from small, single boxes to pallet sized bulk insulated containers. The products contained are used for the treatment, diagnosis and prevention of disease. They may be liquid, solid, and semi-solid or powder. They range from prescription drugs such as pills and capsules, to injectibles such as insulin and vaccines, to diagnostic reagents, medical devices, blood products, organs and tissues.

Market growth combined with new technologies, such as heat labile biologicals, have proliferated. Worldwide biologics products continued their faster-than-average growth, rising by 17.1% to $52.7 billion. That sector has been growing at double-digit rates for several years and is projected to continue for the foreseeable future as new biotech products enter the marketplace. Along with the increase and availability of new drugs, devices, and treatments, there has been a significant increase in global regulatory oversight. New pharmacopeial standards for medicinal products are introduced on a frequent and regular basis and are in many cases broadened to include proper handling,
### Summary:

- Purpose of this chapter is to provide information on the factors that affect temperature-sensitive healthcare products and to indicate critical control points in the air transport logistics that can impact these sensitive products and to provide best practices conforming to regulatory agencies requirements.
  - Factors affecting temperature-sensitive of healthcare products
  - Standard techniques applicable to the commercial handling of most environmentally-sensitive healthcare products by air…
  - Temperature control during transportation and storage
  - GMP’s & GSP’s
  - Cold chain management
  - Active and passive packaging system

### Of Note:

- Quality Management Systems requirements (including exception management)
- Processes and responsibilities of all parties, including the shipper, forwarder, ground handlers/transportation service provider, consignee and air carrier
- Storage and warehousing requirements (including temperature mapping)
- Introduction of new time & temperature sensitive handling label usage requirements
FDA to Revise Component GMP’s to Bolster Supply Chain Security

The FDA is revising GMP regulations for incoming raw materials that would significantly improve drugmakers’ control over suppliers and help secure the pharmaceutical supply chain against economically motivated adulteration.

While there is no concrete timeline for the revisions, they are now under way, Deb Batur, director of CDER’s Office of Compliance, told OGR last month at the 2010 FDA/AMP Pharmaceutical Supply Chain Workshop in Bethesda, Md.

Controlling the risk of counterfeit, adulterated or misbranded products entering the supply chain “really comes down to each company thinking very hard about what its potential vulnerabilities are and building systems around that,” Batur told the audience. The FDA would like to see industry be more proactive in predicting potential economically motivated adulterants and designing test methods and supply chain controls.

The FDA is finding that companies are falling to adequately control raw materials — particularly physical characteristics such as particle size and homogeneity — which contribute to the difficulty of reliably producing a dosage form that performs consistently from batch to batch, CDER Director Janet Woodcock said.

The agency is encouraging manufacturers to warn each other about suppliers and materials that pose hazards. Companies also should notify the FDA as soon as a problem is identified that could pose a health risk.

“People’s instinct is just to drop the supplier and not talk about it,” Woodcock said. “Failing to act could damage the industry’s credibility,” she added.

Some companies already are working toward collaboration on supply chain control. For instance, Johnson & Johnson unit Janssen-Cilag is encouraging other companies to mimic its Drug Validation Portal, which provides EU Customs with electronic images of its product labels and packaging for comparison with incoming shipments, Martin van Tets, vice president of operations and quality for Janssen, said.

Similar images can be used by a drug company’s own employees to help screen incoming raw materials from suppliers, he added.

Limited foreign supplier audits also have become a concern, Edwin Rivera-Martinez, chief of the FDA’s International Compliance Branch, said. Sometimes a company officials, rather than a trained auditor, is sent to the manufacturing site. That can be a problem because auditors must be familiar with the manufacturing processes for ingredients, he said. Even products that meet U.S. Pharmacopeia testing standards may not have been manufactured under GMPs.

Among the solutions suggested by conference participants was auditing suppliers’ control of the chain of ingredients as part of the qualification procedure. Industry also noted more effort is needed to train procurement employees to incorporate quality standards in searches for suppliers.

The FDA also is acting to produce guidelines to promote safe supply chains. A forthcoming final version of the July 2009 draft guidance on physical-chemical identifiers in solid and dosage form drug products is one such guidance, Lisa Berron, director of a pharmacy affairs office in the Office of the Commissioner, Office of Policy, said (OGR, Aug. 2009). — April Hollis
### Summary:

- "FDA is revising GMP regulations for incoming raw materials that would significantly improve drugmakers’ control over suppliers and help secure the pharmaceutical supply chain against economically motivated adulterations."

- Objective of the FDA: to control the risk of counterfeit, adulterated or misbranded products entering the supply chain.

- Industry should be more proactive in predicting potential economically motivated adulterants and designing test methods and supply chain controls.

- FDA encourages Manufacturers to warn each other about suppliers and materials that pose hazards. Plus they should notify FDA as soon as a problem is identified that could pose a health risk.

- FDA noticed limited foreign supplier audits have become a concern.

- Possible solution is to audit suppliers’ control of the chain of ingredients as part of the qualification procedure.

- Other solution is to add more effort to train procurement employees to incorporate quality standards in searches for suppliers.

### Of Note:

- FDA to produce guidelines to promote safe supply chains (final version of the July 2009 draft guidance on physical-chemical identifiers in solid oral dosage form of drug products). **Did not get issued**
USP_Chapter_1118- Monitoring device- Time, Temperature and Humidity

The device described in this section are those most commonly used to monitor temperature in the storage and distribution of drugs in North America. The measurement of temperature at extremes, such as close to absolute zero or above those reasonably expected to be experienced by drugs, is not addressed.

Alcohol or Mercury Thermometers— These devices are based on the change in volume of a liquid as a function of temperature. Mercury thermometers are typically used in the ranges from 0°C to 50°C with a precision of about 0.1°C. Some local regulations apply to mercury-based thermometers. Alcohol thermometers may have a precision as good as 0.01°C, but they must be quite large to measure temperatures in ranges of more than a few degrees. Both types of thermometers may be designed to indicate the maximum and minimum temperatures measured. See Thermometers (11) for further information.

Chemical Devices— This is a device based on a phase change or chemical reaction that occurs as a function of temperature. Examples include liquid crystals, waxes, and lacquers that change phase, and thereby their appearance, as a function of temperature. Such materials represent the least expensive form of temperature measurement, but they may be difficult to interpret.

Other types of chemical sensors include systems in which a reaction rate or diffusion process is used to deduce a temperature equivalent integrated over time rather than the temperature at a specific moment in time such as a spike or critical threshold, for which a separate device may be preferred. Thus, chemical sensors provide a measure of accumulated heat rather than instantaneous temperature. It should be noted that these devices are generally irreversible; once a color change or diffusion process has taken place, exposure to low temperatures will not restore the device to its original state. Accuracy and precision vary widely among different types, to differentiate often limited by their ability or their ability to visually interpret diffusion distances.

Infrared Device— This is a device based on measuring the IR radiation from the article whose temperature is being measured.
## USP_Chapter_1118- Monitoring device- Time, Temperature and Humidity

### Summary:
- Background on science and technology of temperature and humidity monitoring.
- Describes the available technologies and their performance characteristics + provides recommendations for verification and validation of performance.

| Of Note: | • Temperature measurement technologies: Alcohol or Mercury Thermometers, chemical device, thermistor …
|          | • Time-Temperature integrators (TTI’s): Chemical-Physical based, Diffusion based, Enzyme based …
|          | • Electronic Time-Temperature History recorders: data loggers
|          | • Relative Humidity measurement technologies: sling psychrometer, hair hygrometer…
|          | • Validation of Temperature and Humidity monitoring devices: measurement accuracy, time accuracy…
|          | • How many electronic monitors / pallet / shipment
|          | • Are indicators OK |
Saudi Food & Drug Authority

| Author(s): | • Prof. Dr. Saleh. Bawazeer (Vice President for Drug Affairs). |
| Date: | • 09/02/1431H |
| Web Link: | N/A |
Saudi Food & Drug Authority

<table>
<thead>
<tr>
<th>Summary:</th>
<th>• Pharmaceutical products imported in Saudi must be transported in cooled containers and stored accordingly in order to be accepted.</th>
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<tbody>
<tr>
<td></td>
<td>1. March 1st, 2011 all 2-8C products have to have temperature monitoring for import compliance.</td>
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<td></td>
<td>2. By June 1st, 2011 all CRT products have to have temperature monitoring for import compliance</td>
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</tbody>
</table>

| Of Note: | “No shipment of pharmaceutical products imported to the Kingdom will be cleared if it was proved that they were transported in non-cooled containers or stored in such a way contrary to the conditions recommended”. |
Taiwan - Precaution of on-site sampling for vaccine testing and sealing operation [DRAFT]

Precaution of on-site sampling for vaccine testing and sealing operation [DRAFT],
TFDA and companies meeting on 29 Apr 2010

1. This Precaution is announced according to Taiwan DOH’s 2004.05.17DOH Drug No.0930316850 announcement “Operation method of Biol 2005. Dec. announcement “Guidelines on the international packaging and shipping of Vaccines, WHO/IV/05.23”

2. Temperature range of Cold Chain for shipping vaccines should be consistent with labeled storage condition of the package. If carton/pallet by condition of ambient should comply with vaccine’s shipping condition except manufacturer has other instructions.

3. Results of electronic temperature device are major reference for judgment to monitor temperature of cold chain when shipping vaccines. Each is equipped with electronic temperature device. The location and quantity of electronic temperature device should be decided by validation results and its guideline.

4. Except electronic temperature device, if company still insert cold chain monitor card (CCM) and freeze indicator and any one of device functionally recognized as temperature excursion.

5. Unless FDA has agreement to open external package for facilitating move vaccines to cold room. Neither shipping carton/pallet can be open before on-site sampling.

6. The carton/pallet will not be sampling but will be sealed under following condition: if frozen vaccines melt, CCM’s color exceeds WHO guideline beyond the range of labeled storage condition.

7. Once above excursions take place, applying company can guarantee:
   (1) TFDA will only progress sampling for those carton/pallet with passed result of shipping temperature, passed monitoring device, and approved past certificate for those sampled quantity after three vaccines are tested and passed specifications. The rest of vaccines out of above rules, companies on stability data and QA’s evaluation report of the event to TFDA. After evaluation, if the deviation does not impact quality and safety, companies can proceed with above rules.

   (2) TFDA will not progress sampling and seal all vaccines until manufacturer to submit related validation report, shipping SOP, stability data and QA’s evaluation, if the deviation does not impact quality and safety, TFDA will re-use the site for sampling. If companies cannot submit supporting documents, companies voluntarily withdraw the cases.

8. By the deadline of 31 Dec 2010, electronic temperature monitor device should be introduced for cold chain temperature monitoring. After 31.1 those are other device for temperature monitoring.

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Taiwan - Precaution of on-site sampling for vaccine testing and sealing operation [DRAFT]

| Summary: | • Electronic temperature monitor device should be introduced for cold chain temperature monitoring by the deadline of 31 Dec 2010.  
|          | • Standard GDPs |
| Of Note: | “By the deadline of 31 Dec 2010, electronic temperature monitor device should be introduced for cold chain temperature monitoring. After 31 Dec 2010, TFDA will not process sampling for those use other device for temperature monitoring”.

**Summary:**

<table>
<thead>
<tr>
<th>NMA No. 30/24.09.2009 was updated with the following changes:</th>
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<tbody>
<tr>
<td>- a certificate of conformity is no longer requested to be attached to each shipment of medicines.</td>
</tr>
<tr>
<td>- records for temperature and relative humidity measurements during transport should be provided, if applicable, in the conditions imposed by the manufacturer.</td>
</tr>
<tr>
<td>- the copies of the Marketing Authorizations provided to the distributors should be accompanied by the approval letters for variations.</td>
</tr>
<tr>
<td>- distributors should maintain the records for temperature and relative humidity measurements, if applicable, during the transport of medicines from the supplier, so that, when receiving the goods, the conformity of the results of measurements could be verified against the requirements stated in the Marketing Authorization and against the additional information regarding the transport conditions provided by the manufacturer.</td>
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</tbody>
</table>

**Of Note:**

- Changes were made to Romanian NMA Instruction No. 30/24.09.2009 in December 2009 regarding temperature and humidity monitoring during transportation.

**Author(s):**

- N/A

**Date:**

- Dec 2009

**Web Link:**

- N/A
Singapore - Health Sciences Authority Guidance notes on GDP

<table>
<thead>
<tr>
<th>Author(s):</th>
<th>N/A - Health Sciences Authority</th>
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<tbody>
<tr>
<td>Date:</td>
<td>August 2010</td>
</tr>
</tbody>
</table>
### Summary:
- Receiving and incoming checks
- Labels/means to identify cold chain products
- Temperature mapping
- Thermometer and records
- Maintenance program
- Alarm system for temperature excursion
- Backup generator/plan
- Packing procedure and records, and independent check
- Temperature mapping for vehicles or qualified/validated containers
- Monitoring of storage conditions during transportation or simulation study
- Delivery procedure
- Procedure to handle temperature excursion
- Procedure for handling returned products
- Contracts
- Training program and records

### Of Note:
Quick easy read (like IMB)
Czech GDP Guidelines: Monitoring and temperature control during storage and transport of medicinal products (DIS-15 V.1)

Author(s): N/A–Czech GDP guidelines

Date: 2009

Czech GDP Guidelines: Monitoring and temperature control during storage and transport of medicinal products (DIS-15 V.1)

<table>
<thead>
<tr>
<th>Summary:</th>
<th>• Standard GDP to ensure, control and document temperature during storage and transport of medicinal products.</th>
</tr>
</thead>
</table>
| Of Note: | • Temperature map using measuring devices - required for storage.  
• Temperature during transport must be monitored with a measuring devices.  
• Measuring devices must be equipped with an alarm and calibrated (time between 2 subsequent calibrations should not be longer than 24 months).  
• Measuring device error should also be determined during calibration.  
• The used thermometers should not have a greater error than ± 0.5 °C for the monitoring of storage temperature for thermolabile medicinal products.  
• Used thermometers should not indicate greater error than ± 1.0°C for the monitoring of the temperature conditions other than those in the freezing and cooling appliances.  
• Thermolabile medicinal products are transported in cooling vehicles or in cooled transport containers, they are stored in order to avoid freezing (with the exception of medicinal products, which should be transported under freezing temperatures). |
Czech GDP Guidelines: Guidelines for correct distribution practice of human medicinal products (DIS-11)

Author(s): Unknown – Czeck GDP guidelines

Date: 2009

Summary:

- Distributors must observe the rules and guidelines of good distribution practice published by the European Commission
- Standard GDP’s for Storage, Transportation and distribution.
- Medicinal products should be commonly stored separated from other marketable goods
- Temperature is monitored and regularly recorded
- Control should ensure that all parts of particular storage areas keep the temperature within the established temperature range
- System of stock circulation introduced (i.e. “first in - first out”).
- Products should be delivered only to other authorised distributors

Of Note:

This guideline is a translation of the European commission- EU Guidelines on Good Distribution Practice of medicinal products of Human use.
India’s Pharma Mfg’ers Guidelines (not the Gov’t’s)

Organisation of Pharmaceutical Producers of India

OPPI GUIDELINES
- COLD CHAIN PHARMACEUTICAL PRODUCTS

Author(s):
The preparation of these guidelines has been made possible due to the efforts of the Materials Management Committee, spearheaded by its following members:
- Mr. Ashok Bindumadhavan, Eli Lilly (Project Leader)
- Mr. Sikander Yarkhan, Chiron Panacea
- Mr. Uday Shanker Kumar, GlaxoSmithKline Pharmaceutical
- Mr. Rekesh Phadke, Ranbaxy
- Mr. Anil Manjeshwar, Roche
- Mr. Avinash Baskar, Sanofi-Aventis
- Mr. Krishna Prabhu, Sanofi-Aventis
- Mr. Vishwanath Iyer, Wyeth

Date: • June 2010

Web Link: http://www.indiaoppi.com/pubcoldchainproducts.asp
However – endorsed by the Gov’t

FOREWORD

The increasing number of Cold Chain Pharmaceuticals is getting importance in the Indian Pharmaceutical market. In its journey across the supply chain right from the manufacturers to the patient, these medicines are handled and stored by various stakeholders i.e. transporters, Airports, Sea ports, Distributors, Stockists, Retailers, Doctors, pharmacists and Hospitals etc. The storage and handling of Cold Chain Pharmaceutical products are unique in nature and the same is required to be maintained in the entire distribution chain to ensure that the patients get the medicinal product without compromise to it’s quality.
India’s Pharma Mfg’ers Guidelines (not the Gov’t’s)

<table>
<thead>
<tr>
<th>Summary:</th>
<th>Standard GDP’s for Cold Chain Pharmaceutical Products:</th>
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<tr>
<td></td>
<td>• Storing and Handling (seaports/airports, Stockist/Distributors, Retailers/Chemists)</td>
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<tr>
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<td>• Custom Clearance and Sample testing</td>
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<td></td>
<td>• Transportation using refrigerated Vans</td>
</tr>
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| Of Note: | • Temperature loggers in cold rooms |
|          | • Practice FEFO (First Expired First Out) in storage facility. |
|          | • Temperature monitoring device with alarm |
Out of the MOH concern for Egyptian patients’ welfare

GSP = Good Storage Practices
GDP = Good Distribution Practices

Author(s):
- Dr. Madiha Ahmed
- Dr. Abd El-Rahman Maged

Date:
- January 2009

Web Link: [http://www.mohp.gov.eg/](http://www.mohp.gov.eg/)
Messrs.

Out of the MOH concern with attaining Egyptian patients' welfare, providing them with safe and effective drugs at affordable prices, combating adulterated and spoiled drugs. In addition to combating the phenomena of trading drugs of unknown source and expired drugs and non-application of Good Storage & Good Distribution Practices (GSP & GDP) for different drugs and pharmaceutical products, as published on the electronic site of the Central Administration of Pharmaceutical Affairs (WWW.eda.mohp.gov.eg), especially the practices of keeping, storing and transporting the same, along with ensuring the compliance of those working in manufacturing, importing, storing and distributing drugs with the abovementioned practices.
### Summary:

- Rules issued by the MOH and Population (resolution No. 25/2009)
- Standard GDP’s:
  - Temperature monitoring during cold storage
  - Temperature mapping of warehouses

### Of Note:

- Insulated containers may be used for small volumes
- Refrigerated transport for larger volumes
- Temperature must be monitored and recorded
### NATIONAL COORDINATING COMMITTEE ON THERAPEUTIC GOODS

**Australian CODE OF GOOD WHOLESALING PRACTICE FOR THERAPEUTIC GOODS FOR HUMAN USE**

**Draft Revision – June 2006**

This Code supersedes the November 1991 edition of the Australian Code of Good Wholesaling Practice for Therapeutic Goods for Human Use. The provisions of this Code are applied through applicable State and Territory therapeutic goods / drugs and poisons legislation, and/or State or Territory wholesaler licensing arrangements.

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<th>Author(s):</th>
<th>• N/A</th>
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<td>Date:</td>
<td>• June 2006</td>
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**Summary:**

- Standard GDP’s
- Wholesalers are responsible to ensure medicine is stored and distributed within the label requirements of the manufacturer and in accordance with this code. Includes the distribution of temperature sensitive medicines via the cold chain.
- Temperature sensitive therapeutic products (TSTPS)
- Transport
- Management of controlled goods, returned goods, product recalls, documentation.

**Of Note:**

- For TSTPS: temperature monitoring equipment and record
- Goods with a manufacturer-specified temperature range should not be stored in a temporary stock location that could expose them to temperatures outside the specified range.
- Goods requiring temperature maintenance in the range of +2°C to +8°C should be labeled refrigerate – do not freeze. Goods requiring temperature maintenance in the range below 0°C should be labeled keep frozen.
ASEAN GMP GUIDELINES POINT 3 “PREMISES” describes requirements for warehouse facility:

3.15. All premises, including production areas, laboratories, stores, passage ways and external surroundings should be maintained in a clean and tidy condition. The condition of buildings should be reviewed regularly, and repaired where necessary. Special care should be exercised to ensure that building repair or maintenance operations do not adversely affect products.

3.16. Storage areas should be of adequate space, provided with suitable lighting, arranged and equipped to allow dry, clean and orderly placement of stored materials and products.

3.16.1. Such areas should be suitable for effective separation of quarantined materials and products. Special and segregated areas should be available for storage of flammable and explosive substances, highly toxic substances, narcotics and other dangerous drugs and rejected materials and products.

3.16.2. Where special storage conditions e.g. temperature, humidity, and security are required, these should be provided, checked and monitored.

3.16.3. Storage areas should be laid-out to permit effective and orderly segregation of the various categories of materials stored, and to allow rotation of stock.

3.16.4. Segregated storage should be provided for rejected, recalled or returned goods.

3.16.5. Storage arrangements should permit separation of different labels, as well as other printed materials, to avoid mix-up.

### Summary:

- ASEAN GMP guidelines describe requirements for:
- Warehouse facility (temperature monitoring for special storage conditions)
- Handling of product recalls and returned drug products (report and record)
- Quality control
- Documentation (inventory card, record of distribution)

### Of Note:

- Indonesia – GMP Requirements on warehousing or distribution
3.2 Services: Electrical supply, lighting, temperature and humidity controls and ventilation shall be appropriate and such that they do not adversely effect, directly or indirectly the pharmaceutical products during their manufacture and storage, or the accurate functioning of equipment.

(viii) Where necessary, the requirements for storage of the products, including the container, the labeling, and any special storage conditions; and

(ix) Any special precautions to be observed.

(h) Satisfactory arrangements exist to store in appropriate storage conditions;

(e) Provision for special storage conditions;

(d) Storage of starting materials and finished products;

3.7.5 Distribution records: The distribution records shall be readily available to the person(s) responsible for recalls, and they shall contain sufficient information on wholesalers and directly supplied customers (including, for exported products, those who have received samples for clinical tests and medical samples) to permit and effective recall.

3.7.6 Recording of progress: The progress of the recall process shall be recorded and a final report issued, including reconciliation between the delivered and recovered quantities of the products.

3.7.7 Evaluation: The effectiveness of the arrangements for recalls shall be evaluated from time to time.

3.7.8 Storage of recalled drugs: An instruction shall be included to store recalled products in a secure segregated area while their fate is decided.

3.7.9 All concerned to be informed: The Central Licensing and Registration Boards and other concerned government authorities shall be immediately informed if it is intended to recall product(s) or if a product has been recalled. Effective system shall be maintained to inform the doctors, pharmacists and public of the recalled products.

4.1 Capacity: Storage area shall be properly defined of sufficient capacity to allow orderly storage of various categories of materials and products in quarantine, and released, rejected, returned, or recalled products.

4.2 Design: Storage area shall be designed or adapted to ensure good storage conditions. In particular, they shall be clean and dry, suitably lit and maintained within acceptable temperature limits, which should be commensurate with storage requirements of the drugs. Where special storage conditions are required (e.g., controlled temperature and humidity) these shall be provided, checked, and monitored.
Pakistan – Drug Act of 1976

<table>
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<tr>
<th>Summary:</th>
<th>Drug Act not updated since 1976</th>
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<tr>
<td></td>
<td>• Temperature</td>
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<td></td>
<td>• Distribution records</td>
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<td>• Recording of Progress for recall</td>
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<th>Of Note:</th>
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RESOLUTION - RDC No. 234, DATED 08/17/05
DOU (Government Official Newspaper) of 08/26/05

The Collegiate Management Board of “Agência Nacional de Vigilância Sanitária” (Health Control Agency) (ANVISA), within the powers granted to it by art. 11 subparagraph IV of ANVISA approved by the Executive Order no. 3029, of April 16, 1999, combined with art. 111, subparagraph I, clause "b", § 1 of the Bylaws approved by Ordinance no. 593, dated August 25, 2000, republished in DOU of December 22, 2000, at a meeting held August 9, 2005, in the light of provisions of Act no. 6360, dated September 23, 1976 in art 75 and Executive Order no. 79094, dated January 5, 1977, art 130, which regulates Act no. 6360/76;

Whereas the need for regulating the quality control activities relating to biological products in their primary packing and of finished biological products imported by the companies holding the registration has adopted the following Resolution of the Collegiate Management Board and I, the President Director, hereby determine its publication:

Art. 1 The importation of Biological Products in their primary packing and Finished Biological Product subject to the Health Control System may only be performed by a company holding the registration and legally authorized to import drugs by "Agência Nacional de Vigilância Sanitária".

Art. 2 The importing company is responsible for the quality, effectiveness and safety of imported lots of biological products in their primary packing as well as of finished biological products.
### Brazil- Resolution –RDC No. 234

| **Summary:** | • “Agência Nacional de Vigilância Sanitária” (HealthControl Agency) (ANVISA) adopted resolutions to regulate quality control activities for imports of biological products.  
  
  • Importing company must be registered  
  
  • Records of temperature during transport chain and storage and a Quality Assurance Unit must be provided to the importing company.  
  
  • Importing company must, upon clearance of the lots, present the “Custody and Liability Commitment” for the product clearance until they deliver to the General Management of Ports, Airports and Borders the imported lot Clearance Certificate issued by the importing company quality assurance division, as well as a copy of the temperature records with all information |

| **Of Note:** |  |
**Summary:**

Standard GDP’s:

- Warehouse and storage (temperature monitored)
- Transport of products (refrigerated vehicles/transportation containers should be mapped and monitored—if they are the primary means of environmental control).
- “Drug products must be transported in a manner that ensures the products will be maintained within an acceptable temperature range as defined in the approved labeling and supported by stability data. Temperature excursions outside of their respective labeled storage conditions, for brief periods, may be acceptable provided stability data and scientific/technical justification exist demonstrating that product quality is not affected.”

**Of Note:**

- Canadian GMP regulation (0069) was recently revised with the addition of section 4.1 to the requirements for return policy.
- The revised documentation state: “Documentation is available to support the rationale to place returned goods into inventory for further resale. Wholesalers should obtain guidance from importers/distributors to make an informed decision pertaining to the restock of the product.”
IRISH MEDICINES BOARD

GUIDE TO CONTROL AND MONITORING OF STORAGE AND TRANSPORTATION TEMPERATURE CONDITIONS FOR MEDICINAL PRODUCTS AND ACTIVE SUBSTANCES

Author(s): • N/A
Date: • March 2006
Web Link: http://www.imb.ie/search.aspx?q=guide%20to%20control%20and%20monitoring%20of%20storage%20and%20transportation&start=0&section=IMB
| **Summary:** | Standard GDP’s compliant to EU guidelines on GDP’s:  
• Storage (for temperature controlled products)  
• Transportation of cold chain products: (insulated container may be used for small volumes, refrigerated transport vehicles for larger volumes).  
• Temperature mapping and monitoring  
• Returns of Cold chain products (only if cold chain has not been compromised, batch number is known, and entire process is validated).  
• Controlled temperature storage/transportation (temperature mapping of warehouse, MKT) |
| **Of Note:** | • Discuss MKT |
To: Governors of Prefectural Governments,
   Designated Mayor,
   Designated Ward Head,

From: Director of Pharmaceutical and Food Safety Bureau,
       Ministry of Health, Labour and Welfare

The 'Law to Partially Revise the Pharmaceutical Affairs Law and the Blood Collection and Supply Service Control Law' (Law No.96, 2002) (hereinafter referred to as Revision Law) is shown in the MHLW Vice-minister Notification PFSB No. 0731011 from the director of the Pharmaceutical Food and Safety Bureau, MHLW, 31st July 2002. “Concerning the Law to Partially Revise the Pharmaceutical Affairs Law and the Blood Collection and Supply Service Control Law (Order Notification)” (hereinafter referred to as the Vice-minister notification) to Governors of Prefectural Governments.

Since then, the Cabinet Order to Determine the Enforcement Date of the Law to Partially Revise the Pharmaceutical Affairs Law and the Blood Collection and Supply Service Control Law (Cabinet Order No. 212, 2003)” and the “Cabinet Order Relating to Preparations for Related Cabinet Orders Associated with the Enforcement of the Law to Partially Revise the Pharmaceutical Affairs Law and the Blood Collection and Supply Service Control Law (Cabinet Order No. 213, 2003)” were both promulgated on 23rd April 2003.

Today the “Ministerial Ordinance to Partially Revise the Enforcement Regulations of the Pharmaceutical Affairs Law (MHLW Ministerial Ordinance No. 35, 2003)” was promulgated together with the "Partial Revision of Medicines Designated by the Minister of Health, Labour and Welfare as stipulated in Article 15 of Paragraph 3 Item 2b and 2e of the Enforcement Regulations of the Pharmaceutical Affairs Law (MHLW

N.B: This document is protected by international copyright permission to reproduce. It must be obtained in advance in writing from IRAC.
| Summary: | ‘Ministerial Ordinance to Partially Revise the Enforcement Regulations of the Pharmaceutical Affairs Law (MHLW Ministerial Ordinance No. 89, 2003)’ was promulgated together with the ‘Partial Revision of Medicines Designated by the Minister of Health, Labour and Welfare as stipulated in Article 15-4 Paragraph 2 Item 2b and e of the Enforcement Regulations of the Pharmaceutical Affairs Law (MHLW 2 Notification No. 205, 2003)’, and the ‘Complete Revision of Medical Devices Designated by the Minister of Health, Labour and Welfare as stipulated in Article 15-4 Paragraph 2 Item 2 of the Enforcement Regulations of the Pharmaceutical Affairs Law (MHLW Notification No. 206, 2003)’.

• Record and storage

• Handling of medicine with mandatory registration |

| Of Note: | Japan – Biological Pharma revision H15.5.15 |
### Summary:

- Assessment is based on the outcome of an inspection and the classification of any deficiencies found.
- Other factors such as a persistently poor inspection history or action by enforcement may also affect the assessment.

**Current full license holders**

- Inspection frequency will be a minimum of six months to a maximum of four years, dependant on inspection outcome and range of activities.
- Companies awaiting routine inspection will be entered into the risk assessment system following their next inspection.

**New applicants**

- Most full license holders will be re-inspected in a maximum of 15 months. At this point they are risk assessed and their inspection frequency determined.

### Of Note:

---

MHRA- UK- GDP Risk Assessment Strategy
Returns of non-defective refrigerated (2c – 8c) medicinal products.

The requirement for wholesalers to comply with the principles of GDP is stated in European Directive 92/25/EEC Article 10 and Rules and Guidance for Pharmaceutical Distributors 2007.

Guidance for the return of non-defective medicinal products are contained in the Rules and Guidance above, paragraphs 22 – 24, the key element being that:

“products that have left the care of the wholesaler, should only be returned to saleable stock if …… it is known that the goods have been stored and handled under proper conditions” (paragraph 23b) and,

“they have been examined and assessed by a person authorised to do so” (paragraph 23d).

The MHRA reaffirm that the term “proper conditions” can only be interpreted as being under full GDP control by licensed sites. This applies to all categories of medicines. Medicinal products held in retailers’ unlicensed storage and distribution sites are not considered to be within the licensed distribution network.

The MHRA will adopt a pragmatic approach to the return of non-defective refrigerated medicinal products for those products returned from a customer operating from a licensed WLD site.

In such circumstances, the return should be completed as expeditiously as possible. The most expedient and appropriate method of transportation must be used.

In every such instance, the Responsible Person or the authorised person receiving the return must be able to demonstrate evidence of “full knowledge” of the storage of the returned products throughout the period it has been with the customer, including transportation.

For those refrigerated medicinal products returned from unlicensed sites, the return should be completed within 24 hours including transport.

As above, the Responsible Person or the authorised person must be able to demonstrate evidence of “full knowledge” of the storage whilst at the unlicensed site, including transportation.

Steve Todd
Senior GDP Inspector
13th April 2010

Author(s): • Steve Todd

Date: • April 2010

UK – MHRA- Updated Policy on returns of non-defective refrigerated (2-8c) medicinal products

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</tr>
</tbody>
</table>
GDP RISK ASSESSMENT STRATEGY

Author(s): • Cheryl Blake

Date: • Jan 2008

Web Link: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON028448&RevisionSelectionMethod=Latest&noSaveAs=0&Rendition=WEB
UK – MHRA- Cold Chain Distribution

| Summary: | • Guidance on the regulatory requirements and points to consider when developing a distribution strategy (based on the MHRA guidance note 6)  
| | • Control of storage and transportation temperature  
| | • Standard GDP’s:  
| | - Storage and shipping temperature (controlled, compliance, temperature monitoring, temperature mapping, alarms, calibration etc.)  
| | - Risk assessment  
| | - Quality management system |

| Of Note: | Distributors should have in place:  
| | • A comprehensive quality system  
| | • A process for continual quality improvement  
| | • A cold chain distribution strategy  
| | • An ambient and cold chain distribution strategy  
| | • A risk assessment program |
Refrigerated medicinal products: what pharmacists need to know.

Patients and other healthcare professionals are entitled to expect that medicines sold or supplied from a pharmacy are fit for their intended purpose. In this article, Steve Todd looks at preventing breaches in the cold chain.

Steve Todd is a Good Distribution Practice (GDP) Medicines Inspector at the Medicines and Healthcare products Regulatory Agency.

This article draws on some of the findings from inspections performed by the Medicines and Healthcare products Regulatory Agency’s good distribution practice (GDP) inspectorate and focuses on the many issues relating to the storage and distribution of medicinal products that need to be maintained between 2 and 8°C.

To ensure that medicines distributed to retail pharmacies and other persons entitled to sell products to the general public are of the appropriate quality, they must be manufactured in licensed facilities that comply with the principles and guidelines of good manufacturing practice (GMP). They must also be distributed through a network of licensed pharmaceutical wholesalers, who in turn, must comply with GDP. The requirement for wholesalers to comply with the principles of GDP is stated in European Directive 92/25/EEC, which also provides that member states will perform inspections of their premises.

Distribution.
Following manufacture, some medicinal products need to be stored and shipped at lower than ambient temperatures to assure their quality and efficacy. These are often referred to as “cold chain products” or “fridge lines” and wholesale dealers are expected to store and distribute them in strict accordance with the product labelling requirements. (They cannot rely on stability data in the event of temperature deviations).
Summary:

- Medicine be distributed through a network of licensed pharmaceutical wholesalers, who in turn, must comply with GDP.
- The requirement for wholesalers to comply with the principles of GDP is stated in European Directive 92/25/EEC, which also provides that member states will perform inspections of their premises.
- Standard GDP’s: distribution, cold chain returns, transportation, storage, best practices, temperature monitoring.

Of Note:

- “If a cold chain product is to be returned to the wholesaler, this must occur within 24 hours of the original dispatch. After this time, the returned product cannot be considered for resale and must be sent for disposal.”
The Status of Current Good Distribution Practice (GDP) Regulations in Israel

Rachel Karpel, PhD, PCI Pharmaceutical Consulting, Israel

Current Israeli legislation in the area of storage and distribution of medicinal products has typically been legislated in a somewhat piecemeal manner. Over the years, Good Distribution Practice regulations have been addressed both directly and indirectly in various contexts. Moving forward, however, big changes are anticipated with the completion of the formal GDP legislation in Israel at the end of 2010. The changes to the legislation are very much in line with current thinking in the EU and US regarding ensuring the supply chain. While GMPs were legislated many years back and are under constant revision, GDP has been something of a postrule and there seems to be a consensus that updating is needed.

This article will first review the legislation and regulations in Israel, proposed changes in conformance with the World-Health-Organization GDP requirements, and current practices of wholesalers.

In the Pharmacist Ordinance of 1981 there is a requirement for wholesalers to have a "responsible pharmacist" on-site—an advanced requirement even when compared to the current European legislation. Missing from the Ordinance, however, is the description of the duties and expectations of the responsible pharmacist, with respect to Good Distribution Practices. It was assumed that the responsible pharmacist, based on professional knowledge, responsibility, and ethical and legal obligations, would ensure the maintenance of appropriate conditions of shipping and storage, in accordance with the professional standards current at that period.

The first mention of Good Distribution practice in Israeli law appears in the 1999 legislation for parallel import of medicinal products. The law specifies that a medicinal product imported via the parallel import route must be shipped and stored in appropriate conditions. As with earlier legislation, however, this law fails to specify what constitutes "appropriate conditions," other than the requirement for imported product to be stored and shipped by licensed wholesalers from "recognized countries." ("Recognized countries" are those countries that are unilaterally recognized by Israel as having appropriate pharmaceutical regulations and enforcement standards including the United States, all EU member states, Canada, Switzerland, Norway, Iceland, Australia, New Zealand, and Japan.)

In 2008, the "Pharmacist Regulations" (Good Manufacturing Practice for Medicinal Products) were revised in order to achieve harmonization with the European legislation in anticipation of, and as a prerequisite to, signing a trade accord (ACOA—see below) with the European Union. The revised regulations adopted the European GMP (Bd ammonia volume I) as the regulatory standard in Israel, including the requirement for a qualified person (QP) for batch release and direct licensing of medicinal product manufacturers and importers by the Ministry of Health.

The GDP regulations originally included a clause requiring wholesalers to comply with the GDP rules as set out in the European Directive 2001/83/EC, as well as a requirement for direct licensing by the Ministry of Health based on periodic inspections. The regulations primarily designed to address GMPs were somewhat vague regarding GDP. The Ministry of Health therefore decided to issue separate and specific regulations in the area of GDP. Following this decision, in the amendments introduced to the 2008 Pharmacist Regulations—(Good Manufacturing Practice for Medicinal Products), all mention of "Good Distribution Practice" was omitted.
Summary:
• Article review the legislation and regulation in Israel, proposed changes in conformance with the WHO GDP requirements, and current practices of wholesalers.
  • Pharmacist Ordinance of 1981 (requirement for wholesalers to have a “responsible pharmacist” on site”).
  • “Pharmacist Regulations” revised in 2008 to achieve harmonization with European legislation (adopted European GMP and requirement for a QP for batch release and direct licensing).
  • New GDP will include Safeguards to address counterfeiting issues.
  • New GDP will allow better standardization in regards to the supervision of wholesalers.

Of Note:
• Big changes are anticipated with the completion of the formal GDP legislation in Israel at the end of 2010 (adopting WHO guidelines).
Malaysia – NPCB and MOH – Guidelines on Good Distribution Practice (GDP)

Author(s): • National Pharmaceutical Control Bureau (NPCB) Ministry of Health (MOH) Malaysia

Date: • January 2011

Web Link: http://portal.bpfk.gov.my/
Summary:

• Used as a standard to justify status and as a basis for inspection of facilities (e.g. manufacturers, importers, wholesalers…). Procedures include the management of personnel, premises, facilities and adequate documentary procedures to preserve safety and quality of product.

• Appropriate storage conditions should be provided and justified by supportive stability data based on labeling statements. Storage time at a higher temperature is acceptable if justified and supported by suitable data generated under the proposed conditions. Special storage directions (e.g. shipping and transportation need to be requested from the manufacturer or supplier.

• It is recommended that temperature monitors be located in areas that are most likely to show fluctuations

• Quarantine status can be achieved either through the use of separate storage areas or by means of documentary or electronic data processing systems

Of Note:

Malaysia – NPCB – Guidelines on Good Distribution Practice (GDP)
United Arab Emirates
Ministry of Health

Circular No 246/ 2011

Attn: All Importers of Pharmaceuticals/ Medical Equipments and Devices, Chemicals
All Responsible Pharmacists of Stores.

Greetings to you all;

Considering the interest of public welfare and in line with the circulars issued regarding the
importation and storage of Medicines, Pharmaceuticals, Chemicals and Medical Equipments,
you are requested to follow the below instructions:

- In order to protect and ensure proper care for above mentioned substances and to keep
its effectiveness intact, the shipment of medicines and above mentioned materials
should be in temperature controlled and monitored containers (refrigerated containers) from
the countries of origin up to the ports of U.A.E.
- The containers should be temperature monitored and controlled during the shipment till
U.A.E ports.
- The shipment of non medicinal materials such as raw materials used in medicine
production/medical devices should be in containers with temperature <25°C throughout
the shipment (Control room temperature).
- The above mentioned rules are to be followed during the storage and movement of
the materials through the country after arrival.
- The shipments that do not comply with the above mentioned rules will not be released at
the ports and will be returned to the country of origin and no excuses are accepted.
- The product should have at least 2/3 remaining shelf life.

For the protection of the medicinal and chemical products, all are requested to follow the above
recommendations.

With Regards
Dr.Amin Husain Al Amiri.
Undersecretary for Medical Practice and License.

Issued on: 19/01/2011.

Author(s): • United Arab Emirates Ministry of Health
• Attn: Dr. Amin Husain Al Amir

Date: • Jan 2011

Web Link: N/A
### Summary:
- The containers should be temperature monitored and controlled during the shipment till U.A.E ports.
- The shipment of non medicinal materials such as raw materials used in medicine production/medical devices should be in containers with temperature <25 degrees Celsius throughout the shipment (control room temperature).
- Product must be stored and shipped from the original country to U.A.E within the specified temperature requirements on the label.

### Of Note:
LEY DE REGULACIÓN DE LA CADENA DE FRÍO DE LOS MEDICAMENTOS

ARTÍCULO 1°.- En un plazo de dos (2) años a partir de la vigencia de la presente ley, todos los medicamentos de uso humano o veterinario, conteniendo principios activos termolábiles, deberán tener incorporado un testigo de temperatura en el envase individual, de carácter indeleble, insalvable e irreversible, que permita verificar que dicho producto no ha perdido la cadena de frío al momento de llegar al consumidor.

ARTÍCULO 2°.- El testigo será incorporado por la fábrica y deberá permanecer en el medicamento hasta la unidad de consumo individual.

ARTÍCULO 3°.- Para las presentaciones multidosis, el testigo deberá permanecer en el envase, de manera que el consumidor pueda verificar que en el producto en su poder no se interrumpió la cadena de frío, desnaturalizando e inactivando las propiedades originales del medicamento.

ARTÍCULO 4°.- La autoridad de aplicación promoverá en forma directa y/o a través de los actores en la cadena de frío, el mayor conocimiento
### Summary:

- Signed off by the President
- Not enforceable as a law, yet
- Requiring manufacturers to indicate on all biopharma temperature through shelf-life, to the patient

### Of Note:
Guidance for Industry
Standards for Securing the Drug Supply Chain - Standardized Numerical Identification for Prescription Drug Packages

FINAL GUIDANCE

U.S. Department of Health and Human Services: Food and Drug Administration
Office of the Commissioner (OC)
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Office of Regulatory Affairs (ORA)
March 2010

Author(s): • N/A
Date: • Mar 2010
Web Link: http://www.fda.gov/RegulatoryInformation/Guidances/ucm125505.htm

Example of a serialized National Drug Code (SNDC)

NDC 55655 888 77 + 1111111111111111
labeled code + product code + package code
unique, up to 20 characters
## FDA – Standardized Numerical Identifier

| Summary: | • FDAAA Section 913 created Section 505D of the Federal Food Drug & Cosmetic act (Approved by Congress 2009)  
  - To develop an SNI to be applied to a prescription drug at the point of manufacturing at the unit for interstate commerce package level  
  - To be sufficient to facilitate identification, authentication and tracking and tracing of prescription drugs  
  • This is the initial step by FDA to secure the drug supply chain  
  • Repackagers are to link each new package back to the original manufacturer’s SNI  
  • SNIs do not apply to case and pallet level identification  
  • SNI should be a serialized National Drug Code (sNDC) = NDC + serial number  
  • Can append the expiration date and lot number to sNDC using GS1 standards  
  • FDA believes the SNI should be applied in human and machine readable formats  
  • For international standards the sNDC can be represented as a serialized Global Trade Item Number (GTIN) |
| Of Note: | • Enforceable for food already |
In Conclusion - The Transformational Trends for the Pharma Supply Chain are Here

1. From GMP to GDPs
   - Quality systems expanded from mfg’ing into both 1) the Pharma Mfg’ing supply chain (including Clinicals) and the Commercial Dist supply chain
   - Stand alone GDPs are “new” (used to be a subset of GMPs)
2. GxPs specific to pharma (and device) supply chain
   - World wide >35 GDPs (WHO and FDA/EU)
   - All are similar – I showed you some of the specifics
3. Initial Focus was “cold chain”, now expanded to GS1, anticounterfeit and diversion, “normal channel/trade (licensed trade partner), quality agreements and data sharing (to include LSP and TSP)
4. Pedigree (ePedigree) and serialization
   - Turkey, S. Korea, Argentina, etc
5. Increased regulatory focus – standard audit items
   - ANVISA, KFDA, Turkey, Mexico, MHRA, etc
Specifically

• GS1 standards – worldwide
• Pedigree (and ePedigree)
  – Track and Trace (TnT)
• Sharing of Data (license, quality agreement, stability, etc)
• Anti-counterfeit and diversion
• More info 1D → 2D Matrix & QR barcodes → RFID
• Interlinked IT systems (authenticate product flow and its information)
  – Returns/restocks, quarantine, TOT, joint anti-diversion / anticounterfeit procedures and agreements

• Holistic Quality Systems for the supply chain
Questions or Comments??