Review Article
AMERICAN JOURNAL OF PHARMACY AND HEALTH RESEARCH
www.ajphr.com
2016, Volume 4, Issue 1
ISSN: 2321–3647(online)

Pharmaceutical "Good Transportation Practices (GTP)"- An Innovative Concept In 'GXP' Acronym

Nirmal Kumar*[1], **Ajeya Jha**[1]
1.Sikkim Manipal Institute of Technology, Majitar, Rangpo, Sikkim -737132, India

ABSTRACT

There are several approaches of quality system, which adequately take care of pharmaceutical manufacturing and distribution operations. In addition to conventional perspectives there is a need of specialized quality system during transportation and shipment of pharmaceutical products. An exploratory study on transportation quality system shows that as such there is no system with nomenclature 'Good Transportation Practices'. The quality system during transportation is apparently a forbidden concept, although other pharmaceutical quality systems based on GXP nomenclature are available, such as Good Manufacturing Practices (GMP), Good Distribution Practices (GDP), Good Laboratory Practices (GLP), Good Documentation Practices (GDP) etc. Pharmaceutical Good Transportation Practices (GTP) is a novel approach to summarize the elements of quality systems during transit and shipment. The new GTP philosophy is based on core quality system elements like training, documentation, validations, qualification etc. This study on Good Transportation Practices proposes a new concept in pharmaceutical industry, which shall act in alliance with manufacturing and distribution operations to further strengthen the pharmaceutical quality system.

Keywords: GXP, GDP, Pharmaceutical Transportation, Temperature Excursions

*Corresponding Author Email: nirmal.quality@gmail.com
Received 11 December 2015, Accepted 18 January 2016

Please cite this article as: Nirmal *et al.*, Pharmaceutical "Good Transportation Practices (GTP)"- An Innovative Concept In 'GXP' Acronym. American Journal of Pharmacy & Health Research 2016.

INTRODUCTION

In pharmaceutical industry, the good practices are framed under acronym 'GXP'[1]. For example GMP stands for Good Manufacturing Practices, GDP for Good Distribution Practices, GLP for Good Laboratory Practices, GCP for Good Clinical Practices, GEP for Good Engineering Practices (GEP) etc

The logistics and transportation business is growing by leaps and bound.[6] Eventually the quality system for transportation and logistics arrangements have been not conceptualized in a systematic way similar as manufacturing operations. Good Manufacturing Practices (GMP) gives a fare guidance for managing quality operations during production process. In absence of the framed approach of "Good Transportation Practices" for shipment and transference of pharmaceutical products in India there several quality issues are observed, which are contradicting the fundamental prerequisite of medicine business. The transportation and shipment are important aspect of pharmaceutical entrepreneurship, but there is hardly a systematic quality approach which governs and monitors the pharmaceutical product transit. Even though, few unwritten rules of pharmaceutical transportation is available but these lack sincerity and consistency in approaches.

Various quality issues are cropped up during transportation and distribution operations of pharmaceutical products, which may result into a gross business loss and damage to goodwill of organizations, such as [10, 11]:

a. Product mix-up during transportation
b. Deterioration of product quality
c. Discoloration of formulation
d. Microbial contaminations
e. Label mutilation
f. Loss of product integrity
g. Arrival to wrong destination
h. Abnormal delay

The concept of Good Transportation Practices (GTP) shall be helpful to maintain quality during transit in the manner Good Manufacturing Practices (GMP) takes care of quality system during production process.

In order to have consistent performance the transportation process must be validated. In the past, it was not important to validate the transportation of the pharmaceutical products but now it is

recommended by all major regulatory agencies. Storage conditions during transit of the pharmaceutical products should be validated because it may affect the product stability.

MATERIALS AND METHOD

The review paper is based on exploratory study, wherein the data shall be collected from literatures and regulatory guidance, issued by PIC/S, WHO, USFDA etc. The materials from search engines have been collected and the relevant information have been drawn according to exclusion principle. The irrelevant information have been omitted as per consent of both authors. The literatures related to Good Manufacturing Practices and guidance material related to GXP environment were referred from documents like PIC/S guidance. [1]

RESULTS AND DISCUSSION

Pharmaceutical products are maintained at controlled environmental condition during manufacturing and it is also recommended to maintain the controlled environment during transit and transportation.

Pharmaceutical Transportation:

Trucks, vans, cars, trailers, aircrafts, railway carriages, boats and ships are few prominent means for transportation. As per principles of Good Distribution Practice of Medicinal Products for Human Use (GDP Guideline), transportation should be executed in accordance with the storage conditions defined in the marketing authorization and/or technical agreement depending upon product stability study data.

Why 'Good Transportation Practices (GTP)' is important?

Drugs have relationship between the temperature and efficiency, which can be estimated through stability and freeze thaw studies. Most of vaccines have reduced efficacy due to improper handling during transportation and storage. GTP is important for all pharmaceutical products in general and particularly for cold chain pharmaceutical products because:

a. cGMP regulations require temperature between 2-8°C during shipment of cold chain product and specified temperature such as 25 or 27 °C for other products [7]
b. Complete tracking of temperature storage conditions and management of temperature excursion
c. Qualified shipment is required to ensure consistent transit and shipment
d. Documentation of transportation for true representation of traceability and storage condition data for reference during quality issues

The transport risk assessment

The transport risk assessment should be considered in view of following conditions:

a. temperature impact
b. humidity
c. vibration/ Shock impact
d. handling delays during transportation
e. failure of data-loggers
f. topping up liquid Nitrogen (inert coverage to product)
g. environmental conditions monitoring throughout the transport.

Transport Validation

Validation is documented evidence that a process consistently produces result meeting pre-determined specifications. The transport validation refers the evidence for demonstrating that a transportation process or system, when operated within established parameters, can perform effectively and consistently deliver pharmaceutical product meeting its pre-determined criteria and quality parameters during transit from factory premises to the destination. [2]

Increase in temperature beyond specified limit can reduce the efficiency of the drug products. Transportation of pharmaceutical products poses quality risk due to temperature variation; therefore transportation validation is a pre-requisite to ensure quality product delivery.

The transport validation strategy comprises of following steps:

a. The transport validation protocol should be prepared and approved by designated Quality Assurance (QA) officer before starting the validation process, which shall contain various details of transportation and acceptance criteria. The validation protocol should contain following provisions:
    i. Protocol approval
    ii. Scope
    iii. Reason for validation
    iv. Responsibility of validation team member
    v. Validation acceptance criteria
    vi. References
    vii. Instrument to be used
    viii. Procedure
    ix. Observations/ Result recording
    x. Conclusion
    xi. Deviations, if any

xii. Report approval

b. For conducting transport validation during loaded condition, a field shipment test under real operating conditions there are two options.[2]
   - Use real products proposed for regular transportation
   - Use expired or dummy products to simulate the study

c. Define the mode of transportation based on marketing information

d. The vehicles / transport vans should be validated for the controlled environmental conditions before use. Storage cubicle of van should be mapped for temperature and humidity for a time period equal to the actual time taken in transit of product.

e. Acquire documentary evidence that route and mode of transportation is safe for product pack integrity. Generally a longest route for transportation is subjected for transport validation studies.

f. Acquire confidence that product molecule is stable under the defined transportation mode

g. The time taken to exceed the maximum allowable storage temperature limit at the time of control failure should also be studied considering it as a worst case.

Storage conditions

Some pharmaceutical products require specific conditions to be stored and needs special instructions for storage handling.[9]

Table-1: Storage Conditions with meaning

Storage condition	Meaning
Not to exceed 30 Degree Celsius	Temperature range from +2 to +30 Degrees Celsius
Not to exceed 25 Degree Celsius	Temperature range from +2 to +25 Degrees Celsius
Not to exceed 15 Degree Celsius	Temperature range from +2 to +15 Degrees Celsius
Not to exceed 8 Degree Celsius	Temperature range from +2 to +8 Degree Celsius
Should be protected from humidity	Relative Humidity doesn't exceed 60%
Keep away from light	Places not exposed to light i.e should be kept in light proof container

Calibration of temperature measurement devices

Temperature measurement devices must periodically be calibrated in order to ensure their accuracy for full operating temperature range on consistent basis. In addition, there are requirement for which these devices calibration or re-calibration is needed. Some of these circumstances are listed as under:

a. A calibration certificate is lost

b. The device crossed the validity period mentioned on calibration certificate

c. The device was used or treated beyond the instrument safety limitations (e.g. higher temperature, shock, etc.).
d. The battery of the device was replaced after putting off
e. The device's measurement scale is doubtful
f. The device manufacturer specified that a calibration procedure should be carried out at regular intervals

Support from manufacturer entailed

The clear understanding of supplier about the need and strategy to ensure product safety during transportation is the key of successful GTP.

a. During transportation temperature and humidity data loggers are used to generate online record of temperature and humidity. Data loggers are placed at representative locations with the product pack. Data loggers can be packed in shippers accordingly to mapped packaging configuration of the product to get the actual data.
b. Shock measurement stickers should be displayed for shock sensitive material (product).
c. Coding and decoding interpretation of temperature data loggers
d. Stability study and freeze thaw study data generation and interpretation.

In order to ensure pharmaceutical products are safely distributed from manufacturing plant to retailer's each organization must define and document the 'Good Transportation Practices'. The philosophy deserves the equal importance as other GXP practices like Good Manufacturing Practices, Good Laboratory Practices, and Good Distribution Practices etc.

Essential elements of Good Transportation Practices (GTP)

1. For transport and vehicles engaged for pharmaceutical operations, there should be :
    a. Procedures in place for operation and maintenance of equipment involved in distribution process
    b. The vehicles and equipment's used for transportation of pharmaceutical products should have appropriate capacity to maintain orderly storage of the various categories of products
    c. The design of vehicle should aim to minimize temperature exposure, least duct accumulation, free of waste and permit effective cleaning
2. Temperature controlled vehicles are used to transit the medicinal products.
3. Temperature ranges during the storage and transportation may be the constant or varying, they are determined by the product manufacturer, based on stability study programme.

4. Training should be imparted against GTP to the distribution and supply chain personnel, warehouse personnel and other directly associated with transportation and logistics operation of consignment. Transport driver should be trained for handling the data loggers during transit.
5. The drivers of vehicles should be able to produce identity through appropriate documentation to demonstrate that they are the authorized custodian of pharmaceutical products who are aware about quantity and storage conditions of products.
6. The packaging route should be available with logistics personnel. Ideally a flow diagram or pictorial representation comprising the consignment movement and storage should be used for better communication.
7. Dispatch and delivery of pharmaceutical products should be undertaken only after acquiring valid delivery order describing full name and quantity of products. The batch number on invoice / order should exactly match with that on labels.
8. The transport invoice must contain the storage condition of product along with precautions to be taken during transportation. The supply chain personnel and logistics operators should bear and refer 'List of Time and temperature sensitive pharmaceutical product (TTSPP)' [2]
9. The product shippers should contain the packaging profile and packaging configuration.
10. Service Level Agreement (SLA) or Quality Agreement between pharmaceutical company and logistics supplier should contain quality attributed in addition to accountability.
11. Maximum allowable hold time during transit and shipment should be established on the basis of scientific aspects, with following considerations:
    a. Mode of transportation
    b. Duration of transit
    c. Specified temperature and humidity
    d. Container closure system
    e. Stability study results
    f. Freeze thaw studies data
12. Many chemicals used in pharmaceuticals are potentially hazardous for health. An agreement between pharmaceutical company and transporter should ensure they are securely packaged and handled, and special documentation is required.[3] Some types of goods should subject to respective rules and law of land, such as
    a. Psychotropic drugs

b. Narcotic drugs

c. Toxic drugs

13. A risk assessment approach should be used to determine validation scope and extent of product hazard during the course of transportation.
14. Written procedure should be available for the handling of damaged and/or broken shipment containers and appropriate investigations thereto.
15. Labels on shippers should provide sufficient information on handling and storage conditions. National and international accepted abbreviations and symbols for product category and precautions should be displayed on product packs

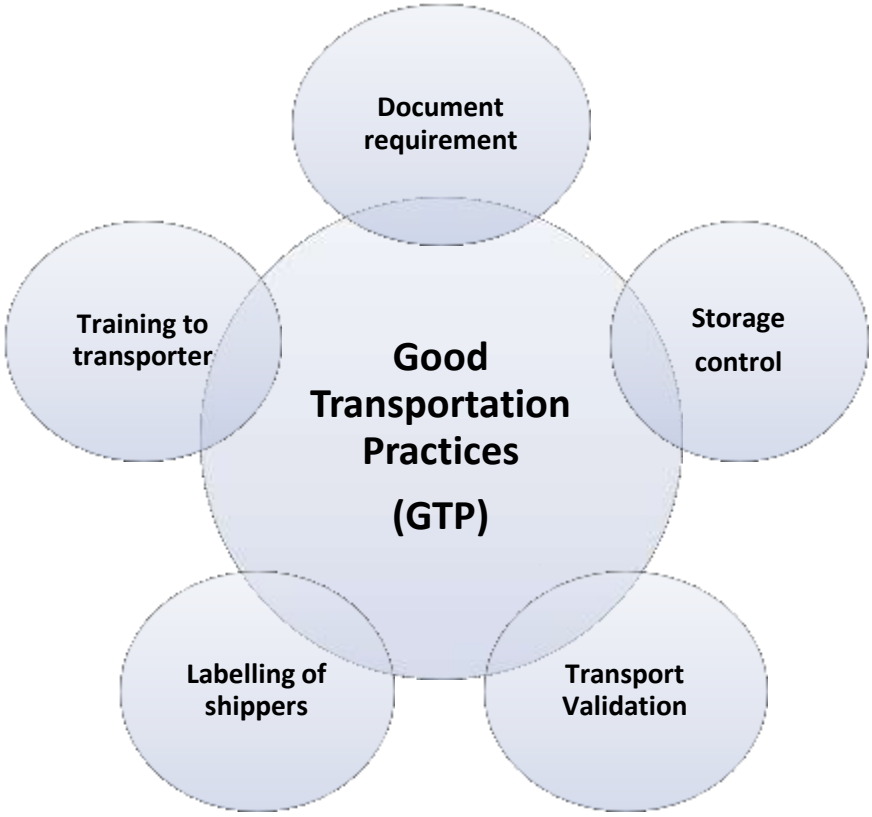

Figure 1: Schematic Representation of Essential Elements of GTP

CONCLUSION

The documentation, validation, labelling, storage control and training form the basics of Good Transportation Practices (GTP). The existing practices are confined to manufacturing, distribution and transport validation studies by manufacturing plant personnel, whereas there is an enhanced requirement of focus on other elements of GTP, in order to consistent and quality product supply of pharmaceutical products in broad interest of corporate and consumers. For consistent quality performance of pharmaceutical business, an organization must maintain

aspects like Transport validation, Transport Documentation, Qualification of transport van, Training to Drivers and Logistics Personnel etc.

RECOMMENDATION:

It is recommended that pharmaceutical product manufacturing plants and supply chain personnel must pay adequate attention to transportation quality system and regard 'Good Transportation Practices' as an integral component of pharmaceutical quality system.

REFERENCE:

1. PIC/S Secretariat ,Good practices for computerized systems in regulated "GXP" environments, September 2007, PI 011-3
2. WHO Technical Report Series, No.961, Model requirements for the storage and transport of time and temperature sensitive pharmaceutical products :2011 : 2.3.2- 6.7.1
3. Practical advice for Northern Ireland Business, Transport regulations for dangerous goods (pharmaceuticals), https://www.nibusinessinfo.co.uk/content/transport-regulations-dangerous-goods-pharmaceuticals, Online Access on 10 Jan-16,
4. GMP News, Transport Validation: new Considerations by Annex 15, http://www.gmp-compliance.org
5. Carli Derifield, You can transport temperature-sensitive products with confidence, http://pharmaceuticalvalidation.blogspot.in, Online Access on 10 Jan-16
6. Jasleen Kaur, Warehousing & Supply Chain Growing by leaps and bounds, Indian Transport & Logistics, Mar-Apr 2013, 10-11
7. Dr. Hans-Jürgen Krause, GMP aspects of cold chain management for pharmaceutical products, Pharmaceutical Development Parenteral Dosage Forms Maha Noujeime, International Technical Service, Abbott GmbH & Co. KG, Ludwigshafen, Germany:7-11
8. Chen Zhu, Good Supply Practice for Pharmaceutical Products, Order of the Ministry of Health of the People's Republic of China No. 90
9. GSDP Report, Edition 3, Guidelines on Good Storage and distribution Practices of Pharmaceutical Products in Lebanon, 2014; 7-35
10. Nirmal Kumar, Dr (Prof) Ajey Jha, ,Quality Perspective of 'Good Distribution Practices' in Indian Pharmaceutical Industry, IOSR Journal of Business and Management (IOSR-JBM). 2015;17(11): 28-32

11. Nirmal Kumar, Prof. Ajeya Jha A Model of Pharmaceutical Customer Complaints and Redressal System Global Journal For Research Analysis, 2015;4(12): 111-113.