GOOD DISTRIBUTION PRACTICE REQURIEMENTS FOR VEHICLES INTEDED FOR TRANSPORT OF TIME AND TEMPERATURE SENSITIVE PHARMACEUTICAL PRODUCTS

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Abstract: *Distribution of medical products is very important, especially for the people that are in need of them. Various people and companies are included in the process of acquisition, distribution and storage of medical products. The problem may occur when several companies are responsible for a segment of a process between manufacturing and selling to the end-buyer, and most commonly their jurisdiction doesn't overlap. World Health Organization published Good trade and distribution practices for pharmaceutical raw materials in 2004 after numerous incidents which included diethylene glycol. The term Good Distribution practice describes all the main requirements for storage and transport conditions which results in the desired quality of a product. Vehicles that are used in this complex supply-chain must be designed in a way to preserve precious cargo from various atmospheric and human factor-like intrusions. Constant monitoring must be achieved in order to preserve the quality and effectiveness of the medical product. Failing to maintain this complex distribution network could cause heavy impact on residency.*

Keywords: *pharmaceuticals, distribution, vehicles, temperature-controlled, cold-chain*

INTRODUCTION

The World Health Organization (WHO) was established as a United Nations specialized agency that has a goal to coordinate available resources related to international public health. The primary function of the WHO is to provide objective and reliable information in the field of human health, and it partially fulfills this responsibility through a large number of publications. The organization strives to support all public health strategies through its publications and enables their use as soon as possible. With this as its goal, practical handbooks, instructions and various materials are being published for the training of health workers. These books are closely related to priority activities of the Organization, which include disease prevention and its management. Progress towards a better health system requires the dissemination and exchange of information on a global level, based on knowledge and experience of all WHO member countries and the cooperation of world leaders in the field of biomedical sciences /1/.

The term cold chain implies a system of activities that include storage and transport from production to application of the product in order to achieve the desired effect. Time and temperature sensitive pharmaceutical product (TTSPP) is a pharmaceutical product that, when not stored, or transported in the given frames and/or in the predicted time, is unusable. Most pharmaceutical products are extremely sensitive to atmospheric conditions and must be stored exclusively on a specific temperature prescribed by the manufacturer. Observing the overall structure of the health system and the cycle itself different temperatures and atmospheric conditions may be required from production to application (example: level of carbon dioxide, oxygen, humidity ...). The usual transport mode is from +2 $^{\circ}$C, to +8 $^{\circ}$C, depending of the type of the product. If temperature at which the pharmaceutical product is stored is out of range, the characteristics of it will be deteriorated, and it is impossible to restore them in any way. Specifications of the devices that define atmospheric and temperature conditions are prescribed by the WHO. Also, a very important factors are employees' ability and adequate knowledge in the distribution system and that there is a clear hierarchy. A responsible person must always be available as well it would provide the right information at the right time and, in case of need, react quickly and correctly. /2/

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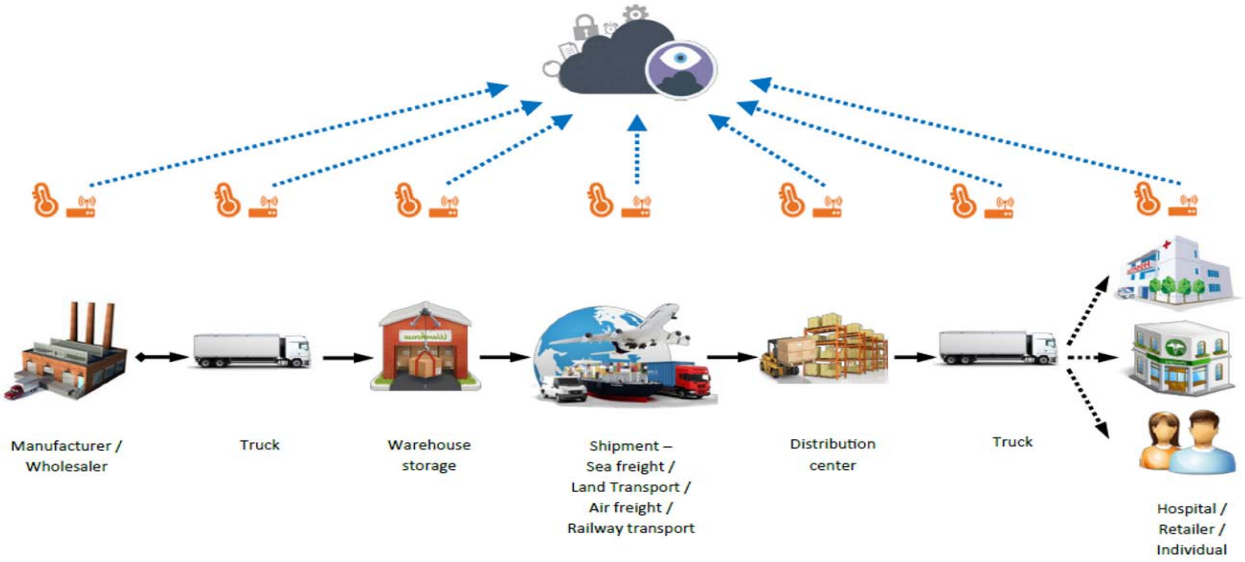
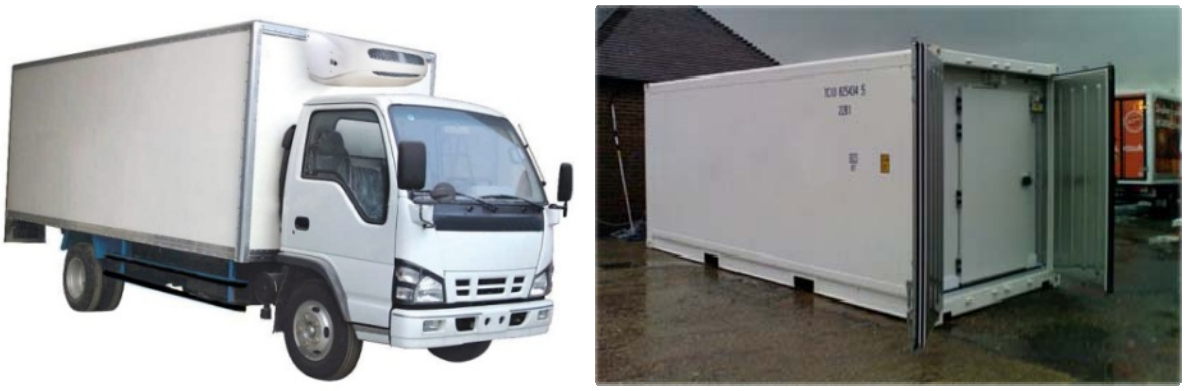


Picture 1. - Graphical representation of cold chain /3/

ATP AGREEMENT

The ATP Agreement is an agreement on the international carriage of perishable foodstuffs and on the special equipment to be used for such carriage. The abbreviation originates from the French name: "*Accord Relatif Aux Transports Internationaux de Denrées Périssables Et Aux Engins Spéciaux à Utiliser Pour Ces Transports*". It is made in Geneva on September 1st 1970 by the United Nations Economic Commission for Inland Transport for Europe. A working party on the transport of perishable foodstuffs (WP.11) of the Committee for Internal Affairs was established for the transport of the Economic Commission for Europe which regularly changes and updates the agreement and its annexes. The latest version is dated on January 1st 2018. /4/, /9/. The ATP agreement can serve as the basis for the construction of the equipment that will transport the medical products.



Picture 2. - Example of refrigerated and insulated equipment

Vehicles and equipment used to distribute and/or store pharmaceutical products should be designed specifically for this purpose in order to ensure the quality of the pharmaceutical product and to prevent contamination. It is desirable to install systems for remote tracking of movement of goods and for monitoring atmospheric and temperature conditions that contribute to the safety of the products. In cases where a vehicle primarily intended for the transportation of pharmaceutical products is used, all safety requirements must be respected /7/.

The basic measure of the quality of temperature insulation is the coefficient "K". It represents total heating or cooling power by degree of temperature difference - between interior and exterior walls and the surface

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of the chamber. It is recommended that all new vehicles which are designed for transport of pharmaceutical products have a value of $K \leq 0{,}4$ W/m^{2}K /5/,/6/.

$$K = \frac{W}{S \cdot \Delta T} \left[\mathrm{W/m^2K} \right]$$

$$S = \sqrt{S_i \cdot S_e}$$

S_i – inner surface of the box

S_e – outer surface of the box

ΔT – the difference between the average internal temperature T_i and the average external temperature T_e at the constant average external temperature T_e

W - heating power or the cooling capacity

Depending on the length of the route, the quantities of products to be transported, the appropriate cooling device must be selected. According to the ATP agreement, it would be desirable that the power of the cooling device be 1.75 times higher than the power that is necessary in order to achieve the desired temperature at an external temperature of 30 °C. If a transport is conducted on the territory where the predicted outdoor temperature is higher than 30 °C, it would be desirable that the power should be 2.25 times higher /5/.

It is of utmost importance to secure the transport of goods from unauthorized access. Also, the interior of the chamber should be constructed in such a way to make the maintenance easy. Hygiene levels must be extremely high. There must be a set of treatments and regular inspections must be carried out /7/.

CONTROL AND TEMPERATURE MONITORING EQUIPMENT

All equipment that affects the storage and distribution of medical products should be constructed, used and maintained in a manner consistent with the exploitation conditions for which it is intended. Devices and equipment used to control the operation of chamber must be calibrated, and its certificates must be available for inspection.

Warning systems must exist and must be active if there is deviation from the specified values and it is recommended to check their function regularly. If there is a failure of a device and/or equipment that is in charge of maintenance of temperature and atmospheric conditions, repair and calibration must be possible, in such a way that the medical product is not compromised in any way.

Basic requirements of vehicles that transport TTSPP:

- capable of maintaining the set temperature throughout the whole transport section, regardless if the vehicle is in motion, if it is stationary or the engine is off;
- equipped with a system that protects medical cargo from too low temperatures;
- cargo bay area equipped with calibrated sensors for temperature and humidity, set at the most unfavorable location;
- device for alarming the driver if there is a temperature deviation from the foreseen range;
- the door of the load compartment is provided with safety markers indicating whether an unauthorized access has occurred.

Basic requirement of equipment that monitors temperature

- sensors for monitoring the temperature with precision of ±5 °C
- temperature record of the state of each sensor (minimum every 10 min).

Basic requirements for humidity monitoring equipment

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- air humidity monitoring sensors with precision ±5% RH;
- record of the humidity of each sensor (minimum every 10 min).

Qualification of temperature-controlled road vehicles

- show that the temperature and humidity of the air in the cargo bay is reflected within the prescribed limits during the planned transport route;
- display areas within the cargo bay which should be exempt from direct exposure temperature sources (cold air flow);
- in case of failure of the temperature control, the time display of the temperature reach out anticipated working range /8/.

CONCLUSION

The goal of the pharmaceutical product suppliers is to provide safe transport from the starting point to the destination point and to deliver products. In most cases transport of these products is time sensitive, especially in emergency situations. If a slightest deviation of the product is noticed, the responsible person should report how the pharmaceutical product was disturbed. Also, additional procedures should be provided to clearly identify the cause of the problem. With enough data acquired, responsible person must resolve and improve all weak spots in cold chain distribution.

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