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REVIEW ARTICLE

COLD CHAIN FOR VACCINES

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ABSTRACT

Vaccines are biological substances that may lose their effectiveness quickly if they become too hot or too cold at any time, especially during transport and storage. The efficacy of vaccines depends on maintaining the cold-chain – that is, a prescribed temperature range during distribution from manufacturer to the point of use. The temperature during transport and storage should be kept at 2-8 degrees centigrade for all vaccines. Inadequate temperature control during storage and transport of vaccines can reduce their efficacy, and result in failure to produce satisfactory levels of immunity. The effect of adverse temperature on vaccines is cumulative and breaks in the cold-chain, which may occur during transportation, will render vaccines subsequently stored in the community more susceptible to loss of potency. Current review paper focuses on the Immunisation and cold chain system in India. Cold chain for vaccines includes different equipment viz (WIC), (WIF), (DF), (ILR), Refrigerated trucks and their management with respect to universal Immunisation Programs.

Key words: vaccines, Immunisation, storage Temprature.

INTRODUCTION

A vaccine is any preparation intended to produce immunity to a disease by stimulating the production of antibodies Vaccines include, for example, suspensions of killed or attenuated microorganisms, or products or derivatives of microorganisms. The most common method of administering vaccines is by injection, but some are given by mouth or nasal spray (Define by WHO).

Cold Chain is a system of storing and transporting vaccine at the recommended temperature range from the point of manufacture to point of use. In order to provide potent and effective vaccine to the beneficiaries a vast cold chain infrastructure is required, which should have a network of Vaccine Stores, Walk-in-coolers (WIC), Walk-in-freezers (WIF), Deep Freezers (DF), Ice lined Refrigerators (ILR), Refrigerated trucks, Vaccine vans, Cold boxes, Vaccine carriers and icepacks from national level to states up to the out reach sessions. The cold chain system and vaccine flow in the country:- The vaccines are transported from the manufacturer through air transport under the temperature range of 2-8 ^{0}C to the primary vaccine stores (GMSDs/State head quarter).

TARGET DISEASES

There are many infectious diseases that can result in the death or disability of infants and young children. Some of the most dangerous of these are:

- Poliomyelitis
- Measles
- Diphtheria
- Whooping cough
- Tetanus
- Tuberculosis
- Hepatitis B
- Mumps

These diseases have one thing in common - they can all be prevented by immunization. Immunization is achieved by the administration of a vaccine, produced from an attenuated, inactivated or killed form of the virus or bacteria. A vaccine is normally injected, or in some cases may be given orally. The vaccine will provoke the development of antibodies in the infant, who thus acquires immunity without suffering the disease.

WHY COLD CHAIN?

- Biotech products often require deep frozen/refrigerated storage like Insulin, vaccines etc.
- Quality of pharmaceutical products is of primary concern
- Chemical and physico-chemical stability depends on temperature
- cGMP regulations enforce the compliance with strict temperature control along the process/distribution chain
- Risks to vaccines of exposure to extremes in temperature
- Compliance with vaccine manufacturer
- Assurance/confidence in potent product
- Ensuring maximum benefit from immunisation

IMMUNISATION IN INDIA

Vaccination is a highly effective method of preventing certain infectious diseases. For the individual, and for society in terms of public health, prevention is better and more cost-effective than cure. Vaccines are generally very safe and adverse reactions are uncommon. Routine immunization programmes protect most of the world's children from a number of infectious diseases that previously claimed millions of lives each year. For travelers, vaccination offers the possibility of avoiding a number of dangerous infections that may be encountered abroad. However, vaccines have not yet been developed against several of the most life threatening infections, including malaria and HIV/AIDS.

The UIP in India is one of the largest Universal immunization program (UIP) in the world in term of quantities of vaccines used, almost 27 million infants and 30 million pregnant women are covered. India spends about Rs.2000 crores annually for immunization (***Sokhey, 1988***) The UIP covered 6 deadly vaccines preventable Disease viz, TB, Diphtheria, Tetanus, Pertussis, Polio and Measles. In addition, Hepatitis B and Japanese Encephalitis vaccines have been introduced in some districts.

VACCINES DISTRIBUTION SYSTEM IN INDIA

During transport between one level and the next, all vaccines must be maintained at a temperature between 0 ^{0}C and +8 ^{0}C ***(Annual Report 2002-03 MoHFW)***..

Table 1: Milestones In The Immunization Program In India

1978	Expanded Program of Immunization (EPI) introduced BCG, DPT, OPV, Typhoid
1985	Universal Immunization Program (UIP) introduced Measles added Close monitoring of <1 yr age group
1990	Vitamin-A supplementation
1992	Child Survival and Safe Motherhood Program
1995	Polio National Immunization Days
1997	Reproductive and Child Health Program (RCH I)
2005	RCH-II and the National Rural Health Mission (NRHM)

If unopened and OPV, Measles or Mumps vaccines become unfrozen during transit, they can be safely re-frozen at the next level without any harm or loss of potency to the vaccine. The distribution system in India for Vaccines may be existing as indicated in Flow chart

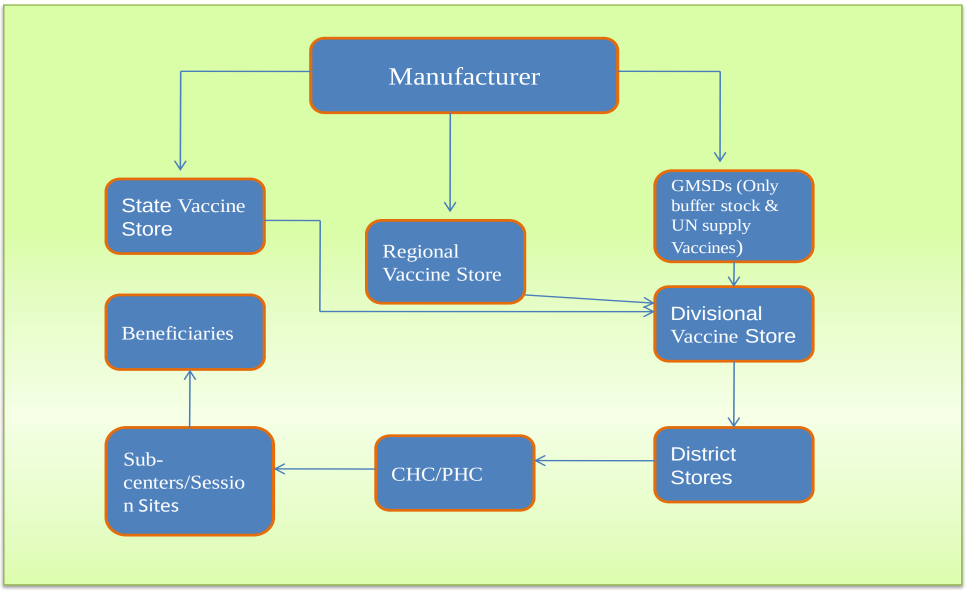

Figure 1: Vaccine distribution system in India (CHC = Community Health centre, PHC= Primary Health centre)

(Source: Handbook for Vaccine & Cold Chain Handlers. Govt. of India)

Table 2: Number Of Vaccines Store In India As In August 2009*

Store level	Number
Government Medical Supply Depots	4
State vaccines store	35
Regional Vaccines stores	20
District Vaccines Store	96
District Store	626
Community Health centre/Primary Health centre	26439

****Handbook for Vaccine & Cold Chain Handlers. Govt. of India***

CRITICAL PARAMETER ABOUT COLD CHAIN

The stability of vaccines completely depends on the cold chain system if cold chain is break that's lead to the instability of vaccine. The cold chain depends upon following parameter:

Transport Parameters

- Transport duration time limit
- Transport duration time limit in case of excursions
- Temperature continuous monitoring : Max & Min and Avg
- No and locations
- Quantity & position of cooling packs

Product Parameters

- General Appearance of drug product

- Physical condition of packaging
- Chemical checks
- Microbiological checks where necessary

Challenges faced during Transportation

- Weather
- Unexpected delays
- Traffic jams
- Break-downs
- Power failures
- Agitation or Strikes

COLD CHAIN EQUIPMENT FOR VACCINES (MODULE 3, THE cold chain WHO 98)

The cold chain equipments are the most essential part of cold chain management system, without their proper handling cold chain is nothing to be done. The equipments for storage of vaccines must have recommended temperature conditions for vaccine storage round the year. There are different equipments of different capacity for storage of vaccines at different levels. Some of the equipments are dependent on electric supply to maintain the recommended temperature, while others can maintain the desired temperature range even in the absence of power supply for a specific time period.

Refrigerated Truck and Insulated Vaccines Vans

Refrigerated trucks are used infrequently in India for transportation of vaccines. Insulated vans (photo) are used for bulk transportation of vaccines by road .Up to 10 lakh mixed antigen vaccines can be transported at a time .All vaccines are transported in cold boxes with frozen or conditioned ice packs or with dry ice (Rotary International).

Walk-in-Freezers (WIF)

These are used for bulk storage of OPV, and also to prepare frozen ice packs at state stores. They maintain a temperature around (-) 20oC. They are available in sizes of 16.5 Cum. and 32 Cum. These are provided with two identical cooling units and standby generator set. The Generator set starts automatically as soon as the power cuts off. An alarm system is also provided. As soon as the temperature crosses the safe range a hooter hoots loudly. Bulk quantities of ice packs are also made and stored in the Walk-in-Freezers.

Walk-in-Coolers (WIC)

These are used for bulk storage of vaccines at State and Regional/Divisional Stores. They maintain a temperature of +2 ^{0}C to +8 ^{0}C. They are available in sizes of 16.5 Cum. and 32 Cum. These are used for storage of large quantities of vaccines, like DPT, DT, TT, Measles, BCG, and Hepatitis B They have two identical cooling units and standby generator sets with automatic start and stop facilities. They are also provided with temperature recorder and alarm systems. Once the temperature of WIC is more than +10 ^{0}C, alarm system gets activated. Walk-in Coolers are established at regional levels, which store vaccines for about 4-5 districts.

Deep Freezer

The cabinet temperature is maintained between -15 ^{0} C to -25 ^{0}C. This is used for storing of OPV (district level and above only) and also for freezing ice packs. In case of power failure, it can maintain the cabinet temperature in the range of -15 ^{0} to -25 ^{0}C for 18 & 26 hours at ambient temperatures of 42 ^{0}C and 32 ^{0}C respectively, if not opened. The deep freezers have vaccine storage capacity and ice pack freezing capacity. These are available in different sizes (Large and small). The Deep Freezer is provided with special insulation, which helps in maintaining inside temperature in the range of (-) 25 ^{0}C to (-) 15 ^{0}C.

Ice Lined Refrigerator (ILR)

These type of refrigerators are top opening because they can hold the cold air inside better than a refrigerator with a front opening. It can keep vaccine safe with as little as 8 hours continuous electricity supply in a 24-hour period. Inside the ILR there is a lining of water containers (ice packs or tubes) fitted all around the walls and held in place by frame. When the refrigerator is functioning the water in the containers freezes and if the electricity supply fails, then the ice lining maintains the inside temperature of the refrigerator at a safe level for vaccines. Therefore the temperature is maintained in ILR for much longer duration than in deep freezers and ILRs can keep vaccine safe. The ILR has got two sections – the top and bottom. The bottom of the refrigerator is the coldest place and is shown as section A. The DPT, DT, TT and BCG vaccines should never be kept directly on the floor of the refrigerator as they can freeze and get damaged. The top section of the

ILR is known as section B and it maintains the temperature of +2 ^{0}C to +8 ^{0}C. All the vaccines should be kept in the basket provided with the refrigerator. OPV and Measles can be kept at bottom of the basket while BCG, DPT, DT and TT vaccines are kept in upper part of the baskets. In case basket is not available keep two layers of empty ice packs laid flat on the floor; do not keep the vaccines on the floor of the ILR.

Solar Refrigerators

A solar refrigerator operate on the same principle as normal compression refrigerators but incorporate low voltage (12 or 24V) DC compressors and motors, rather than mains voltage AC types. A photovoltaic refrigerator has higher levels of insulation around the storage compartments to maximize energy efficiency, a battery or number of batteries depending upon the size of panel for electricity storage, a battery charge regulator and a controller that converts the power from the battery to DC form required by the compressor motor.

Cold boxes:

Cold boxes are big insulated boxes. These are of different sizes- 5, 8, 20 and 22 liters with requisite number of ice packs. The 5 & 8 liters cold box can transport about 1500 & 2400 doses of mixed antigen vaccines respectively Cold Boxes are mainly used for transportation of vaccines. In emergency they can also be used to store vaccines as well as frozen ice packs. The cold boxes are use in Collect, transport large quantities of vaccines and Store vaccines for transfer up to five days.

Vaccine Carriers

Vaccine carriers are used for carrying small quantities of vaccines (16-20 vials) to the sub-centers or session sites. The vaccine carriers are made of insulated material, the quality of which determines the cold life of the carrier. Four ice packs are laid in the vaccine carrier as per manufacturer's guidelines. Conditioned icepacks should only be placed and the lid of the carrier should be closed tightly (***Apex International Noida***).

Ice Packs

Ice packs are key component of the cold chain. It is used for ice lining inside the cold box and vaccine carrier. The ice packs are frozen inside the deep freezer under the temperature range of (-) 15 to (-) 25 ^{0}C. The specifications of ice packs vary with the manufacturers. The ice packs for cold box are different from vaccine carrier and these should be used as per the manufacturer's guidelines.

MONITORING OF THE COLD CHAIN

All vaccines are damaged by temperatures more than +8 ^{0}C, whether they are exposed to a lot of heat in a short time (e.g., as a result of keeping vaccine in a closed vehicle in the sun) or a small amount of heat over a long period (e.g., as a result of the frequent opening of lid of ILR).

Reconstituted BCG, measles and JE vaccines are the most sensitive to heat and light. Since these live vaccines do not contain preservatives, there is risk of contamination with staphylococcus aureus leading to Toxic Shock Syndrome and, therefore, they should not be used after 4 hours of reconstitution.

THE VACCINE VIAL MONITOR (VVM):

To check the heat damage Before opening a vial, A Vaccine Vial is inspect by volunteer which l containing a heat-sensitive material as label to register cumulative heat exposure over time. The combined effects of time and temperature cause the inner square of the VVM to darken gradually and irreversibly (***Chudasama et al. 2009*).**

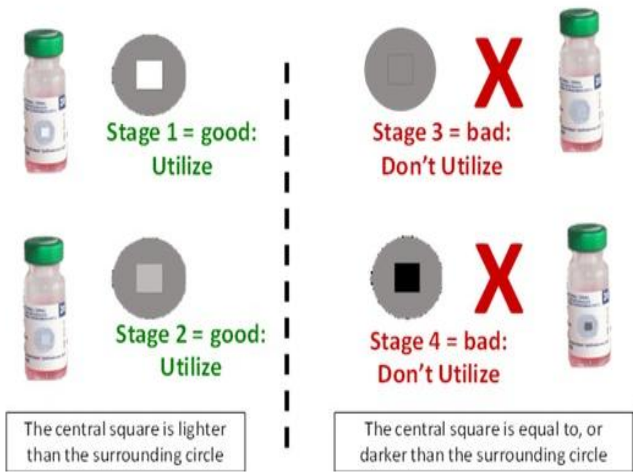

Figure 2: VVM

Table 3: The UIP guidelines for light and Temperature of the cold chain at which they are maintained

Vaccine PHC	Exposure to heat/light	Exposure to cold	Temperature at
Heat and light sensitive vaccines			
BCG	**Relatively heat stable, but sensitive to light**	**Not damaged by freezing**	**+2°C to +8°C**
OPV	Sensitive to heat	Not damaged by freezing	**+2°C to +8°C**
Measles	Sensitive to heat and light	Not damaged by freezing	**+2°C to +8°C**
Freeze Sensitive Vaccines			
DPT	**Relatively heat stable**	**Freezes at -3°C (Should not be frozen)**	**+2°C to +8°C**
Hepatitis B	Relatively heat stable	Freezes at -0.5°C (Should not be frozen)	**+2°C to +8°C**
DT	Relatively heat stable	Freezes at -3°C (Should not be frozen	**+2°C to +8°C**
TT	Relatively heat stable	Freezes at -3°C (Should not be frozen	**+2°C to +8°C**

At the PHC (Primary health centre) level, all vaccines are kept in the ILR for a period of one month at temperature of +2 ^{0}C to +8 ^{0}C
(:Immunization Handbook for Medical Officers,Govt of India.)***

CONCLUSION

India has, over the years, built a large cold chain for vaccines to support its UIP. The challenges of maintaining temperature within close limit to increase the shelf life of vaccines, transportation to reach the vaccines to inner areas in the country, and perennial power outage that can cause instability to vaccine, are being overcome with innovative ideas.

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