Temperature monitoring of the vaccine cold chain to assess the level of freezing

National Institute of Epidemiology
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Chennai

With technical support from UNICEF, India, New Delhi

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Generous financial support from Norway Indian Partnership Initiative (NIPI) has facilitated this National Study on Temperature Monitoring of the Vaccine Cold Chain and to assess the level of freezing.

NATIONAL INSTITUTE OF EPIDEMIOLOGY, CHENNAI

Dr. Sanjay Mehendale, MD MPH
Director

Preface

While the public health policy makers and program managers are gearing up to address the huge burden of non-communicable diseases, the burden, morbidity and mortality associated with communicable diseases in India continues to be high. Even the vaccine preventable diseases constitute a significant public health burden. In addition to issues related to coverage and acceptance by the communities; storage and potency of the available vaccines often gets questioned. Traditionally the program mangers focus on avoiding exposure of vaccines to high temperatures during vaccine storage and shipment. In India, several studies have assessed the exposure of vaccines to high temperatures. However, there appears to be very little information about exposure to subzero temperatures in the national cold-chain system. Exposure to subzero temperatures can reduce the potency of diphtheria, tetanus and pertussis (DPT), diphtheria and tetanus (DT), tetanus toxoid (TT), hepatitis B and pentavalent vaccines.

A robust and systematic study to generate evidence of reliability and dependability about the temperatures in the vaccine cold chain was the need of the hour. NIE conducted a study in 10 Indian states to estimate the frequency of exposure of vaccines to freezing temperatures at various levels in vaccine cold chain and results presented in this report have a very significant contribution to make in that regard. The findings of the study after >130,000 hours of temperature monitoring indicated that exposure to freezing temperature was frequent at the peripheral health facilities as well as during transport of vaccines whereas exposure to higher temperatures was common at all the levels of the cold chain. While the main aim of the present study was to evaluate exposure of vaccines to extremes of temperature at various storage levels, the investigators also identified several reasons why vaccines were being exposed to suboptimal temperatures, such as, incorrect setting of thermostat and presence of gaps between the plates forming the walls of the walk-in cooler.

India has one of the largest immunization programmes in the world, in terms of the quantity of vaccines used, numbers of beneficiaries covered, geographical spread and the cold-chain equipment and human resources involved. Every year, the programme targets more than 27 million infants and 30 million pregnant women. Several new vaccines are likely to be introduced in the national immunization programme in the near future. Since most of the childhood vaccines are sensitive to extremes of temperature, an adequate and optimal cold-chain system will have to be created and maintained to preserve the quality of all vaccines before they are administered.

I am confident that the study findings and the recommendations would result in an appropriate programmatic response and policy decisions to support more effectively temperature monitoring in storage facilities at all levels and shipment of vaccines under the most ideal conditions.

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1. EXECUTIVE SUMMARY

WHO guidelines for the use of diphtheria–tetanus–pertussis, diphtheria–tetanus, tetanus toxoid and hepatitis B vaccines specify that these vaccines must not be frozen and should not be used if thought to have been frozen. Exposure of these vaccines to sub-zero temperatures leads to the loss of potency and compromises protective immunogenicity in recipients. While several studies conducted in developed and developing countries have reported frequent exposures of vaccines to sub-zero temperatures both during their storage and transport, very limited data is available about the level of freezing occurring in vaccine cold chain in India.

To provide this important information to the programme, the National Institute of Epidemiology (NIE), Chennai conducted a study to estimate the frequency of exposure to freezing temperatures at various levels in vaccine cold chain. The study was conducted following the WHO protocol for temperature monitoring in the vaccine cold chain and involved monitoring of the temperatures during the storage and transport of the vaccines using electronic data logger, a WHO prequalified device as well as freeze event indicators. The study was conducted in 10 Indian states representing different regions of the country. From each state, two districts were selected and from each of the selected district, two peripheral health facilities where vaccine is stored were selected for temperature monitoring.

The study commenced with placement of test boxes containing programmed data loggers, two un-frozen DPT vaccine vials and two freeze event indicators (FreezeAlert, Sensitech and Trans Tracker C, TempTime) at the state or regional vaccine store. The test boxes were placed at the vaccine store at the same place where DPT vaccine was stored and remained at each level of the cold chain (state, regional, district, community health centre/Primary Health centre) for a minimum duration of pre-determined period of time. The test boxes were shipped towards the selected health facility in the same carton as the other vaccines and according to typical loading and transport procedures. No special arrangements were made to transport the test boxes to the selected health facilities (Last cold chain points). As the goal of the study was to monitor the temperatures of a typical cold chain, the test boxes were handled and stored in the same way the vaccine shipments are handled, without any changes to routine procedures. The date and time of arrival of the test boxes as well as the date and time when the vaccine boxes were shipped to the next level were recorded in the monitoring sheet. The test boxes were collected from the last cold chain points at the end of the study and transported to NIE at the room temperature. The data from the data-loggers were downloaded and analyzed to calculate the extent of sub-optimal exposure (<0 and >8^{0}C) at national, state, regional, district and peripheral vaccine stores as well as during transportation. A shake test was conducted on the DPT vials to find if the vaccine vials were damaged due to freezing.

The study was conducted for a total duration of 138,476 hours of monitoring temperatures at different levels of cold chain. At the state vaccine stores, the exposure to sub-zero temperature and >8^{0}C was recorded respectively for 1.5% and 14.3% of the total time at these stores. Exposure to sub-zero temperature was recorded only at the state vaccine store in Tamil Nadu while higher temperatures were recorded at the state stores of Manipur, Madhya Pradesh, Bihar, Karnataka, Andhra Pradesh for a variable period of time. At the regional and district vaccine stores, exposure to below zero temperature occurred for less than 1% of the time, however exposure to higher temperature was recorded for 13.2% and 8.3% of the total time of storage at the regional and district vaccine stores. At the peripheral health facilities as well as during the transport of the data loggers, exposure to <0 and >8^{0}C were frequently recorded. Freezing events were recorded only in Tamil Nadu during the conduct of the outreach sessions.

In several state/regional vaccine stores, temperatures were monitored using manual methods. The temperature monitoring data was not regularly reviewed to identify temperature excursions. Records of manual temp recording did not match with the readings of data loggers. The temperature monitoring devices in the cold chain were never calibrated. Long hours of power cut, shortage of trained cold chain handlers (CCH) affected the maintenance of cold chain.

Based on the findings of the study, we propose a number of recommendations to improve the maintenance of the vaccine cold chain and avoid the temperature excursions. First, a visit by the technical team from the immunization division of the Ministry and the National Cold chain Training Centre, SHTO, Pune is necessary to identify the reasons for exposure to sub-optimal temperatures at the state vaccine stores at Andhra Pradesh, Bihar, Karnataka, Madhya Pradesh, Manipur and Tamil Nadu as well as the regional vaccine store at Dharmasala, Himachal Pradesh. Second, all the state and regional vaccine stores need to have a real-time data logging system with a remote viewing option and the state EPI/immunization officers need to ensure that the data collected is reviewed regularly and take corrective action for any temperature excursions. Third, for improving the cold chain maintenance at the district and sub-district level, there is a need to (a) update the cold-chain infrastructure by replacing old cold-chain equipments, (b) calibrate the temperature monitoring devices, (c) consider the use of alternate source of electricity for power back-up in areas with frequent power cuts and (d) conduct refresher training for the CCH with emphasis on periodic de-frosting of ILR and packaging of vaccines during the transportation.

2. BACKGROUND

Childhood vaccination is one of the most important and cost-effective public health interventions.[1] The Universal immunization programme (UIP) was launched in India with the objectives of (a) universal vaccination of newborns against six vaccine preventable diseases and pregnant mothers with tetanus toxoid and (b) achieving the self sufficiency in vaccine production and the manufacture of cold chain equipment. In some states, hepatitis-B and Japanese encephalitis vaccine is included in the programme. Adequate cold-chain infrastructure and compliance is paramount for preserving the quality of these vaccines as they are distributed.

World Health Organization (WHO) guidelines recommend that all vaccines except oral polio vaccine be kept at 2–8^{0}C during in-country distribution. Emphasis has long been placed on avoiding high temperatures during vaccine shipments.[2] However, a poorly functioning cold chain may deviate from this target range and expose vaccines to freezing temperatures. Exposure to sub-zero temperatures can result in potency loss for freeze-sensitive vaccines such as diphtheria, tetanus, pertussis, hepatitis B, haemophilus influenzae type b (Hib) and inactivated polio vaccine.[3, 4, 5,6,7,8, 9] Several studies conducted in developed as well as developing countries have reported the exposure of vaccines to freezing temperatures, during the storage as well as the transport segments of the vaccine cold chain.[10]

In India, several studies have assessed the exposure of vaccines to high temperatures.[11, 12,13,14,15] However, very little information is available on vaccine exposure to subzero temperatures in the national cold-chain system. With this background, the National Institute of Epidemiology (NIE) conducted a study to estimate the level of freezing in cold chain in different Indian states.

3. OBJECTIVES

Primary objective:

- Estimate the frequency of vaccine exposure to sub-optimal temperatures <0 or >8^{0}C at various levels in vaccine cold chain in selected Indian states

Secondary objective:

- Describe the maintenance of cold chain in the selected health facilities to identify possible reasons for freezing

4. METHODS

The study was conducted during February August 2012 by following the WHO protocol for temperature monitoring in the vaccine cold chain.[2] The study involved monitoring of the temperatures during the storage and transport of the vaccines using WHO approved temperature measuring devices like data loggers and supplemented by freeze event indicators.

4.1. Selection of the study states:

The study was conducted in 10 Indian states representing different regions of the country. The details of the states selected from each region are given in table-1. The selection of the study states was not random.

Table 1: Study states and districts

Region	Study states
Eastern	(1) West Bengal
	(2) Bihar
North-eastern	(3) Manipur
	(4) Arunachal Pradesh
Northern	(5) Himachal Pradesh
Southern	(6) Andhra Pradesh
	(7) Tamil Nadu
Western	(8) Gujarat
	(9) Karnataka
Central	(10) Madhya Pradesh

4.2. Selection of the study districts and last cold chain points:

From each of the selected states, two districts (one largest in terms of number of cold chain points/population and one furthest district) were selected. In each of the 20 selected districts, two peripheral health facilities where vaccine is stored (last cold chain points, LCP) – generally the two that were most distant from the district vaccine store – were selected, to give four peripheral vaccine stores – one urban and three rural – for investigation in each study state. We consulted with the managers of the Universal Immunization Programme to ensure that the peripheral vaccine stores that we selected for study were both accessible and

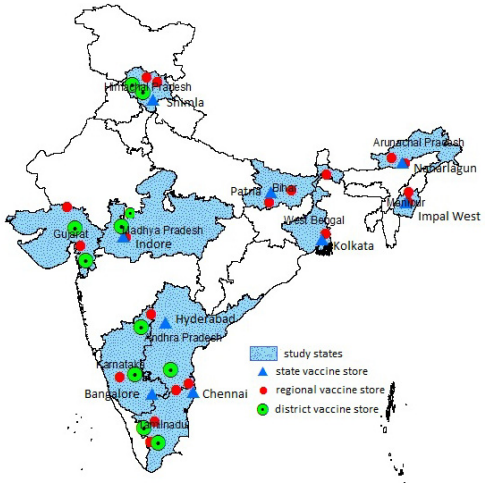


Fig 1: Location of 10 Indian states selected for the temperature monitoring study.

staffed. In each study state, one or two researchers were responsible for planning, coordinating and monitoring the study. The location of the state, regional and district vaccine stores in the 10 selected states is given in Fig 1.

4.3. Temperature monitoring

The temperatures during the storage at different vaccine stores and transport of the vaccines from the state stores up to the last cold chain point (defined as peripheral health facility where vaccine is stored) were monitored using electronic temperature loggers (data loggers). The data loggers were programmed to record the temperature readings at 30-minute interval and had a capacity to record temperatures for a period of 5.5 months. DPT vaccine was used as the study vaccine for monitoring the temperature during the storage and transport.

4.4. Preparation of test boxes

Test boxes containing (a) programmed data logger (Log Tag TriX-8*, LogTag Recorders, Auckland, New Zealand, measurement range: -40^{0}C to +85^{0}C), (b) 2 DPT vaccine vials and (c) two freeze event indicators (FreeAlert, Sensitech* Sensitech, Beverly, USA and Trans Tracker C, Temp Time, Morris Plains, USA) were prepared at NIE and sent to all the participating states. DPT vaccine vials of the same batch (Batch No. 906, Expiry date: Jan 2013) were procured from the Directorate of Public Health, Govt of Tamil Nadu for the study. Shake test was performed on these vials in order to ensure that the test vials were not damaged by freezing prior to the study. Only those vials which passed the shake test were put into the test boxes.

Test box contained, datalogger, un-frozen DPT vials (2) and freeze event indicators (2)

4.4.1. Temperature monitoring during the storage and transport up to last cold chain point:

The study commenced with placement of four test boxes (one each for the selected last cold chain point in the state) at the state vaccine store (or regional vaccine store in case there are no state stores). The name of the last cold chain point and its route starting from state vaccine store was mentioned on the test boxes.

Study commenced with placement of four test boxes in the state/regional vaccine stores

* *Approved by the World Health Organization's Performance, Quality and Safety (PQS) standard*

As the goal of the study was to monitor the temperatures of a typical cold chain, the test boxes were handled and stored in the same way the vaccine shipments are handled, without any changes to routine procedures. The test boxes were placed in the vaccine store in the same place where DPT vaccine was stored and remained at each level of the cold chain (state, regional, district, community health centre/Primary Health centre) for a minimum duration of the prior-determined period of time (Table-2). The test boxes were shipped towards the selected health facility in the same carton as the other vaccines and according to typical loading and transport procedures. No special arrangements were made to transport the test boxes to the selected health facilities (Last cold chain points).

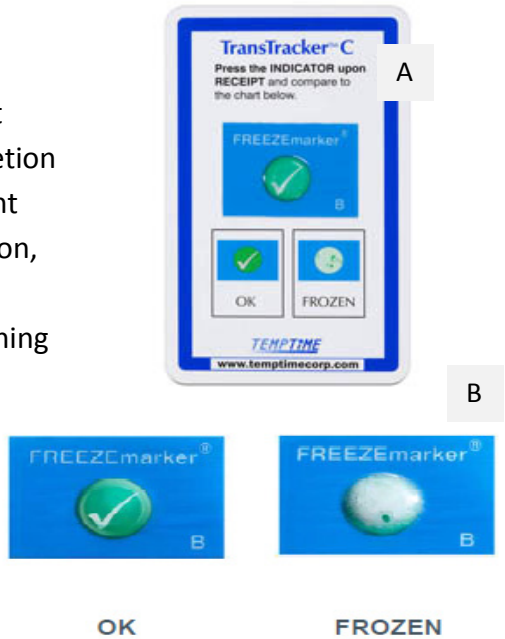
Table 2: Minimum duration of storage of test boxes at different levels in vaccine cold chain

Vaccine store	Minimum duration of time for storage of test boxes
State vaccine store (SVS)	1 month
Regional vaccine store (RVS)	1 month
District vaccine store (DVS)	1 month
Community Health centre	15 days
Primary Health Centre	15 days

Every study box was accompanied by a monitoring sheet to record the movement of vaccine. Co-investigators/cold chain staff at each point in the cold chain recorded the date and time of arrival of the test boxes as well as the date and time when the vaccine boxes were shipped to the next level.

4.4.2.Temperature monitoring during outreach session:

The temperature during shipment of vaccines from the last cold chain point to the outreach session and till the completion of the vaccination session was monitored using freeze event indicator. Before taking the vaccines for the outreach session, the co-investigators placed the indicator (TransTracker C, TempTime Morris Plains, USA) in the polythene bag containing the vaccine or pasted the markers on the vaccine vials (FreezeMarker, TempTime Corporation, USA). At the end of the vaccination session, the status of the freeze event monitors was examined to find if the vaccines were exposed to freezing after they had left the peripheral vaccine stores.



TransTracker (A) and Freeze Markers (B) showing exposure to freezing

4.4.3. Ambient Temperature monitoring:

In addition to the monitoring of temperatures during the storage and transport of the cold chain, ambient temperature during the storage and transport was also monitored at one of the four last cold chain points (LCP) selected in the district. The LCP which was furthest from the state vaccine store was selected for ambient temperature monitoring. The box containing the data logger for ambient temperature was kept in the same room where the Walk-in-cooler (WIC)/Ice-lined refrigerator (ILR) was located but out of direct sunlight and away from heat sources. This box was shipped along with the test boxes containing data loggers and DPT vials from the State vaccine store towards the selected health facility (last cold chain point).

4.4.4. Interview of cold chain handlers:

The cold chain handlers of the health facilities selected for temperature monitoring were interviewed to collect information about their knowledge levels about freezing in the cold chain, training needs, as well as maintenance of different cold chain equipments using a questionnaire. Records of temperature monitoring during the last 3 months in these facilities were also reviewed.

4.4.5. Collection of the data loggers at the end of the study:

The co-investigators collected the test boxes from the last cold chain points and transported them to NIE at room temperature.

4.4.6. Shake test:

The shake test was conducted jointly by NIE and experts of immunization programme following the standard procedures.[2] The shake test was conducted (1) at the time of preparation of test boxes in order to ensure the test vials were not damaged by freezing and (2) at the end of the study to find out the if the vaccine vials were damaged due to freezing.[‡] Shake test has 100% specificity and 100% sensitivity for detecting freeze damage in aluminium-based, adsorbed, freeze-sensitive vaccines.[16]

4.5. Study time frame:

In all the states, except Arunachal Pradesh, the study commenced in the month of February 2012 with placement of test boxes in the state (or regional vaccine stores) during 10-15 February 2012. The study in Arunachal Pradesh commenced on 14 May 2012. The last data logger was retrieved on 25 August 2012.

[‡] *The DPT vaccine vials used in the test boxes were procured from SVS, Tamil Nadu. For preparation of the test boxes, we conducted the shake test on 90 vials of which about 15 vials failed the shake test indicating the damage due to freezing. As a result, additional 50 vials were procured from SVS, Tamil Nadu and all the vials which passed the test were included in the study.*

4.5.1. Data analysis:

The data from the dataloggers were downloaded and analyzed. We calculated the proportions of the 40 boxes that had been exposed to a temperature of <0 or > 8°C at each level of the cold chain and while in transit and the percentages of the time that – while stored at each level of the cold chain or in transit – each datalogger had been exposed to a temperature of < 0 or > 8°C. For each datalogger, we also estimated the longest period of exposure to a temperature of < 0 or > 8°C, assuming that the datalogger had remained at a similar temperature between two consecutive temperature recordings of < 0 or > 8°C. We also measured the exposure to freezing temperatures using the freeze-event indicators (FreeAlert, Sensitech, TransTracker C, TempTime). A shake test was conducted on all DPT vials retrieved from the peripheral vaccine stores.

4.6. Approvals:

The study protocol was approved by the institutional ethics committee of the National Institute of Epidemiology. Permission to conduct the study was obtained from the Ministry of Health and Family Welfare, Govt of India and the health authorities in each study state. The Technical Advisory Group (TAG) consisting of experts from Ministry of Health and Family Welfare, Govt of India, Indian Council of Medical Research, UNICEF and WHO was established prior to the study (Annex-1). The study protocol was reviewed and approved by the TAG during its meeting on 2nd December 2011. The findings of the study were reviewed by the TAG during its meeting on 3rd October 2012.

5. RESULTS

The 40 dataloggers recorded temperatures over a total of 138 476 hours. The total time of observations during the storage and transportation of the vaccine is given in Table 3. The temperature data recorded while the test boxes were in vaccine stores and in transit accounted for > 99% and < 1% of this total time, respectively.

Table 3: Total hours of observation at different levels in vaccine cold chain

Location	Total hours of observation	Percentage
State Vaccine Store	44630.5	32.2
Regional Vaccine Store	18260.5	13.2
District Vaccine Store	34680.0	25.0
Primary/Community Health Centre	39,948.0	28.8
Transportation of the vaccine	957.0	0.7
Total	**138,476.0**	**100**

5.1. Proportions of boxes exposed to sub-optimal temperatures

During their storage at state and regional vaccine stores, 11% (4/36) and 26% (5/19) of the test boxes were exposed to subzero temperatures while 89% and 58% of the boxes were exposed to temperatures of > 8°C, respectively (Table 4). The corresponding proportions at peripheral vaccine stores were 63% (25/40) and 88% (35/40), respectively. During their transportation – and depending on the level of the cold chain at which the transport began – 18–36% of the test boxes were exposed to subzero temperatures and 0–66% were exposed to temperatures of > 8°C (Table 4).

Table 4: Number of study boxes exposed to freezing and high temperatures during storage or transportation of vaccines, India

Distribution stage	No. of test boxes (%)		
	Monitored	Exposed to temperature of < 0°C	Exposed to temperature of > 8°C
Vaccine storage			
State vaccine store	36	4 (11)	32 (89)
Regional vaccine store	19	5 (26)	11 (58)
District vaccine store	36	8 (22)	15 (42)
Community or primary health centre	40	25 (63)	35 (88)
Vaccine transportation			
State to regional store	15	5 (33)	2 (13)
State to district store	19	6 (32)	8 (42)
Regional to district store	17	3 (18)	6 (35)
District store to community or primary health centre	35	8 (23)	6 (17)
Community health to primary health centre	14	5 (36)	0 (0)
Other route	3	1 (33)	2 (66)

5.2. Temperatures at the vaccine stores:

5.2.1. Temperatures at the state vaccine stores (Table 5)

The total monitoring time at the state vaccine stores in different states was 44, 630.5 hours. Exposure to below zero temperatures was recorded at the SVS, Tamil Nadu for 660.5 hours which amounted to about 11% of the time the data loggers were at this location (Fig 2). None of the other state vaccine stores recorded exposure to sub-zero temperatures.

Exposure to temperatures above 8^0C was recorded at the state vaccine store Manipur (Fig 3), Madhya Pradesh, Bihar, Karnataka, Andhra Pradesh, for 83.3%, 28.8%. 16.6%, 6.6% and 6% of the total time of the observation at the respective state stores (Table 5).

Overall, the temperatures at the state vaccine stores ranged between 2-8^0C for about 79% of the total time, and were exposed to sub-zero temperatures and higher than recommended temperatures for 1.5% and 14.3% of the time respectively.

Table 5: Temperatures during storage at state vaccine stores

States	Total hours of observation	Percentage of observation period at different temperatures (^{0}C)				Temperature range
		<=-0.1	0-1.9	2-8	>8	
Andhra Pradesh	6770	0	0.0	94.0	6.0	2.3 to 10.6
Arunachal Pradesh	3082	0	0.0	98.1	1.9	3 to 14.2
Bihar	4733.5	0	0.6	82.8	16.6	1 to 16.2
Gujarat	–	–	–	–	–	–
Himachal Pradesh	4855.5	0	0.0	99.8	0.2	3.8 to 17.4
Karnataka	4351	0	1.5	91.9	6.6	0.2 to 15.1
Madhya Pradesh	4522	0	0.1	71.1	28.8	1.7 to 16.9
Manipur	4211.5	0	0.0	16.7	83.3	3.8 to 17.5
Tamil Nadu	6147	10.7	35.4	53.9	0.0	-2.1 to 5.1
West Bengal	5958	0	0.4	98.9	0.7	1.4 to 17.9
All states	**44630.5**	**1.5**	**5.1**	**79.1**	**14.3**	**-2.1 to 17.9**

(– indicates n*o state vaccine store)*

Fig 2: Temperatures during the storage at State Vaccine Store, Tamil Nadu, 10 Feb-16 April 2012

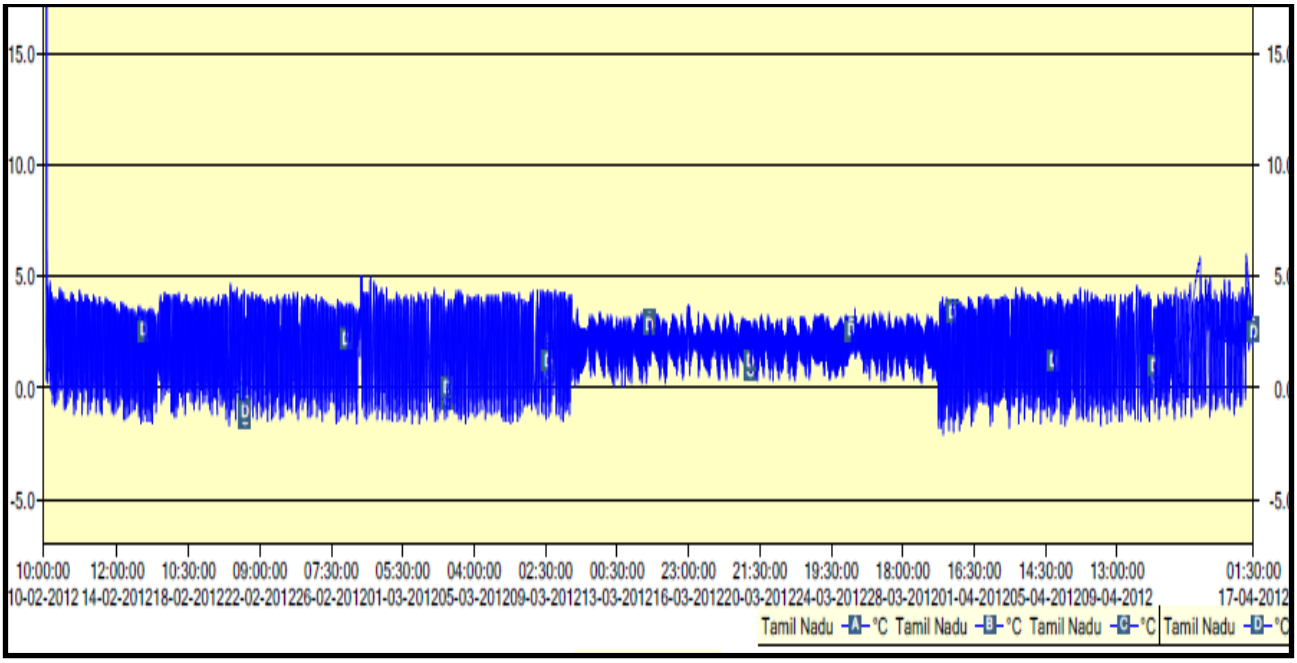
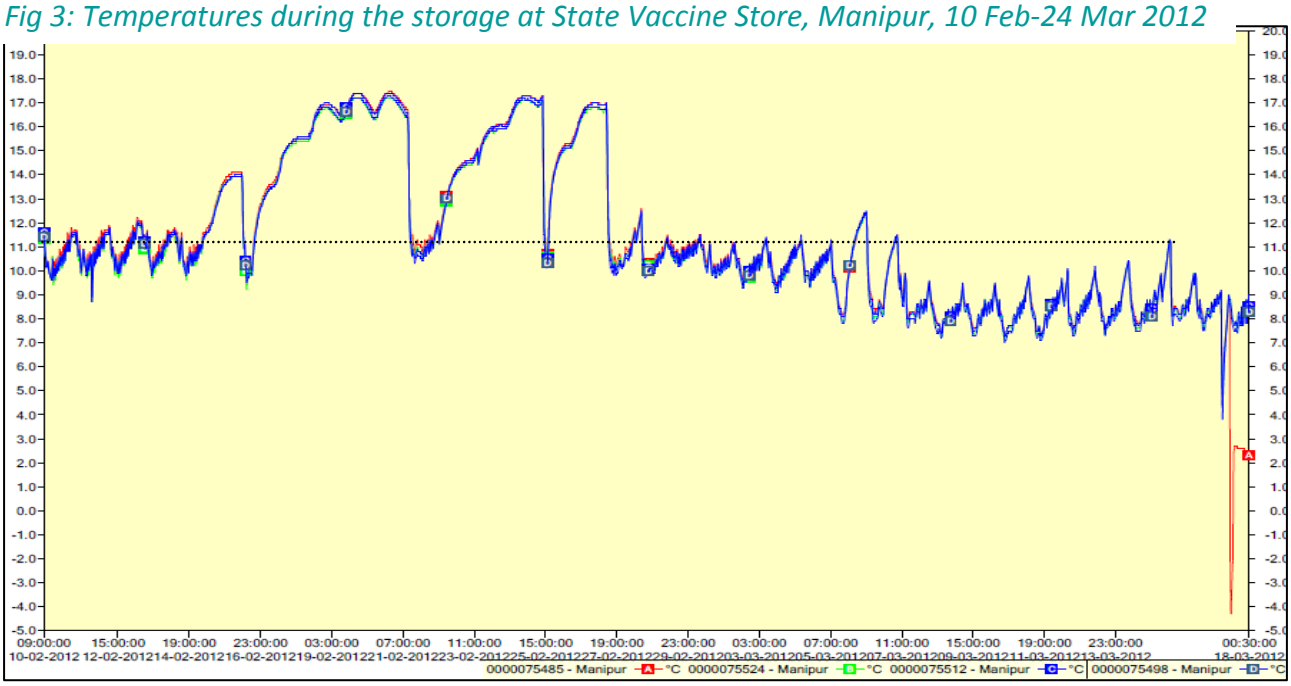


Fig 3: Temperatures during the storage at State Vaccine Store, Manipur, 10 Feb-24 Mar 2012



5.2.2. Temperatures at the Regional vaccine stores (Table 6)

Of the 18260.5 hours of observation at the regional vaccine stores in different states, temperatures below zero temperatures was recorded for 27.5 hours (0.2% of the total time) while the temperatures were above 8^0C for 2410 hours (13.2%). Exposure to sub-zero temperature occurred at the stores in Tamil Nadu and Karnataka respectively for 0.7% and 0.2% of the total time of observations while the temperatures above 8^0C were recorded at the RVS, Himachal Pradesh (51.3%, Fig 5), Karnataka (3.5%), Madhya Pradesh (0.3%) and Andhra Pradesh (0.1%) (Fig 4).

Table 6: Temperatures during storage at regional vaccine stores

	Total hours of observation	Percentage of observation period at different temperatures (^{0}C)				Temperature range
		<0	0-1.9	2-8	>8	
Andhra Pradesh	1769	0.0	56.4	43.4	0.1	0.3 to 9.8
Arunachal Pradesh	–	–	–	–	–	–
Bihar	–	–	–	–	–	–
Gujarat	3557	0.0	29.7	70.3	0.5	1.2 to 8.3
Himachal Pradesh	4465.5	0.03	5.7	43.0	51.3	-3.6 to 15
Karnataka	3176	0.2	3.5	92.8	3.5	-2.2 to 18.7
Madhya Pradesh	2359	0.0	3.2	96.6	0.3	1.3 to 11.4
Manipur	–	–	–	–	–	–
Tamil Nadu	2934	0.7	20.0	79.3	0.0	-0.8 to 7.1
West Bengal	–	–	–	–	–	–
Overall	18260.5	0.2	16.9	69.8	13.2	-3.6 to 15

(– indicates no *regional vaccine store at these states)*

Fig 4: Temperatures during storage of test boxes at Regional vaccine stores

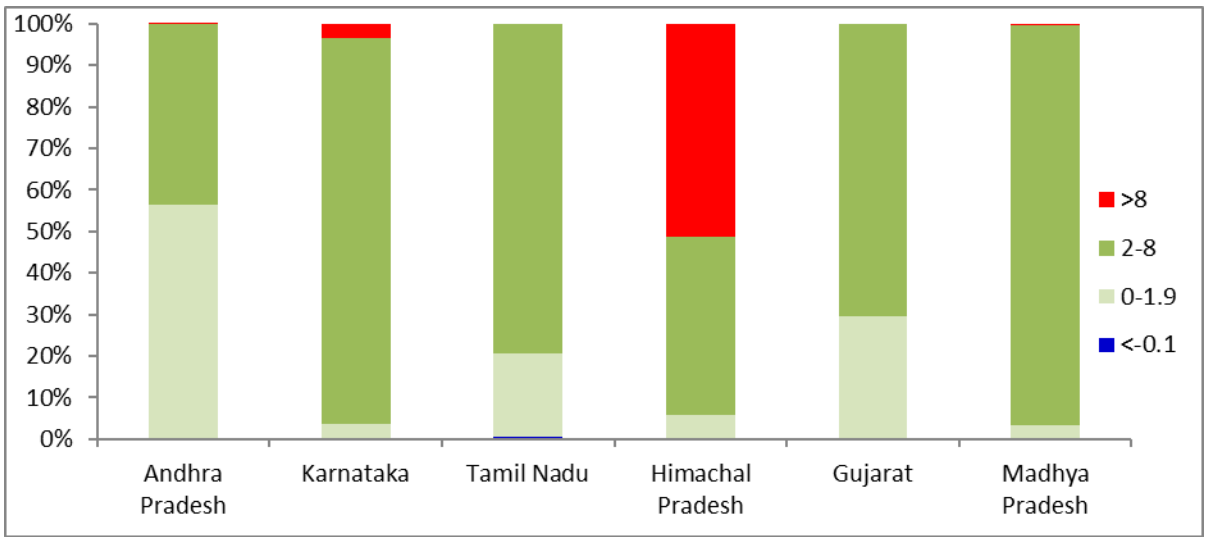
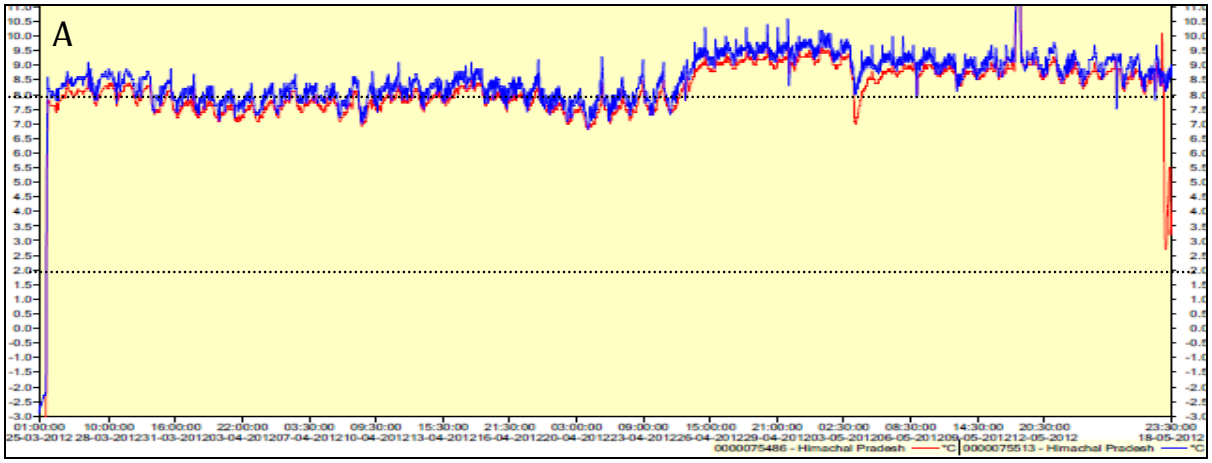
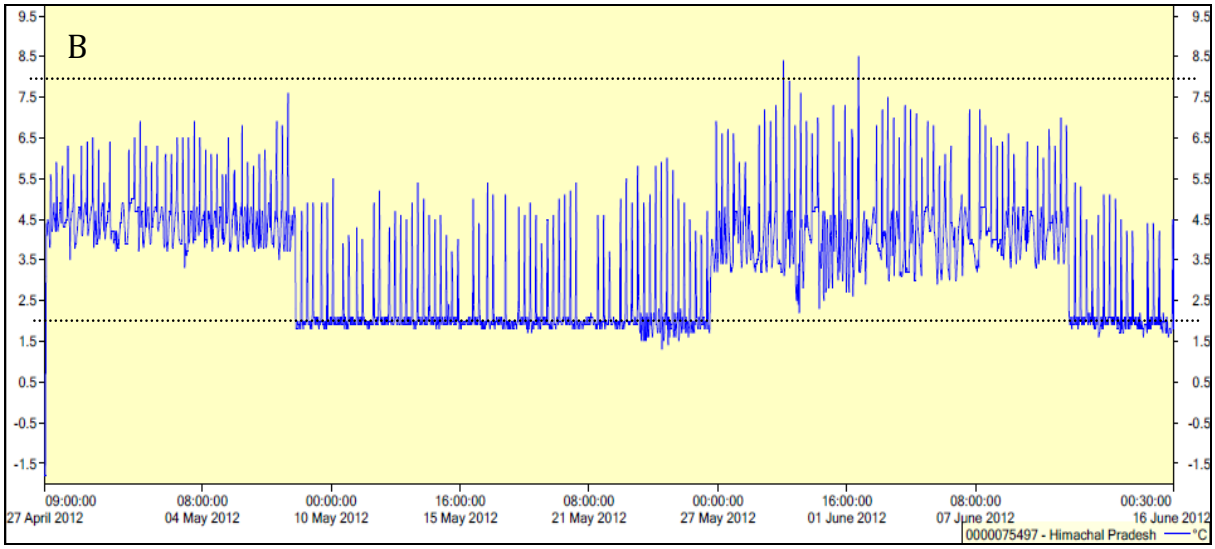


Fig 5: Temperatures during the storage at Regional Vaccine Stores: (A) Dharmasala, (B) Mandi





5.2.3. Temperatures at the District vaccine stores (Table 7)

The data loggers were at the district vaccine stores for 34,680 hours. Of the total hours of observation, exposure to sub-zero temperature was recorded for 205 hours (0.6%) while temperature above 8^0C was recorded for 2866 (8.3%) hours. The DVS at Bihar, Arunachal Pradesh, West Bengal and Andhra Pradesh recorded the temperatures above the recommended limits (Fig 6). The temperature at the two district vaccines stores in Bihar is presented in fig 7.

Table 7: Temperatures during storage at district vaccine stores

States	Total hours of observation	Percentage of observation period at different temperatures (^{0}C)				Min Max
		<-0.1	0-1.9	2-8	>8	
Andhra Pradesh	3164	0.0	0.3	96.4	3.3	1.6 to 14.4
Arunachal Pradesh	5576.5	3.1	14.8	74.7	7.4	-2.7 to 16.9
Bihar	4652.5	0.0	0.0	51.0	49.0	1.8 to 24
Gujarat	3576	0.0	0.0	100.0	0.0	2.6 to 7.9
Himachal Pradesh	745	0.0	0.0	100.0	0.0	2.1 to 4.6
Karnataka	3366.5	0.0	3.1	96.9	0.0	0.7 to 10.2
Madhya Pradesh	4273	0.0	7.0	93.0	0.0	0.1 to 9.2
Manipur	2323	0.1	23.7	76.2	0.0	-0.4 to 7.1
Tamil Nadu	2956	0.0	3.2	96.8	0.0	0.5 to 5.5
West Bengal	4047.5	0.8	4.5	93.0	1.7	-2.4 to 18.2
Overall	34680	0.6	6.0	85.2	8.3	-2.7 to 18.2

Fig 6: Temperatures during storage of test boxes at District vaccine stores

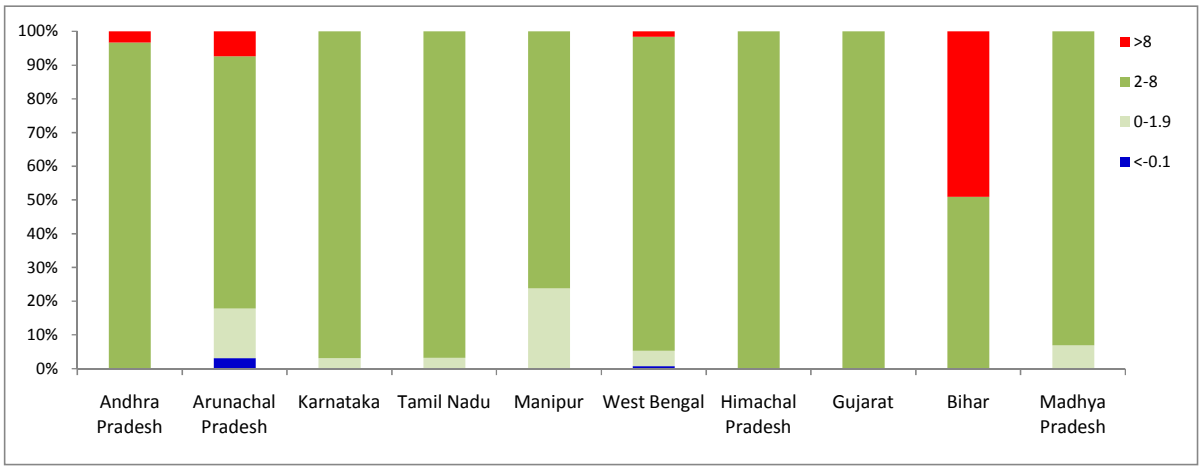
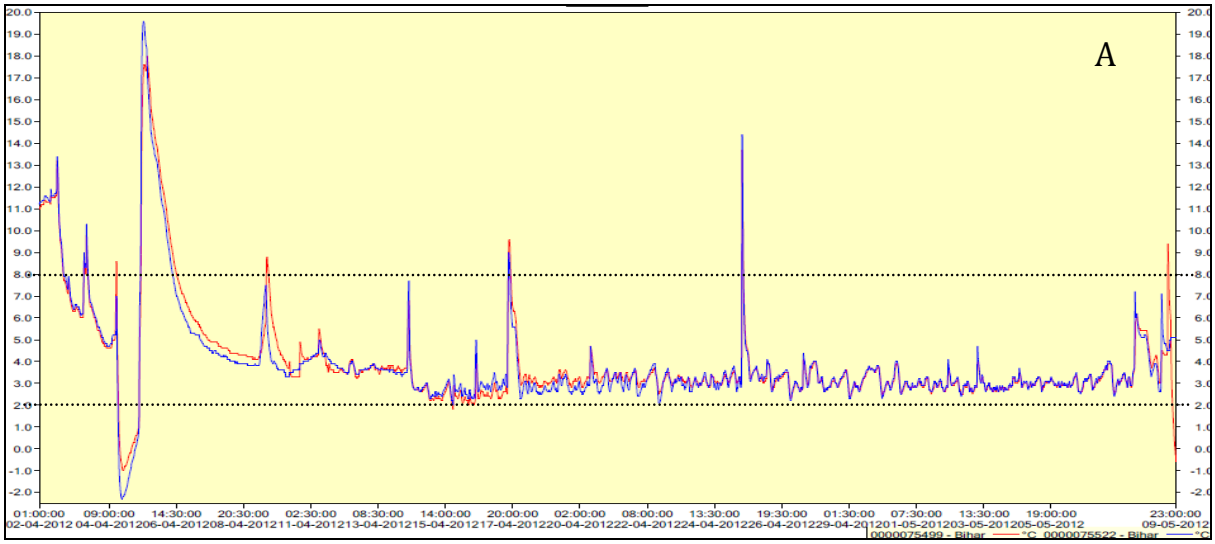
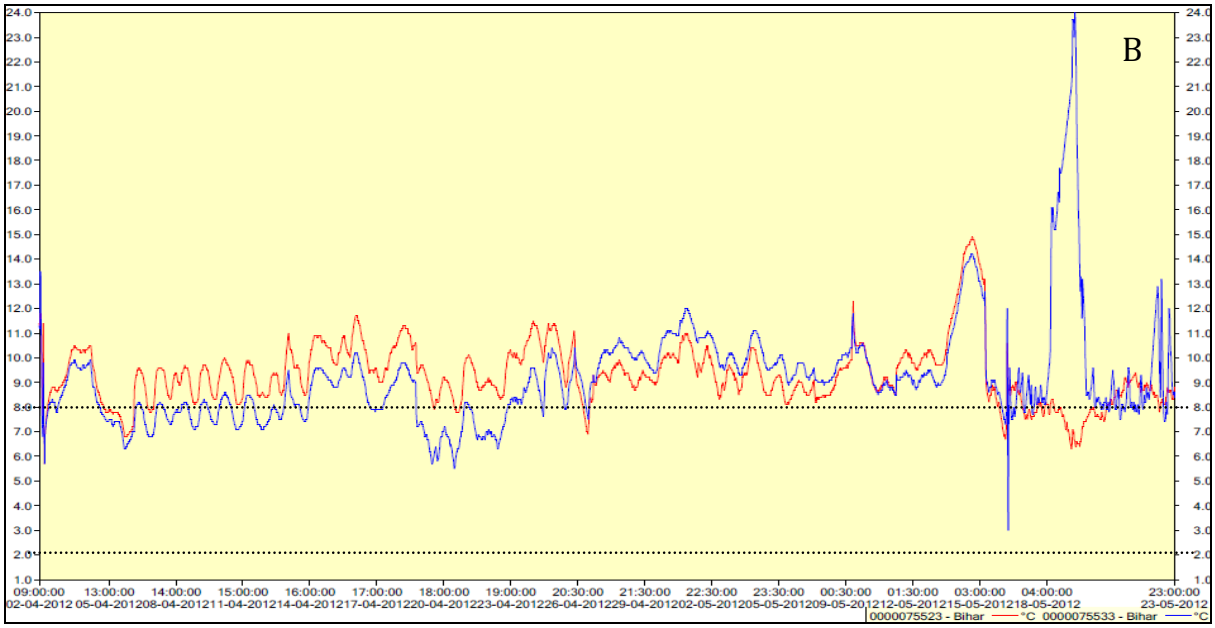


Fig 7: Temperatures during the storage at the district Vaccine Stores, Bihar: (A) Khagaria, (B) Gaya





5.2.4. Temperatures at the vaccine stores at primary health centre/community health centres

During the 39,948 hours of observation at the vaccine stores at CHC/PHCs in 10 states, exposure to freezing temperatures was recorded for 4200 hours (10.5%) while temperatures above 8^0C was recorded for 5866 (14.7%) hours (Table 8). The exposure to temperatures below zero degrees was recorded in all the 10 states at CHC/PHCs for a variable amount of time, ranging from less than 1% of the time Tamil Nadu, Arunachal Pradesh and Manipur to 38.4% of the total time at these stores at Andhra Pradesh. The vaccines stores at the PHC/CHCs in Manipur (41% of the total time at CHC/PHC), Bihar (40% of the total time) and Madhya Pradesh (17%) were exposed to temperatures above 8^0C for a considerable amount of time (Table 8).

Table 8: Temperatures during storage at community health centre/primary health centre

States	Total hours of observation	Percentage of observation period at different temperatures (^{0}C)				Temperature range
		<-0.1	0-1.9	2-8	>8	
Andhra Pradesh	2074	38.4	21.9	37.5	2.2	-10.3 to 16.1
Arunachal Pradesh	2711	0.2	4.2	92.5	3.1	-4.1 to 22.1
Bihar	6056.5	2.6	20.1	37.8	39.5	-1.9 to 30.6
Gujarat	4404.5	11.4	26.3	61.0	1.3	-4.8 to 26.9
Himachal Pradesh	4527.5	4.8	55.8	37.9	1.5	-6.5 to 18.5
Karnataka	4121.5	21.6	16.1	62.1	0.2	-8.2 to 16.6
Madhya Pradesh	4770	11.4	26.4	44.9	17.4	-8.9 to 14.7
Manipur	5462	0.7	5.6	53.1	40.6	-6.4 to 27.8
Tamil Nadu	2060	0.2	42.3	57.5	0.0	-2.6 to 5.3
West Bengal	3761	27.8	11.6	56.2	4.4	-21.3 to 30.6
Overall	39948	10.5	22.5	52.3	14.7	-21.3 to 30.6

5.3. Temperatures during transit

Temperatures during transit between vaccine stores were recorded for a total of 957 h. Exposures to temperatures of < 0 and > 8°C were recorded for 173.5 (18.1%; 95%CI: 15.8–20.8) and 69.5 h (7.3%; 95% CI:5.8–9.2) in transit, respectively. Exposure to subzero temperatures was particularly frequent during the shipment of the vaccines in Himachal Pradesh (52.2% of transit time), Manipur (25.9%), Arunachal Pradesh (23.6%) and Bihar (18%), whereas exposure to a temperature of > 8°C during transit was most common in Bihar (23.3% of transit time) and Andhra Pradesh (16.2%) (Table 9).

Table 9: Temperatures during transport of vaccines from vaccine stores

States	Total hours of observation	Percentage of observation period at different temperatures (^{0}C)				Temperature range
		<-0.1	0-1.9	2-8	>8	
Andhra Pradesh	89.5	0.0	6.7	77.1	16.2	2.7 to 14.1
Arunachal Pradesh	101.5	23.6	65.0	11.3	0.0	-5.8 to 7.8
Bihar	122.5	18.0	13.5	45.3	23.3	-2.3 to 16.1
Gujarat	52	0.0	30.8	69.2	0.0	0.5 to 7.6
Himachal Pradesh	189.5	52.2	10.3	32.2	5.3	-9.1 to 20.2
Karnataka	76	8.6	47.4	37.5	6.6	-15 to 13.5
Madhya Pradesh	35.5	12.7	43.7	35.2	8.5	-7.2 to 9.6
Manipur	13.5	25.9	11.1	63.0	0.0	-4.3 to 7.8
Tamil Nadu	145.5	8.2	45.4	46.4	0.0	-6.7 to 6
West Bengal	131.5	1.5	38.4	53.6	6.5	-0.9 to 15.8
Overall	957	18.1	30.7	43.9	7.3	-15 to 20.2

5.4. Temperatures during the outreach session

The temperature during transport of the vaccines from the last cold chain point (PHC/CHC) to the outreach session and till the completion of the vaccination session was monitored using Freeze Marker/TransTracker C. Freezing events were reported in 2 of the 40 outreach sessions monitored. Both the events were reported from the state of Tamil Nadu (Table 10).

Table 10: Freezing during the outreach vaccination session

State	Number of outreach sessions monitored	Number of freezing events
Andhra Pradesh	4	0
Arunachal Pradesh	4	0
Bihar	4	0
Gujarat	4	0
Karnataka	4	0
Madhya Pradesh	4	0
Manipur	4	0
Tamil Nadu	8	2
West Bengal	4	0

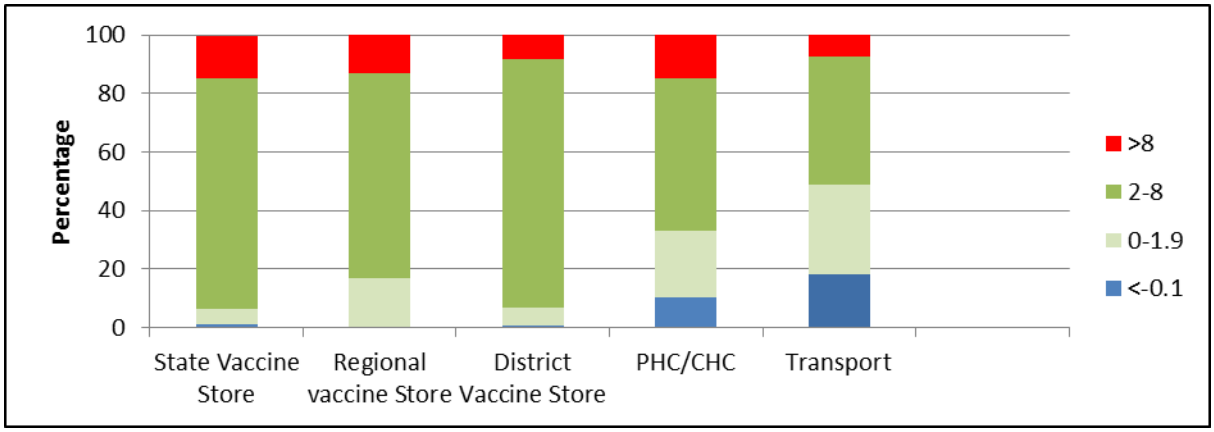
5.5. Summary of temperature monitoring during storage and transport

The findings of the temperature monitoring during the storage of data loggers at different vaccine stores and during their transport are summarized in the following table (Table 11, Fig 8). At the state vaccine stores, exposure to sub-zero temperature and temperature more than 8^0C was recorded respectively for 1.5% and 14.3% of the total time at these stores. At the regional and district vaccine stores, freezing occurred for less than 1% of the time, however exposure to higher temperature was recorded respectively for 13.2% and 8.3% of the total time of storage at the regional and district vaccine stores. At the last cold chain points as well as during the transport of the data loggers, both freezing and higher temperatures were frequently recorded. Freezing events were recorded only in Tamil Nadu during the conduct of the outreach sessions.

Table 11: Summary of temperature monitoring during storage and transport

	Total hours of observation	Total duration (%) in hours at different temperatures			
		<-0.1	0-1.9	2-8	>8
State Vaccine Store	44630.5	660.5	2293.5	35276.5	6400.0
	(32.2)	(1.5)	(5.1)	(79.0)	(14.3%)
Regional vaccine Store	18260.5	27.5	3084.0	12739.0	2410.0
	(13.2)	(0.2)	(16.9)	(69.8)	(13.2)
District Vaccine Store	34680.0	205.0	2065.0	29544.0	2866.0
	(25.0)	(0.6)	(6.0)	(85.2)	(8.3)
PHC/CHC	39,948.0	4200.5	9000.0	20881.5	5866.0
	(28.8)	(10.5)	(22.5)	(52.3)	(14.7)
Transport	957.0	173.5	293.5	420.5	69.5
	(0.7)	(18.1)	(30.7)	(43.9)	(7.3)
Overall	138476.0	5267.0	16736.0	98,861.5	17611.5
	(100)	(3.8)	(12.1)	(71.4)	(12.7)

Fig 8: Summary of temperature monitoring during storage and transport



5.6. Consecutive exposure below zero degrees

"Continuous spells" – that is, periods that covered at least two consecutive readings by a datalogger – accounted for about 85% of the exposure to subzero temperatures (Table 12) and 94% of the exposure to temperatures of > 8°C (Table 13) that we recorded.

Table 12: Spells of continuous exposure of vaccines to temperatures of <0°C, India, 2012

State	Exposure to temperatures of < 0°C					
	Total duration (h)	Continuous spells[a]				
		Combined duration (hours)	Total number	Number of spells lasting:		
				≤ 1 h	2–9 h	≥ 10 h
Andhra Pradesh	796.5	786.0	23	2	6	15
Arunachal Pradesh	200.5	166.5	55	9	44	2
Bihar	181.5	134.5	63	35	26	2
Gujarat	503.5	487.5	20	1	4	15
Himachal Pradesh	316.0	254.5	58	42	6	10
Karnataka	903.5	871.5	44	23	3	18
Madhya Pradesh	547.0	517.0	54	15	24	15
Manipur	41.0	34.0	14	4	10	0
Tamil Nadu	697.0	113.0	178	168	10	0
West Bengal	1080.5	1041.0	56	15	24	17
All 10 study states	**5267.0**	**4404.5 (83.6%)**	**565**	**314**	**157**	**94**

[a]*A "continuous spell" at < 0°C was indicated by a datalogger that showed two or more consecutive readings of < 0°C.*

Table 13: Spells of continuous exposure of vaccines to temperatures of >8°C, India, 2012

State	Exposure to temperatures of > 8 °C					
	Total duration (h)	Continuous spells[a]				
		Combined duration (hours)	Total number	Number of spells lasting:		
				≤ 1 h	2–9 h	≥ 10 h
Andhra Pradesh	573.5	468.5	78	24	33	21
Arunachal Pradesh	557.5	491.0	39	4	17	18
Bihar	5488.0	5368.5	194	50	69	75
Gujarat	56.5	53.5	4	1	2	1
Himachal Pradesh	2374.5	2256.5	141	49	59	33
Karnataka	410.0	357.5	70	38	26	6
Madhya Pradesh	2140.5	1833.5	662	490	135	37
Manipur	5726.5	5514.5	249	44	104	101
Tamil Nadu	0.0	0.0	0	0	0	0
West Bengal	284.5	239.5	45	23	14	8
All 10 study states	**17 611.5**	**16□583.0 (94.2%)**	**1482**	**723**	**459**	**300**

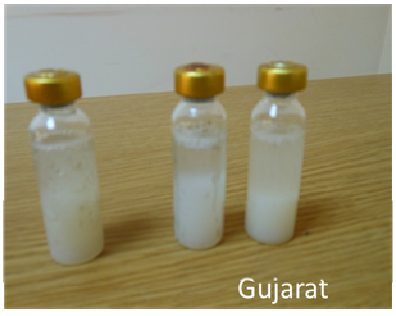
[a]*A "continuous spell" at > 8°C was indicated by a datalogger that showed two or more consecutive readings of > 8°C.*

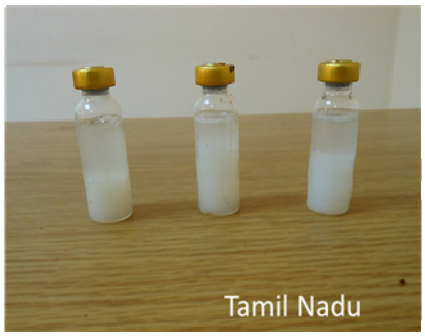
5.7. Shake test

Of the 80 DPT vaccine vials sent along with the 40 test boxes for temperature monitoring, 67 were returned to NIE. Of the 67 vials subjected to shake test, 51 (76%) failed the test indicating damage to the vaccine due to freezing (Table 14).

Table 14: Results of the Shake test

State	Number of DPT vials tested	Number of vials failed
Andhra Pradesh	8	7
Arunachal Pradesh	1	0
Bihar	6	2
Gujarat	8	2
Himachal Pradesh	8	8
Karnataka	8	6
Manipur	8	6
Madhya Pradesh	4	4
Tamil Nadu	8	8
West Bengal	8	8
Overall	67	51 (76%)





5.8. Findings of temperature monitoring with other freeze event indicators:

Each study box had two freeze event indicators (Freeze Alert and Trans Tracker) besides the data loggers. The findings of freeze event indicators were read at the end of the study. Thirty four of the 40 data loggers recorded temperatures below zero degrees at any point during the study. Thirty one Freeze Alert indicator and equal number of Trans Tracker showed evidence of freezing (Table 15).

Table 15: Findings of the temperature monitoring using Freeze event indicators

State	Data loggers		Freeze Alert (# frozen)	Trans Tracker (# frozen)
	Number	Temp <0 deg		
Andhra Pradesh	4	4	3	3
Arunachal	4	4	3	3
Bihar	4	2	2	2
Gujarat	4	2	1	1
Himachal Pradesh	4	4	4	4
Karnataka	4	3	3	3
Madhya Pradesh	4	4	4	4
Manipur	4	3	3	3
Tamil Nadu	4	4	4	4
West Bengal	4	4	4	4
Overall	40	34	31	31

5.9. Knowledge of the Cold chain handlers, temperature monitoring and equipment maintenance:

5.9.1. Knowledge of the cold chain handlers:

We interviewed 127 cold chain handlers (CCH) working at different cold-chain points. Majority of them had correct knowledge about the storage range of temperatures for each vaccine (112, 88%), and most (108, 85%) could correctly tell the names of the freeze sensitive vaccines. Eighty-two (65%) of them told that they had received hand-on training on CCH module. None of the CCH from Himachal Pradesh had received hand-on training on CCH module.

5.9.2. Temperature monitoring and recording

Various devises were used for temperature monitoring at different levels in the cold chain. The salient findings are summarised below:

Temperature monitoring

- The temperature monitoring at five state vaccine stores (Andhra Pradesh, Bihar, Madhya Pradesh, Tamil Nadu, West Bengal) was done using wireless data-loggers (Cobalt-60). At the SVS at Arunachal Pradesh, Manipur, Himachal Pradesh and Karnataka, manual methods (such as external panel display and/or dial thermometers) were used for temperature monitoring.
- In the RVS, DVS and CHC/PHCs, temperatures were monitored using one or more of the following devices: graphic trace recorder, stem/dial/digital thermometer, external panel display.
- There was no evidence that any of the devices used for routine temperature monitoring in the vaccine stores had ever been calibrated.

Availability of temperature records

- The records of temperature monitoring were available at all the SVS (except Manipur), and RVS. No records of temperature monitoring were available at the DVS West Bengal, DVS Himachal Pradesh and the one of the four last cold chain points in Manipur, West Bengal and Himachal Pradesh.

Review of temperature records by CCH

- Across all the states, there was no evidence to show that these records were routinely reviewed to identify any deviations from the recommended temperatures. Almost all of the routine records of temperature indicated values of 2–8°C.
- At the SVS, Tamil Nadu the exposure to sub-zero temperature was also recorded by wireless data loggers. However this data was not reviewed.

5.9.2.1. Equipment maintenance

The salient findings about the maintenance of cold chain equipment are summarized below:

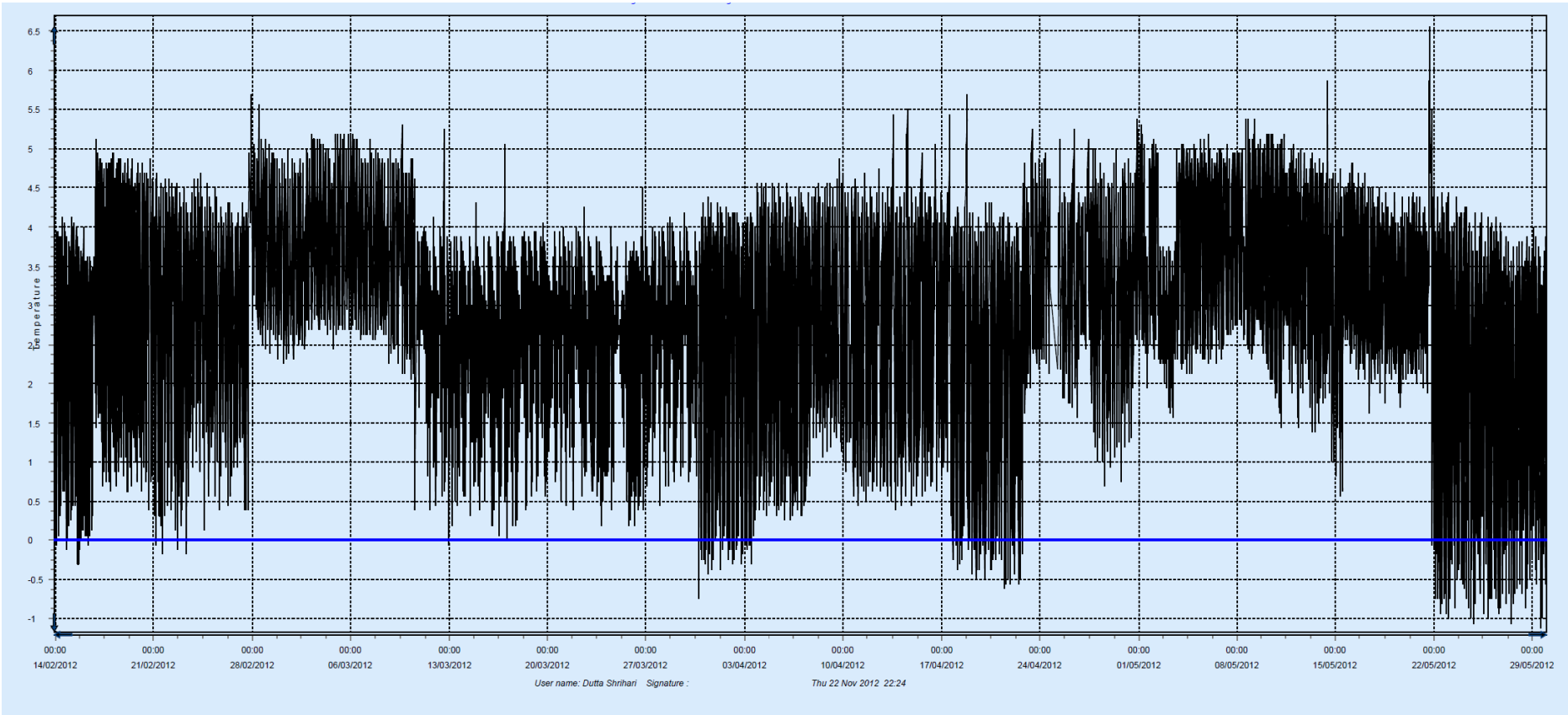
- The equipment maintenance at State/Regional stores, Karnataka, Himachal Pradesh and West Bengal was outsourced to the private sector while in the remaining states, the maintenance was in house. For the states where maintenance was outsourced, the cold chain technicians periodically visited these stores, though the frequency of their visits varied greatly. Most of the CCH informed that the response time for repair was less than 24 hours while the downtime to repair depended on the type of problem and ranged between less than 24 hours to 1-2 weeks for major problem.
- For states having maintenance outsourced, the visits of cold chain technicians to district and sub-district level facilities were highly irregular.

- The frequency of de-frosting of ILR at the district vaccine stores was variable, ranging from once a week to once a month. The DVS at Manipur did not have a fixed frequency of de-frosting the ILR.
- In Tamil Nadu, there was a shortage of CC Technicians for maintenance of cold chain equipment.
- The median age of the walk in cooler at the state/regional vaccine stores was 12 years (range: 2 to 27 years) while the median age of ILR was 11 years (range: 1-23 years)
- Irregular power supply was a major issue in all the states especially Manipur, Bihar, Madhya Pradesh and Tamil Nadu. Some CCH also mentioned about budgetary constrains in the purchase of POL required for running the generators.
- In Himachal Pradesh, cold boxes were over-filled with ice-packs by keeping additional ice-packs on the top of vaccine boxes.

5.10. Additional observations supporting the findings of the study

SVS, Chennai: A team from UNICEF, NIE and the State Immunization Officer visited the SVS, Chennai in September 2012. Review of the data of wireless data loggers from previous 3-4 months revealed frequent exposure to sub-zero temperature, a findings consistent with the present study (Fig 9). The team also identified technical issues with respect to the adjustment of thermostat as the probable reason for freezing temperatures. A shake test conducted on four pentavalent vaccines failed, indicating the damage to the vaccine due to freezing. It was suggested to shift the vaccines to another walk-in-cooler (WIC) maintaining the recommended temperatures.

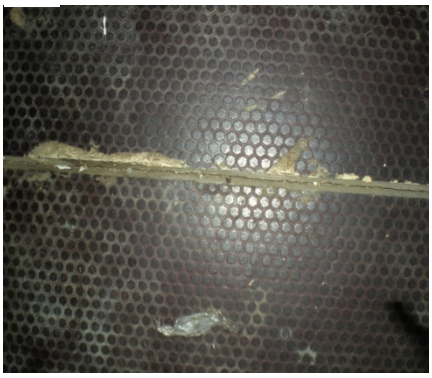
Fig 9: Data from wireless data logger, SVS, Chennai, Tamil Nadu, 14 Feb-29 May 2012



SVS, Manipur: Following the findings of exposure to high temperatures at the SVS, Manipur, the co-investigator along with the state Immunization Officer visited the state store. During their inspection, several gaps in the plates of WIC were detected. These gaps were sealed subsequently.

Picture showing the gaps in the (A) floor, (B) roof and (C) walls of the walk-in-cooler at SVS, Manipur

A



B

C

6. LIMITATION

Our study had certain limitations. First, the temperatures during the transport of the vaccine from peripheral stores to outreach sessions were monitored using freeze event indicators and not using the data loggers. Second, although the data loggers were exposed to higher temperatures (>8^{0}C), we were not able document if these had damaged the vaccine as the labels (including the VVMs) on the test vials were removed. We made no attempt to test the potency of the vaccine in each of the vials in the test boxes at the end of the study. Third, all of the DPT vials used in the study had been procured from the state vaccine store in Tamil Nadu – the only state vaccine store where our dataloggers recorded subzero temperatures. Although shake testing of these DPT vials indicated that none had been frozen before the start of our study, it remains possible – and perhaps probable – that they had already been exposed to subzero temperatures at that stage. The high number of DPT vials that failed the shake test at the end of our study may therefore have reflected the cumulative effect of exposures to subzero temperatures in the cold-chain system during our study and similar exposures at the state vaccine store at Tamil Nadu before the study began.

7. CONCLUSIONS

- Exposure to freezing temperature was frequent at the peripheral health facilities as well as during the transport of vaccines whereas exposure to higher temperatures was common at all the levels of the cold chain.
- Though the vaccines were in transit for a small proportion of time in the cold chain, exposure to sub-zero temperature was high during the transportation.
- In several state/regional vaccine stores, temperatures were monitored using manual methods. The temperature monitoring data was not regularly reviewed to identify exposure to sub-optimal temperatures. Records of manual temp recording did not match with the readings of data loggers.
- The temperature monitoring devices in the cold chain were never calibrated.
- Long hours of power cut, shortage of trained CCH affected the maintenance of cold chain.

8. RECOMMENDATIONS (Box-1)

1. Identify the reasons for temperature excursions (freezing and/or exposure to higher temperatures) at the state and regional vaccine stores.
   - *This would involve visit by the technical team to the SVS, Andhra Pradesh, Bihar, Karnataka, Madhya Pradesh, Manipur and Tamil Nadu and the RVS, Himachal Pradesh (Dharmasala) to identify reasons related to cold chain equipment and its maintenance at the state and regional vaccine stores leading to temperature excursions and temperature mapping of the cold rooms*
2. Ensure that the temperatures of the state and regional vaccine stores are recorded using a digital method or graphic chart recorder and reviewed regularly
   - *All state and regional vaccine stores with WIC storing bulk vaccines should have real time data logging system with remote viewing option.*
   - *State EPI/immunization Officer/Cold Chain Officer needs to ensure temperature recording of WIC using digital methods and regularly review the temperature monitoring and take corrective action for any temperature excursions.*
3. Improve the temperature monitoring at the District and sub-district levels
   - *To ensure this, it is necessary to (a) calibrate the temperature monitoring devices regularly, (b) Train the state/regional vaccine store team on calibration of CCE and (c) strengthen supervision of cold chain staff*
4. Introduce newer WHO PQS devices for recording the temperatures (especially the freezing) during shipment.
5. Conduct refresher training for the CCH
   - *Emphasis should be given on (1) periodic de-frosting of ILR, (2) conditioning of Ice packs, and (3) packaging of vaccines during the transportation.*
6. Update cold-chain infrastructure by replacing old cold chain equipments
7. Consider the use of alternate source of electricity as a power back up in areas with frequent power cuts.
8. Generate more information on how vaccines are transported and use temperature monitoring devices to detect freezing or exposure to heat.

Box-1: Key issues in vaccine cold chain in India and proposed recommendations

Level of cold chain	Issues	Recommendations
State and regional vaccine stores	• Exposure to sub-zero or high temperatures during storage	• Identify reasons for temperature deviations and fix the cause with highest priority • Undertake regular review of temperature monitoring records • Install real time temperature monitoring devices • Do calibration of Thermostat, Thermometers and other monitoring devices • Sensitize store and programme managers on temperature monitoring and action to be taken in case exposure to sub-optimal temperature is recoded
	• Manual method of temperature monitoring	• Ensure that the temperatures are recorded using digital method at least two times daily • Ensure functionality of graphic chart recorder that records automatic temp recording 24X7 of the WIC/WIF • Consider using acoustic alarm in all WIC/WIF to alert store and programme manager when vaccine has reached unsafe temperature range
District and sub-district vaccine stores	• Temperature monitoring devices not calibrated	• Calibrate the temperature monitoring devices regularly • Train the state/regional/district vaccine store team on calibration of cold-chain equipments
Sub-district vaccine stores	• Exposure to sub-zero or high temperatures during storage • ILR not defrosted regularly • Cold chain equipments are old	• Check the equipment setting as per the season • Check equipment functionality by the trained technician • Twice daily temperature recording and validation of these recording through of 30 days electronic Data loggers • Refresher training with focus on periodic de-frosting of ILR • Fixed day schedule for ILR defrosting • Review temperature monitoring records weekly/monthly
	• Long hours of power cut or low voltage	• Provide at least 8hrs electricity through alternate source i.e. generator, UPS, Inverter • Consider use of solar equipment for areas with inadequate power supply (<8 hrs in a day)

All levels	• Records of temperature monitoring not reviewed	• Review temperature records regularly; weekly /monthly
	• Records of manual temp recording did not match with the readings of data loggers	• Strengthen supervision of cold chain monitoring
	• Exposure to sub-zero and high temperature during transportation of the vaccine	• Refresher training emphasizing on packaging of vaccines (method of packing the vaccine, insulating the packed boxes for transportation) and conditioning of ice packs • Use temp monitoring devices to detect freezing • Generate more information on how vaccine are transported

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