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# A vaccine cold chain freezing study in PNG highlights technology needs for hot climate countries

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**Abstract**

Fourteen data loggers were packed with vaccine vials at the national vaccine store, Port Moresby, Papua New Guinea (PNG), and sent to peripheral locations in the health system. The temperatures that the data loggers recorded during their passage along the cold chain indicated that heat damage was unlikely, but that *all vials* were exposed to freezing temperatures at some time. The commonest place where freezing conditions existed was during transport. The freezing conditions were likely induced by packing the vials too close to the ice packs that were themselves too cold, and with insufficient insulation between them. This situation was rectified and a repeat dispatch of data loggers demonstrated that the system had indeed been rectified. Avoiding freeze damage becomes even more important as the price of freeze-sensitive vaccines increases with the introduction of more multiple-antigen vaccines. This low-cost high-tech method of evaluating the cold chain function is highly recommended for developing and industrialized nations and should be used on a regular basis to check the integrity of the vaccine cold chain. The study highlights the need for technological solutions to avoid vaccine freezing, particularly in hot climate countries.


*Keywords:* Data logger; Cold chain; Vaccine vial; Vaccine store; Freezing-sensitive vaccine

## 1. Introduction

Global immunization coverage for DTP-3[1] has risen to 78% [1], resulting in increasing numbers of lives saved and disease episodes averted. However, the impact of this increased coverage will be blunted if vaccines administered are not potent at the moment of use. The tremendous effort expended in reaching children with immunizations services will be lost if vaccines are improperly handled so that they are damaged by incorrect temperature maintenance. Improperly maintained or outdated refrigeration equipment, poor compliance with cold chain procedures, inadequate monitoring and poor understanding of the dangers of vaccine freezing contribute to the weakness of the existing cold chain in many countries [2]. Emphasis has long been placed on keeping vaccines cold, with less attention devoted to prevention of vaccine damage from freezing. Published reports and field evidence now demonstrate that freezing of vaccines in the cold chain is commonplace, potentially resulting in the widespread delivery of vaccines whose potency has been compromised by the disassociation of antigen from the adjuvant. The World Health Organization (WHO) and manufacturer guidelines clearly state that adjuvant vaccines (hepatitis B vaccine, DTP, tetanus toxoid (TT) and *Haemophilus Influenzae* type B (Hib)) must not be exposed to freezing temperatures and should be stored at temperatures between 2 and 8 °C [3].

Freezing of vaccines containing diphtheria, tetanus, pertussis or hepatitis B antigens can compromise their immunological potency [4]. Low sero-conversion rates have been

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[1] DTP-3: third dose of diphtheria-tetanus-pertussis "triple vaccine".

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reported following episodes of vaccine freezing [5]. Vaccines should not be used if thought to have been frozen. Yet recent studies have found widespread freezing at many levels of the vaccine distribution system. These studies have been in hot climate countries such as Ethiopia [6], India [7,8], Indonesia [9], Iraq [10] and Malaysia [11]; mixed climate countries such as Australia [12–18], Taiwan [19] and Turkey [20]; and cooler countries. The first cold chain study in Europe was conducted in Hungary in 1990 [21], followed by studies in other cooler climate countries such as Canada [22], Kazakhstan [23], Mongolia [24], New Zealand [25], Rumania [26], United States [27–31], United Kingdom [32,33] and Ukraine [34]. The results of these studies were often surprising, revealing that freezing events were commonplace, even in industrialized countries (e.g. 70% of refrigerators were below freezing [30]).

For many years, the "shake test" has been used as an easy field guide to whether a liquid vaccine has become frozen. While it is still useful, it is clear that this test lacks the precision required for scientific assessment of the cold chain [35].

The Global Alliance for Vaccines and Immunization (GAVI) is actively supporting the introduction of combination vaccines into developing countries. These vaccines contain DTP and hepatitis B vaccines, both of which are liquid vaccines that are sensitive to freezing. Formally, multiple-antigen vaccines cost only a few cents per dose. Now, with the addition of Hep B and Hib and inactivated polio vaccine (IPV) to the combination vaccines and the possibility of pneumococcus and other antigen being added soon, the potential cost for each dose of combination vaccines has soared. Each dose is even more precious and will need to be handled correctly so that it is not wasted through heat/freezing damage or any other error.

In a recent study in Indonesia [9], Papua New Guinea's (PNG) nearest neighbour, it was found that 75% of hepatitis B vaccine shipments were exposed to freezing temperatures, potentially damaging a significant portion of this expensive vaccine. The study identified the segments of the cold chain primarily responsible for freezing, allowing Indonesia to focus corrective actions on specific equipment and procedures.

In PNG, the cold chain had fallen into considerable disrepair, and restoring it became a major priority of the Women's and Children's Health Project (1998–2004). Cold chain reviews in 2001 and 2002 suggested widespread heat damage to vaccines at all levels of distribution. The end-of-project report [36] noted that a large and positive impact had been made on the whole of the programme through ensuring the appropriate provision of cold chain equipment to virtually the whole country. Some gas cylinders and fridges were still needed. Refurbishing was not complete everywhere—15–20% of health centres did not have new equipment, but 95% had some form of functioning cold chain equipment. Only 5% had no equipment or their status was uncertain. The present study was the first to test scientifically how well the refurbished cold chain was functioning. It was also intended that the study should build capacity in national staff who managed the cold chain, raising their awareness of the importance of their jobs and enabling them to be become more robust in problem-solving in the future.

## 2. Method

The purpose of the study was to document if freezing occurred in the vaccine cold chain, and to identify specific problem areas where corrective actions might be warranted. In this study, the temperature of vaccine vials was monitored continuously as vaccine shipments traveled through the cold chain from the national store to the provincial stores, to health centres, and finally to the outreach delivery site.

The outcome was designed to demonstrate whether vaccines destined for use in the peripheral health units were being subjected to freezing temperatures, and to identify the precise locations where such freezing might be taking place. The study needed strong central coordination and the cooperation of many individuals along the vaccine distribution system. Guidelines for individual responsibilities, budgetary considerations and equipment requirements were drawn up. Five days of planning and design were conducted in December 2004 immediately prior to the first data collection.

The selection of end-of-the-line health centres was made in consultation with the provincial advisors for the cold chain. Health centres were chosen to provide as wide a range of conditions as possible while representing the approximate distribution of each criterion:

- Location—four provinces were arbitrarily selected: Oro, Sandaun, New Ireland and Chimbu.
- Method of transport from Provincial Vaccine Stores (PVSs): four by air, seven by road and two by boat.
- Method of transport from health centre to outstations was by road.
- Type of refrigeration: nine gas-powered, two solar-powered, two electric.
- Type of health centre—eight run by government and five by Church Health Services.

The study required the use of electronic temperature loggers to monitor temperatures. The data logger is a small cylindrical computer (the approximate size of a vaccine vial) that records temperatures at selected time intervals. Several continuous temperature monitoring devices were considered. This study selected the Gemini TinyTalk logger[2] to provide continuous temperature data, but other commercially available loggers could have been used. Recording accuracy was suggested by the manufacturers to be $\pm 1\ ^{\circ}C$. A computer was required to programme and download temperature information so that it could be analyzed and printed (Fig. 1).

[2] More details of this and other data loggers can be found in the WHO Product Information Sheets (PIS E6/43).

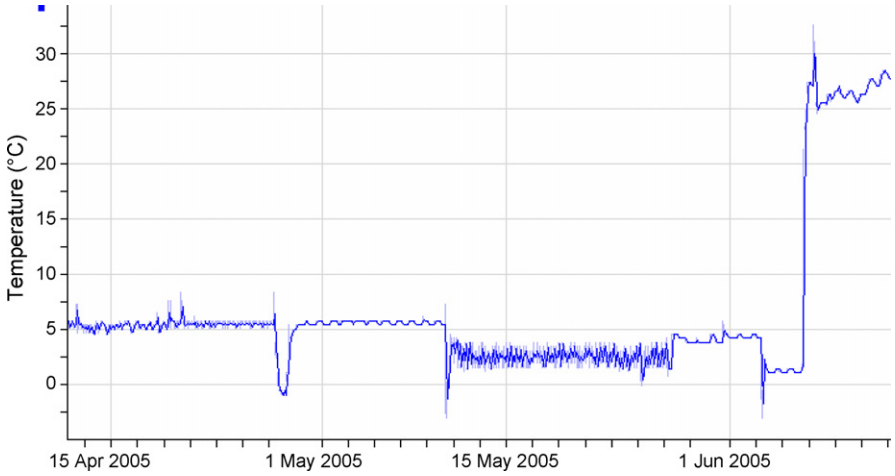


Fig. 1. Typical logger data.

Using a computer connection, the data loggers were activated and programmed to read at 50 min intervals. The data loggers have a limited life for recording data, they do not continue indefinitely but stop automatically when the memory is full. They register temperature at moments in time (not a continuous monitor) so it is possible to choose very short intervals between points but use up the memory quickly, or have longer intervals between recorded points and sustain the study for longer. This study chose to monitor the temperature every 50 min for a maximum of 1806 readings (6 weeks). By using these parameters, it was possible to follow each logger the entire length of the cold chain to peripheral clinics, and to hold each logger (in its vaccine box) for 2 weeks at the central vaccine store, the Provincial Vaccine Store and the health centre. In this way, temperatures were recorded not only during transport but also for a considerable time at each storage point.

Staff at the national vaccine store placed a data logger and monitoring form in each of 13 boxes (typically containing five vials of DTP) marked with the name of the target health centre. On the monitoring form was written the date and time that the box arrived at, and departed from, the various storage areas. Each box with a logger was sent down a different distribution chain to 13 peripheral health centres (one health centre received a logger for the vaccine and a second logger to measure the external ambient temperature). Since the goal was to monitor the temperatures of the typical cold chain, the shipments were packed, handled and stored normally, without any changes to routine procedures. As part of the process of capacity-building, staff at each point in the cold chain were instructed in the use of the data loggers and were trained to direct these monitored shipments toward the target health centres.

When the boxes arrived at peripheral health centres, they were kept in the fridge for 2 weeks before being used in clinics. At the end of the static or outreach session, the vaccinator recorded the time and date on the Monitoring Form. This marked the end of the study. Once the study had ended, data loggers and the related monitoring forms were stored at room temperature until the supervisors came and collected them. They were then sent back to Port Moresby where the data were extracted from the loggers directly onto a computer.

The study coordinator facilitated the training of the supervisors (regional cold chain officers) who were given the responsibility to identify and train cold chain officers and vaccinators at each point through which study vaccines would pass. Key training topics included:

- Purpose and methodology of the study.
- Importance of treating the study vaccine according to normal practices and schedules.
- Identification of study vaccines.
- Receiving and shipping study vaccines.
- Completion of the study monitoring form.

In addition, the supervisors informed counterparts, such as Provincial Health Advisor, Family Health Services Coordinators, health centre staff and/or local officials, who needed to be aware of the study. Health personnel at the target province, district and health centres were briefed on the study procedures and instructed to handle the monitored box using standard procedures.

## 3. Results

At the point of retrieval of data from the loggers, it was discovered that there was no data on one of them (sent to Health centre 6). The reason for this is unclear, it may have been incorrectly programmed, there may have been an error in the data retrieval process or the logger may have malfunctioned. This reduced the number of effective logger lines to 12, plus one measuring ambient temperature. The maximum and minimum temperatures for each logger during each phase of the journey to the periphery are recorded in Table 1.

Table 1
Maximum and minimum temperatures (°C) for each targeted health centre as recorded on data loggers

| Target health centre | Maximum/minimum | At AMS | Transport to PVS | At PVS | Transport to Health centre | At health centre | At clinic or outreach | Final status |
|---|---|---|---|---|---|---|---|---|
| 1 | Max | 10.5 | 5.0 | 5.8 | 3.0 | 9.0 | 32.0 | FROZEN |
| | Min | 4.5 | −2.8 | −1.0 | −8.0 | 1.0 | 3.0 | |
| 2 | Max | 8.0 | 4.3 | 5.8 | 2.0 | 5.5 | 5.8 | FROZEN |
| | Min | 4.5 | −3.5 | −0.6 | −13.4 | −5.8 | −1.8 | |
| 3 | Max | 8.0 | 4.0 | 7.3 | 2.0 | 5.5 | 5.6[a] | FROZEN |
| | Min | 4.5 | −3.5 | 0.3 | −7.2 | −7.0 | −6.5[a] | |
| 4 | Max | 8.9 | 3.9 | 4.6 | 3.9 | 3.0 | 32.0 | FROZEN |
| | Min | 4.5 | −1.5 | −0.5 | −13.1 | −0.5 | 5.4 | |
| 5 | Max | 8.4 | 3.0 | 8.2 | 4.0 | 9.5 | 11.7 | FROZEN |
| | Min | 4.5 | −2.8 | 2.0 | 1.4 | 4.2 | 8.4 | |
| 6[b] | Max | No data | | | | | | |
| | Min | | | | | | | |
| 7 | Max | 7.0 | 3.5 | 6.1 | 5.9 | 9.5 | 27.3 | FROZEN |
| | Min | 4.8 | −7.7 | 1.9 | −6.5 | 0.5 | 0.3 | |
| 8 | Max | 7.2 | 3.5 | 5.0 | 10.5 | 9.0 | 4.5 | FROZEN |
| | Min | 4.5 | −9.1 | 2.5 | 3.0 | 3.0 | 1.0 | |
| 9 | Max | 8.0 | 2.3 | 5.4 | −5.8 | 5.0 | 2.7 | FROZEN |
| | Min | 4.5 | −3.1 | 4.0 | −7.7 | 0.3 | −2.7 | |
| 10 | Max | 8.4 | 5.5 | 7.3 | 4.5 | 3.8 | 2.2 | FROZEN |
| | Min | 4.5 | −1.0 | 5.5 | −3.0 | 0 | −3.0 | |
| 11 | Max | 8.4 | 3.5 | 5.4 | 6.2 | 7.7 | 4.3 | FROZEN |
| | Min | 4.5 | −2.7 | 3.0 | 0.3 | 0.2 | −3.5 | |
| 12 | Max | 10.2 | 5.0 | 5.4 | 11.3 | 6.9 | 2.5 | FROZEN |
| | Min | 4.6 | −2.7 | 5.0 | −9.2 | −1.0 | −4.0 | |
| 13 | Max | 9.5 | 3.9 | 6.5 | 3.1 | 14.2 | ND[a] | FROZEN |
| | Min | 1.9 | −9.2 | 0.7 | −4.9 | 3.9 | ND | |
| Number of freezing episodes | | 0/12 | 12/12 | 3/12 | 10/12 | 4/12 | 5/12 | 12/12 |

AMS, Area Medical Store; PVS, Provincial Vaccine Store.
[a] Logger left in solar-powered fridge even though vaccines went to outreach clinic.
[b] No data obtained.

### 3.1. Storage at the central vaccine store, Port Moresby

The temperature of all the loggers was constant at around 5–8 °C during the 2 weeks' storage. There were only minor fluctuations.

### 3.2. Transport from central vaccine store, Port Moresby to provincial medical/vaccine stores

For all 12 loggers, there was a drastic drop in temperature as soon as they left the central store. Mostly the temperature dropped to −3 °C, but one shipment dropped to −9.2 °C. The duration of the low temperature varied from 6 to 48 h.

### 3.3. Storage at Provincial Vaccine Store

There were three loggers that experienced freezing episodes at PVS level. The temperature loggers were generally at a constant temperature for the entire 2 weeks at the PVS, showing around 3–5 °C. Exceptions to this were health centre 1, 2 and 4 that exhibited temperature drops to −0.5 to −1.0 °C.

### 3.4. Transport from PVS to health centre

Ten of the 12 loggers showed a major drop below freezing during transport out of the PVS. The drop tended to be lower than that experienced in transport from the national medical store dropping to as low as −13.4 °C. Transport time was generally brief, around 6 h.

### 3.5. Storage at health centre

Four of the 12 loggers experienced freezing episodes while stored at the health centre level. Power to store the vaccines in fridges varied—it was either electric power from the public grid (two health centres), gas from portable LP gas cylinders [8], or solar power [2].

The loggers showed greater variation at this level than at other stages of the cold chain. Of the two electric fridges, one

Table 2
Some possible solutions to avoid vaccine freezing

| Problem | Strategy | Possible response[a] |
|---|---|---|
| Freezing in transport | Remove vaccines from cold chain during transport between centres | Avoid direct sunlight that might "bake" vials |
| Temperature in fridges fluctuates due to power surges, brown-outs and black-outs | Improve fridges' ability to maintain even temperatures | Install surge protection to prevent temperature variations due to fluctuation in power source |
| Temperature of vaccines uncertain. Temperature monitors are unable to read the actual temperature of vaccine vials | Improve temperature monitoring devices | Design a heat probe that could be viewed from outside the vaccine container that would give readings of actual vaccines |
| Ice packs over-cool vials (1) | Improve insulation between vaccines and ice packs and fridge cooling parts | Design a simple packing tray that prevents vaccines coming too close to ice liners (this would prevent the most severe temperature drops). Modify design of ice packs to prevent direct contact with vials |
| Ice packs over-cool vials (2) | Ensure transport packs contain water that has recently thawed (i.e. around +1 °C) | Use chilled water packs to transport vaccines in vaccine carriers - shake each pack to ensure it contains liquid and is not frozen |
| Liquid vaccines are damaged by freezing | Change presentation of liquid vaccines | Reformulate liquid vaccines to presentations that are more cold-robust, e.g. powder vaccines that are freeze dried and accepting of low temperatures without damage |

[a] Responses are suggested directions to consider and would need field testing as to their practicability, suitability and effectiveness. There are surely other solutions to the problems not mentioned in this table.

was constant at 5 °C. The other showed marked irregularity although it maintained the temperature within the acceptable range.

Of the eight gas fridges, two were regular at around 3 °C, but the other six showed marked irregular swings in temperature, one even dropping to −5.8 °C.

One solar-powered fridge showed excellent control at a constant 3–5 °C. The other one showed irregular control with daily incursions into freezing, dropping as low as −5.8 °C each day.

### *3.6. Transport to outreach immunization sessions*

Five of the 12 loggers experienced a freezing episode after leaving the health centre, either in transport or during the outreach session. All other loggers experienced a rise in temperature after they left the refrigerated cold chain on the way to outreach clinics. Most rapidly reached ambient temperature, but it was not possible to tell whether the vaccines themselves had already been administered prior to the loggers warming up, or whether the vaccine vials heated up before administration. One health centre dispatched the vaccines to the outreach clinic but kept the logger at the health centre!

To measure ambient temperatures along the distribution route, one data logger was shipped with the vaccines to one of the study health centres, but at ambient, rather than cold chain, temperatures. It was shipped and stored in the same room or vehicle as the vaccines and according to the same schedule as the vaccines, but out of direct sunlight and away from heat sources. The temperature logger recording ambient temperature was not put in the cold boxes or refrigerators used for the vaccines. A monitoring form was included in the box and used to record the date and time of its arrival and departure from each cold chain point. The ambient temperature ranged from 23 to 32 °C.

## 4. Discussion

Over the last 5 years, the cold chain in PNG had been progressively renovated, resulting in appropriate hardware in place at appropriate locations. This study went the next step beyond simply counting refrigerators—it measured function. It was reassuring to note that heat damage of vaccines as they passed down the cold chain was not observed (although not all parts of the distribution network were surveyed). But this study did reveal the human behavioural element of the cold chain, namely the incorrect packing of vaccines in vaccine carriers for transport between stores and the field.

The data loggers provided extremely accurate data that measured temperature related to time, approximating to the temperature of the actual liquid vaccine in the vial (but did not measure the actual temperature of the vaccine to indicate whether it has been frozen). The loggers responded virtually instantaneously to temperature change, whereas the vaccines would have taken a finite time to cool down. Those vials exposed to very low temperatures for long periods of time (e.g. 48 h at −7 °C) would almost certainly have been damaged by freezing. Those with milder temperature exposures for less time may not have been damaged. This study made no attempt to measure possible loss of potency associated with freezing—that link has already been well established [4,5].

While the data loggers revealed with great precision and clarity what was happening at any one time, there was one

health centre that defied explanation. Health centre 3 logger exhibited irregular temperature control with daily incursions into freezing, dropping as low as −5.8 °C each day. The fridge was powered by solar energy, and while some variation in power might be expected between cloudy days and full sun, it did not explain why the temperature dropped so low below freezing. The reason for this was not identified but a repeat passage of the data logger subsequently did not show the same abnormality.

Despite the establishment of a chain of refrigerators and transport between stores, this study showed that vaccines were not maintained at correct temperatures. Retraining in the way vaccines are packed should improve the situation in the short term. But is there a better way? When faced with a staff behaviour problem in relation to syringe use in the 1980s (staff were re-using disposable syringes), the WHO Expanded Programme on Immunization (EPI) went back to the drawing board and created an auto-disable syringe. This technological solution to a human behavioural issue was extremely successful to the point where auto-disable syringes are now the syringe of choice for immunization. Because the current cold chain will always be vulnerable to human error, there may be some way that this potential weakness could be bypassed. We suggest that a number of approaches could be explored that would reduce the possibility of vaccines freezing (Table 2). For instance, tetanus toxoid and hepatitis B vaccine are sufficiently stable at high temperatures that they could reasonably be removed from the cold chain during transport when the risk of freezing is highest [37,38]. The most radical solution (and most costly) would be to change the presentation of liquid vaccines so that all vaccines were more heat-robust. We have suggested elsewhere [39] that it is time to rethink the entire needle/syringe approach to delivery of vaccines, and if this were implemented at the same time, it might be possible to avoid liquid injectable vaccines (and the accompanying risk of freezing) all together.

## 5. Conclusions

Most of the static fridges in PNG functioned well in maintaining the vaccines at correct temperatures most of the time. But there is clear evidence of vaccines having been exposed to freezing temperatures during transport at multiple locations in the cold chain. The ice packs were presumably too cold when placed in the vaccine carriers, and there was insufficient distance between them and the vials, causing the vaccines to cool below freezing. Short exposure to high temperatures was not a problem despite very high ambient temperatures. The National Department of Health has already begun corrective training for relevant staff, and at least in the short term, it is anticipated that there will be much lower numbers of vaccine freezing incidents.

For over a decade, the use of data loggers has been shown in many countries to be useful. This technology has proved itself again in the challenging environment of PNG, and will hopefully be used repeatedly in the future to monitor for freezing events.

There is surely a wider lesson to be learned from the PNG study–that the entire cold chain system (however well it is installed) is vulnerable to human error. Can this vulnerability be reduced in hot climates by simple or not-so-simple technological solutions? We offer some potential solutions such as changing the presentation of liquid vaccines to a more heat-stable form. The Global Alliance for Vaccines and Immunization is already supporting the introduction of combination vaccines (that include DTP, HepB and Hib vaccines) in many countries. We believe that hot climate countries will increasingly need to avoid cold damage in anticipation of an era when increasing numbers of costly, freeze-sensitive vaccines will be introduced. Investing in studies such as this as a means to identify and solve problems, and to strengthen staff capacity is time and money well spent.

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