

Study protocol for temperature monitoring in the vaccine cold chain

Immunization, Vaccines and Biologicals



**World Health
Organization**

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immunization, vaccines and biologicals may be requested from:**

World Health Organization
Department of Immunization, Vaccines and Biologicals
CH-1211 Geneva 27, Switzerland

• *Fax:* + 41 22 791 4227 • *Email:* vaccines@who.int •

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Acknowledgements

This *Study Protocol* was initially developed by the Program for Appropriate Technology in Health (PATH) in 2003 and was used in several countries. Critical evaluation of the results of these studies stressed the risks of freezing in the cold chain and the need to introduce innovative approaches to prevent freezing in many settings.

The *Protocol* was further revised in 2004 by the Access to Technologies Team, Department of Immunization, Vaccines and Biologicals of the World Health Organization.

With the introduction of Performance, Quality and Safety for prequalification of equipment and devices used in immunization services, the *Protocol* was revised by the Quality, Safety and Standards Team, Department of Immunization, Vaccines and Biologicals of the World Health Organization.

The World Health Organization thanks PATH for initiating this significant *Protocol*.

Abbreviations

DT	diphtheria–tetanus (vaccine)
DTP	diphtheria, tetanus (toxoid) and pertussis vaccine
HepB	hepatitis B (vaccine)
LTA	LogTag Analyzer
PATH	Program for Appropriate Technology in Health
Td	tetanus–diphtheria (vaccine)
TT	tetanus toxoid (vaccine)
UNICEF	United Nations Children’s Fund
VVM	vaccine vial monitor
WHO	World Health Organization

1. Introduction

Improperly maintained or outdated refrigeration equipment, poor compliance with cold-chain procedures, inadequate monitoring and poor understanding of the dangers of vaccine freezing contribute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. Emphasis has long been placed on keeping vaccines cold, with less attention devoted to preventing vaccine damage by freezing. Published reports and field evidence 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. In response to this danger, WHO guidelines clearly state that adjuvant vaccines must not be exposed to freezing temperatures.

This Protocol¹ is designed to:

- 1) document temperature exposures throughout the vaccine cold chain with a special emphasis on the level of freezing; and
- 2) identify specific problem areas where corrective actions are warranted.

In this *Protocol*, temperatures are monitored continuously as vaccine shipments travel through the cold chain, from primary stores, to intermediate stores, to health centres and, finally, to the outreach delivery site/s. This *Protocol* can be tailored to meet the individual resources of any programme: either a simple, low-cost study can be conducted – without sophisticated monitoring tools – or a more comprehensive approach can be taken to provide more details.

The outcome of the study should help programmes determine the most appropriate interventions. If evidence demonstrates, for example, that exposure of vaccines to freezing temperatures occurs most commonly during vaccine transport, new procedures for conditioning of ice packs, or ice-free transport can be implemented. If there is a correlation between specific types of refrigerators and freezing, equipment replacement may be required or, alternatively, more attention should be given to the training of cold-chain supervisors.

As with any study, this *Protocol* requires strong central coordination and the cooperation of many individuals along the vaccine-distribution cold chain. Guidelines for individual responsibilities, budgetary considerations, and equipment requirements are provided.

¹ This protocol replaces the document “*Protocol for a cold chain survey WHO/EPI/LHIS/94.9*”

Freezing of diphtheria, tetanus, pertussis, hepatitis B vaccines and combination vaccines can compromise their immunological potency.² WHO guidelines and manufacturers' vaccine labels state that hepatitis B, DTP, DT, and TT vaccines should be stored at temperatures between 2°C and 8°C and should not be used if thought to have been frozen. Yet recent studies in Canada, Hungary, Malaysia, Mongolia, Pakistan, United Kingdom, United States of America and other countries have found widespread freezing at many levels of the vaccine-distribution system.³ Emphasis is frequently placed on preventing vaccine heat exposure, with many immunization providers unaware that monitoring and preventing vaccine freezing is also essential.

Using this *Protocol*, a study in Indonesia found that 75% of its hepatitis B vaccine shipments were exposed to freezing temperatures, potentially damaging a significant portion of this expensive vaccine.⁴ The study identified the segments of the cold chain primarily responsible for freezing, allowing Indonesia to focus corrective actions on specific equipment and procedures.

² PATH. Effects of freezing on vaccine potency: Literature review. February 2003 (unpublished document, Presented at the WHO Technology and Operations Panel, 23 February 2003, Geneva) http://www.path.org/files/TS_cc_effects.pdf

³ PATH. *Evidence of vaccine freezing in the cold chain: literature review*. February 2003 (unpublished document; Presented at the WHO Technology and Operations Panel, 23 February 2003, Geneva). http://www.path.org/files/TS_cc_evidence.pdf

⁴ Nelson CM, Wibisono H, Purwanto I et al. Hepatitis B vaccine freezing in the Indonesian cold chain: evidence and solutions. *Bulletin of the World Health Organization*, February 2004, 82 (2):99-105.

2. Equipment requirements

This *Protocol* uses electronic temperature loggers to monitor temperatures. In addition to electronic temperature loggers, vaccine vial monitor (VVM) will be used as visual reference for heat exposure.

Data logger

Several continuous temperature monitoring devices are available. This *Protocol* describes the **LogTag TRIX-8 data logger**⁵ to provide continuous temperature data; other loggers could, however, be used.

Recording accuracy is $\pm 0.3^{\circ}\text{C}$. A computer is required to configure the logger and to download temperature information so that it can be analyzed and printed. **Annex 1** provides detailed step-by-step instructions on how to configure the data loggers and download the data.

Figure 1: LogTag TRIX-8 data logger with interface

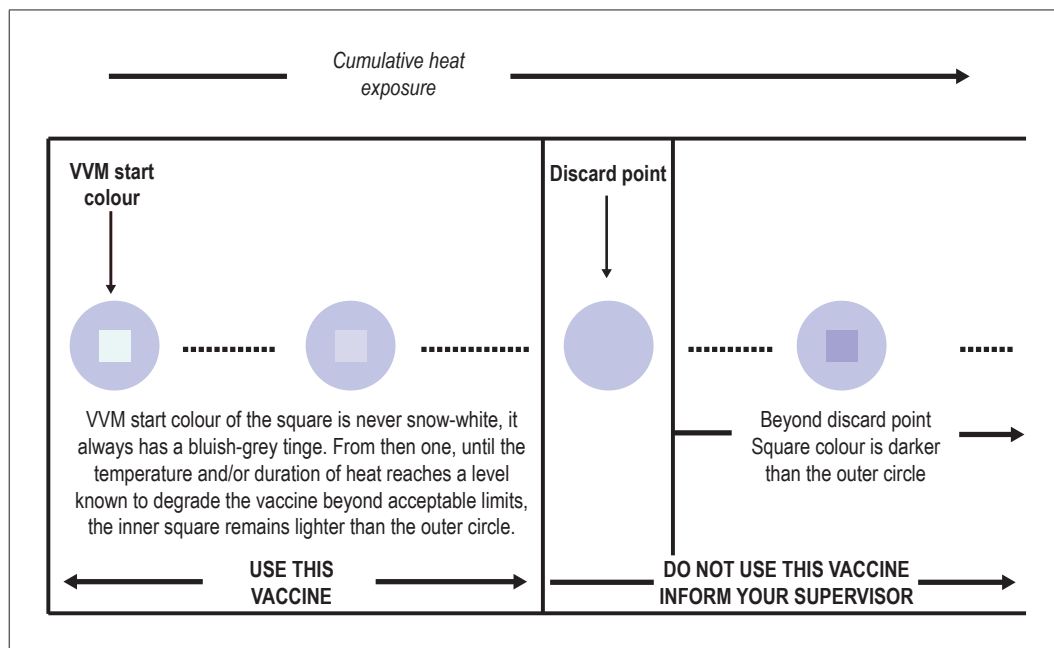


⁵ Included in the *WHO Performance, Quality and Safety* database, and described under reference WHO/PQS/E6/06.

Vaccine vial monitor

A vaccine vial monitor or VVM⁶, is a circular indicator, printed directly on the vaccine vial label or affixed to the top of the vial or ampoule. The **inner square** of the VVM is made of heat-sensitive material that is initially light in colour and **becomes darker** when exposed to heat over time. By comparing the colour of the square to the reference ring, health workers can determine the extent to which the vaccine has been exposed to heat. The vaccine can be used as long as the colour of the inner square is lighter than that of the reference ring.

Figure 2:



6 Included in the *WHO Performance, Quality and Safety* database, and described under reference WHO/PQS/E6/01.

3. Study design

3.1 Study overview

Small data loggers will be packed within inner vaccine boxes (**Annex 2**) and accompany vaccine shipments to eight different health centres (**Annex 3**). Since the goal is to monitor the temperatures of a typical cold chain, the shipments should be packed, handled and stored normally, without any changes to routine procedures. Cold-chain staff at each point in the cold chain will direct the monitored shipments toward the target health centres. At each point they will record the date of arrival and the date of departure on the *Monitoring Form* (**Annex 4**) enclosed in each inner vaccine box, as illustrated in **Annex 2**.

3.2 Study planning and preparation

Responsibility: study coordinator

It is important to prepare for this study. A study coordinator must be identified, capable of designing and overseeing this cold-chain study, as discussed in paragraph 3.12 (Personnel and responsibilities) below. Planning discussions should include input from the country's ministry of health officials, those responsible in-country for national immunization services, and available cold-chain experts. A budget must be prepared (see **Annex 5**) and this *Protocol* should be modified to reflect the specific characteristics of the country. A realistic study schedule should be established (see **Annex 6**).

Some countries may wish to use an international technical advisor with prior experience in conducting cold chain monitoring studies to assist with study preparations and training the local study coordinator. Technical advisors may be available from WHO, UNICEF, PATH or other organizations. Spending about five days with the study coordinator and local ministry officials, a technical advisor would be expected to fully train the study coordinator and provide advice on study implementation, data analysis, and follow-up.

3.3 Study sites selection

Responsibility: study coordinator

Study provinces, districts, and health-centre sites should reflect broad areas of the country. While it is inadvisable to select the most poorly managed cold-chain sites with the fewest resources if this is atypical, it is important to choose study sites where it would be most valuable to identify vaccine freezing. On the basis of discussions with immunization programme personnel, select areas that are average to below average in terms of performance, accessibility, and temperature extremes, and that are staffed with responsible personnel who would be able to fulfil study requirements.

Depending on the climatic diversity, equipment variations, and available budget, each country should select an appropriate number of provinces to monitor. In this protocol we suggest selection of two provinces to keep the study to a manageable size. Within each province, two districts should be selected. Within each district, two health centres should be selected, representing two different immunization scenarios (for example, one rural and remote, one urban). In summary, there should be a total of eight health centres selected as study destinations. **Annex 3** demonstrates the distribution of data loggers through the cold chain, from the primary stores to the health-centre destination. The actual names of the provinces, districts, health centres and outreach posts should be written on this diagram or on a separate sheet that can then be used for study planning and as a supervisory tool.

3.4 Selecting a study vaccine

Responsibility: study coordinator

One type of vaccine should be selected as the vaccine to be monitored during distribution. It should be one of the freeze-sensitive vaccines (HepB, DTP, DT, TT or Td) that is distributed widely. Although many types of vaccines may be shipped in a single cold box or stored in a single refrigerator, selection of one type of vaccine will assist in identifying monitored shipments. Data loggers will be packed and shipped with the vaccine. This *Protocol* refers to vaccines shipped with a data logger as “study vaccines.” The location of the data logger within the vaccine box is demonstrated in **Annex 2**.

3.5 Activating the data logger

Responsibility: study coordinator

Using a computer connection, the data logger will be activated and programmed to read at 20-minute intervals, thus allowing temperature recording for 111 days (**Annex 1**). Each data logger will be given the name of its target health centre. To direct the shipment, this name will be clearly marked on the vaccine inner box, the vaccine shipping carton and recorded on the *Monitoring Form* (**Annex 4**).

3.6 Vaccine shipment preparation and storage at primary level

Responsibility: study coordinator

At the primary vaccine stores, data loggers and *Monitoring Forms* will be placed in eight inner boxes (typically containing 10 to 20 vials) clearly marked with the name of the target health centre (see **Annex 2**). One of these study vaccines should be fully frozen solid at -20°C overnight and clearly labelled “Frozen” with a permanent marker. All these packed boxes should be stored at the primary vaccine stores for a period of one month. The *Monitoring Form* for each vaccine box with a data logger must be completed with the date and time of start of storage and should be placed inside the inner box. Normal loading and handling procedures should be followed so the data loggers will be exposed to typical cold-chain conditions.

3.7 Ambient-temperature monitoring

Responsibility: study coordinator and health staff

To measure ambient temperatures along the distribution route, one data logger should be shipped with the vaccines to each of the study health centres, but at ambient – rather than cold-chain – temperatures (see **Annex 3**). For each health centre, a data logger should be put into a small box, labelled with its destination, and shipped with the vaccines. It should be stored and shipped 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 should not be put in the cold boxes or refrigerators used for the vaccines. A *Monitoring Form* must be included in the box and used to record the date and time of its arrival and departure from each cold-chain point.

3.8 Distribution and monitoring

Responsibility: health staff

Storage at primary stores: At primary stores, two study-vaccine cartons should be prepared. One carton should be shipped to each of the two study provinces using normal shipping procedures (see **Annex 3**). Each carton should contain four data loggers, with each data logger enclosed in a separate box of monitored vaccines. Each of these four boxes must be labelled with the destination health centre and shipped with a routine vaccine shipment to the appropriate province. Eight additional data loggers, each in small boxes, should accompany the four boxes to monitor ambient temperature during the study. Study-vaccine boxes should remain at the primary store for one month to adequately measure storage temperatures.

Transport to provincial stores: The primary stores cold-chain manager will follow the normal vaccine supply schedule for each the two study provinces. However, with the subsequent scheduled shipment to each study province, they will include the two study-vaccine boxes, labelled with the name of the two districts located within each province. Before sending this shipment, the central cold-chain manager will record the time and date on each *Monitoring Form* and will then pack the vaccines for shipment according to standard practice. The study-vaccine boxes should be shipped in the same carton as the other vaccines being delivered and according to typical loading and transport procedures. In addition to study-vaccine boxes, eight small boxes containing data loggers - only for ambient-temperature monitoring - with appropriate labels should also be sent at ambient temperature.

Storage at provincial stores: Upon delivery of the vaccine shipment to the provincial vaccine stores, cold-chain personnel will accept the study-vaccine carton and small boxes containing ambient-temperature-monitoring data loggers, open them and the four inner vaccine boxes containing the data loggers and *Monitoring Forms*. They will record the time and date of arrival on the *Monitoring Form*, then store the inner box containing vaccines, data logger, and *Monitoring Form* in the cold room or refrigerator along with other vaccines, following standard practice. Data loggers for ambient-temperature monitoring should be placed in the room where vaccines are kept but out of direct sunlight and away from heat sources. Study-vaccine boxes should remain at the provincial store for one month to adequately measure storage temperatures.

Transport to district stores: In each of the two study provinces, the provincial cold-chain managers will follow the normal vaccine supply schedule for each of the two study districts in their respective province. However, with the next scheduled shipment to each of the two study districts in this province, provincial cold-chain personnel will include the two study-vaccine boxes, each labelled with the name of the health centre located within the district to which it will be sent. Before sending this shipment, the provincial cold-chain manager will record the time and date on each *Monitoring Form* and will then pack the vaccines for shipment according to standard practice. The study-vaccine boxes should be shipped in the same carton as the other vaccines being delivered and according to typical loading and transport procedures. In addition to study-vaccine boxes, two small boxes containing data loggers only for ambient-temperature monitoring should also be sent, appropriately labelled, at the ambient temperature.

Storage at district stores: Upon delivery of the vaccine shipment from the provincial level to each of the four study districts, district cold-chain personnel will open the two study-vaccine boxes labelled for the respective health centre destinations within their district. They will record the time and dates of arrival on the enclosed *Monitoring Form*. They will store the inner box containing vaccines, data logger, and *Monitoring Form* in the cold room or refrigerator along with other vaccines, following standard practice. For the ambient-temperature-monitoring data logger, time and date of arrival should also be noted. This box should be kept in the same room where the refrigerator is located but out of direct sunlight and away from heat sources. Study-vaccine boxes should remain at district vaccine stores for two weeks to adequately measure storage temperatures.

Transport to health centre: Following the normal vaccine-distribution schedule, the district cold-chain manager will prepare vaccine shipments to study health centres. Upon preparation for shipment to each health centre, the district cold-chain manager will record the time and date on each *Monitoring Form* (**Annex 4**), then pack the vaccines for shipment according to standard practice. One study-vaccine box – labelled with the destination health centre and containing a data logger – will be sent to each study health centre (**Annex 3**). The study vaccines should be shipped in the same vaccine carriers with the other vaccines, according to typical loading and transport procedures. In addition to study-vaccine boxes, one small box containing a data logger – only for ambient-temperature monitoring – with a proper label should also be sent at ambient temperature.

Storage at health centre: Upon arrival of the vaccine shipment from the district, cold-chain personnel at each study health centre will open the enclosed study-vaccine box containing the data logger and *Monitoring Form* (**Annex 4**). They will record the time and date of arrival on the *Monitoring Form* and handle and store the study vaccines according to standard procedures. For ambient-temperature-monitoring data logger, time and date of arrival should also be noted. This box should be kept in the same room where the refrigerator is located but out of direct sunlight and away from heat sources. Study vaccines should remain at the health centre for two weeks to adequately measure storage temperatures.

Shake test at the health centre: After at least two weeks of storage at the health centre, the health staff should conduct the shake test with study vaccines. The marked frozen vial should be used as control vial. All other vials in the box should be tested against this frozen control vial. Results should be noted on the *Monitoring Form* shake-test table (**Annex 4**). If vials fail the shake test, they should not be used. However, the study-vaccine box and the small box containing the data logger for ambient-temperature monitoring should be taken to outreach to complete temperature data recording.

Outreach immunization: After conducting the shake test following at least two weeks of storage at the health centre, the health centre staff should prepare to monitor the next outreach session by including the study-vaccine box. When preparing for an outreach session, the health centre cold-chain manager will record the time and date on the *Monitoring Form* then load the data logger into a vaccine carrier, along with other vaccines, according to standard procedures. On completion of the outreach session, the vaccinator will record the time and date on the *Monitoring Form*. This completes the study. Once the study has been completed, data loggers can be stored at room temperature.

3.9 Data collection and analysis

Responsibility: health staff and study coordinator

Use of the *Monitoring Form* (Annex 4): One person at each point should be trained to use the *Monitoring Form* and be responsible for completing it upon receipt and reshipment of each study-vaccine shipment and ambient-temperature monitoring. This form should be modified to indicate each of the cold chain points and the study vaccine.

3.10 Interviews

Responsibility: study coordinator

To collect additional information about health worker attitudes and practices toward vaccine freezing, the study coordinator should interview all cold-chain staff participating in the cold-chain study. Sample interview questions are given in **Annex 7**.

3.11 Collection of data instruments

Responsibility: study coordinator

After all health centres have completed the study, the study coordinator should visit each centre to collect the data loggers and monitoring forms. The coordinator may also conduct health staff interviews at this time.

3.12 Data analysis

Responsibility: study coordinator

Preparing a Temperature Profile for Each Monitored Shipment: The study coordinator should retrieve the temperature data from the data loggers. The data from the monitoring forms and data loggers should be combined to create temperature profiles of each shipment. The exact time of transition of the vaccine from transport to storage and back to transport should be clearly indicated on the monitoring form. Annex 8 shows a sample temperature profile of a vaccine shipment as it travels through each part of the cold chain. From these profiles, the severity of freezing and number of freezing incidences at each point in the cold chain can be determined.

Preparing a Data Summary for all Shipments: To compare different shipments and draw overall conclusions, a summary table should be made showing the temperature extremes for each shipment at each point in the cold chain. A table, as shown in Annex 9, is a useful way to compare and summarize data.

Additional Analysis: Further analysis can show not only the occurrence of freezing, but the frequency or severity of the problem. Annex 10 shows one possible analysis by summarizing the percent of time the vaccines were stored at temperatures below zero degrees. Other analyses can be made depending on local needs.

3.13 Study report

Responsibility: study coordinator

Data from the data loggers and interviews should be combined into a report characterizing the incidence of vaccines being exposed to freezing temperatures and the likely causes. Interview information can provide additional insights into knowledge, attitudes, and practices that might be contributing to cold chain freezing. Descriptions of the refrigerators monitored in the study should be included along with any conclusions that can be drawn about the types of equipment involved in freezing episodes. A completed report should be sent to all participants and partners in the study.

3.14 Using the study findings

Responsibility: study coordinator

The outcomes from this study should provide clarity on the severity and causes of vaccine freezing in the cold chain. Recommended next steps should include:

- **Presentation of findings:** Findings should be presented to immunization partners such as ministry of health, WHO, UNICEF, and other partner agencies.
- **Expert review:** An expert group should be established to review findings and make recommendations for improvements. Training, equipment, and programmatic issues should be analyzed and considered in any cold chain improvement plan.
- **Building awareness and support:** Study findings could be a valuable tool in gaining upper-level commitment to cold chain improvements. Cultivation of donor funding for new equipment or training programmes could also be facilitated with data clearly documenting the problem.

-
- **Field test and validate solutions:** Possible solutions might include revised training programmes, new equipment, revised operating procedures, new ice-pack conditioning procedures, and limited ambient temperature transport or storage.
 - **Implementation and monitoring of solutions:** Approaches to reducing freezing should be refined and expanded. To evaluate the effectiveness of the new systems, a follow-up cold chain study could be conducted and compared to the baseline findings.

3.15 Personnel and responsibilities

Study coordinator: A study coordinator will oversee implementation of the cold-chain study. The coordinator's responsibilities include:

- Design and planning (e.g. customizing this *Protocol*, providing data loggers)
- Site selection
- Training of staff participating in the cold-chain study
- Programming of data loggers
- Oversight of shipment preparation
- Supervision and troubleshooting
- Interviewing staff participating in the cold-chain study
- Collection of data loggers at end of study
- Data analysis
- Report preparation

Health staff: The appropriate person responsible for cold-chain management at each point of the cold chain in all study areas must be identified and trained. Their responsibilities include:

- Receiving study shipments
- Filling out the *Monitoring Forms* for each study-vaccine shipment
- Directing shipments to study sites
- Conducting the shake test prior to outreach (vaccinators)
- Transporting data logger with study vaccine for outreach (vaccinators)
- Sending data logger back to study coordinator at end of study (vaccinators)

3.16 Training and information

The study coordinator must identify and train staff participating in the cold-chain study and vaccinators at each point through which study vaccines will pass. Key training topics include:

- 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*
- How to conduct shake test⁷

In addition, the coordinator will inform counterparts, such as immunization coordinators, health centre doctors and/or local officials, who should be aware of the study. Ministry of health personnel at the target province, district, and health centres will be briefed on the study procedures and instructed to handle the monitored box using standard procedures.

⁷ The attached shake-test learning guide should be used in this training (Annex 11).

Annex 1:

Configuring and downloading the LogTag TRIx-8 data logger

1. Coding of the file names for programming

Before configuring the data loggers the vaccine boxes and ambient-temperature boxes should be prepared as described in the Study Protocol.

The computer used for configuring the data loggers must be set to the correct date and time.

In a typical cold-chain study, 16 **TRIX-8 data loggers** should be used. Eight of these will be for recording internal temperatures, and eight will record ambient temperature.

Figure 1 and Table 1 (below) provide an example of file-name coding. However, different coding such as using name of the province and district in full could be used.

Figure 1: Coding of the file names for configuration of the data loggers

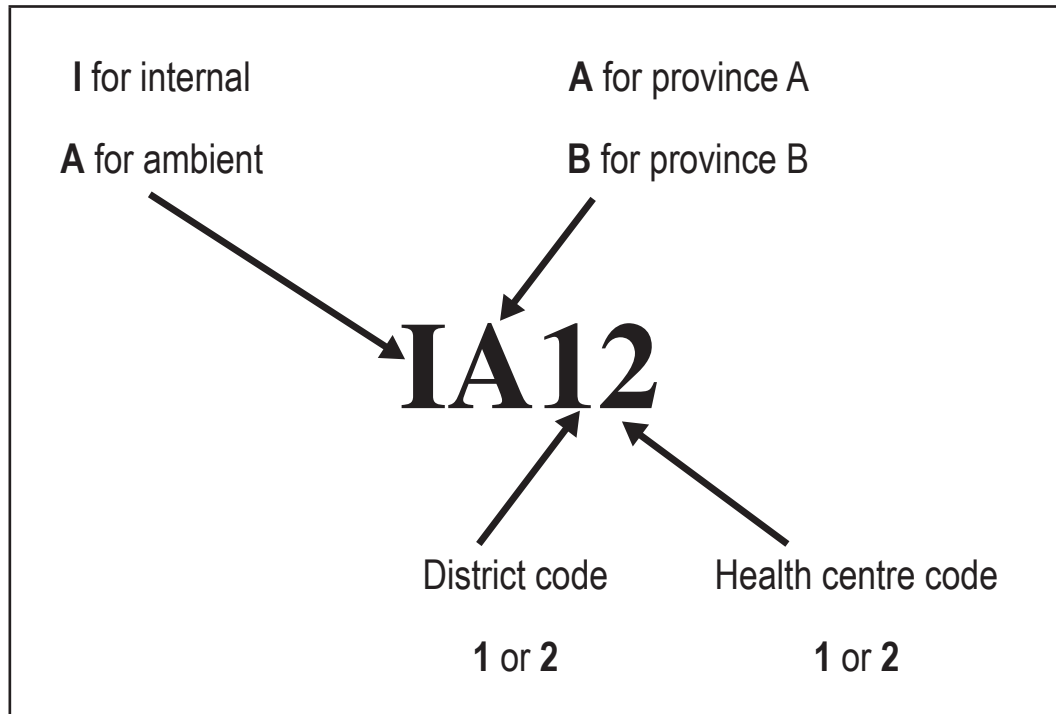


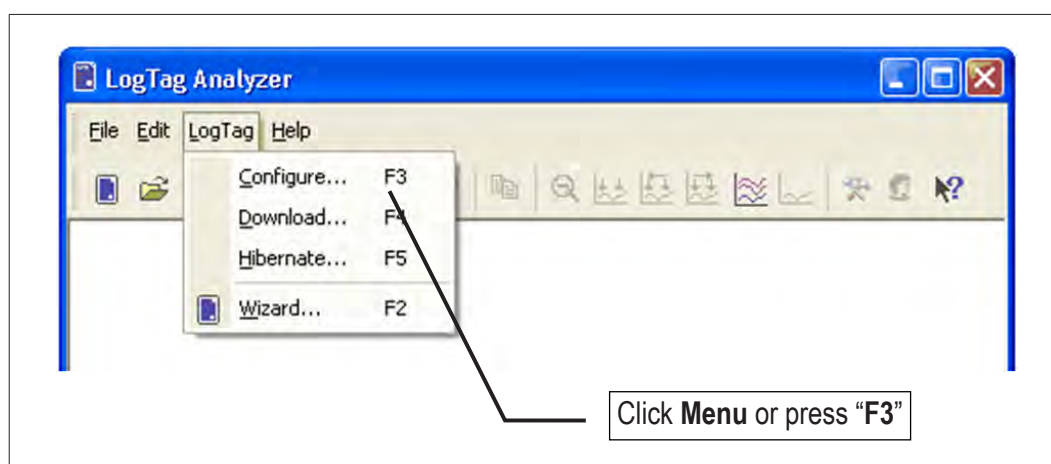
Table 1: Suggested file-name coding for data loggers

			Internal temperature	Ambient temperature
Province A	District 1	Health centre 1	IA11	AA11
		Health centre 2	IA12	AA12
	District 2	Health centre 1	IA21	AA21
		Health centre 2	IA22	AA22
Province B	District 1	Health centre 1	IB11	AB11
		Health centre 2	IB12	AB12
	District 2	Health centre 1	IB21	AB21
		Health centre 2	IB22	AB22

2. Configuring the data loggers

- 1) Insert the data logger into the interface and open the **LogTag Analyzer** programme (LTA)
- 2) Select “LogTag” – “Configure” from the menu, or press “F3”.

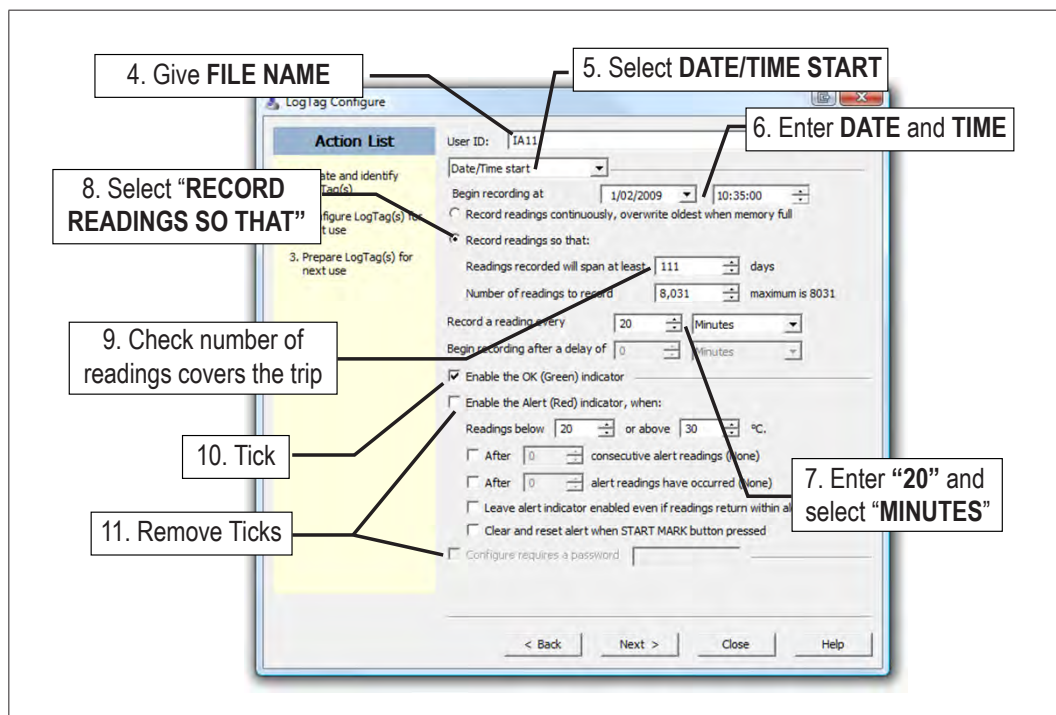
Figure 2: Configuring the data logger: Step 2



- 3) The programme will look for a connected interface and data logger. Once confirmed, the **configuration screen** will appear.
- 4) Fill in the “**User ID**” with a file name as explained above. For example for internal temperature monitoring of Province A, District 1, Health centre 1 route, file name should be given as IA11.
- 5) From the drop down box choose “**Date/Time start**”.
- 6) In “**Begin Recording at**” enter date and time when the loggers must start. The date and time set in all data loggers should be the same (the time and date should allow you enough time to configure and pack all 16 data loggers so that all recordings will begin at the same time in packed boxes.)

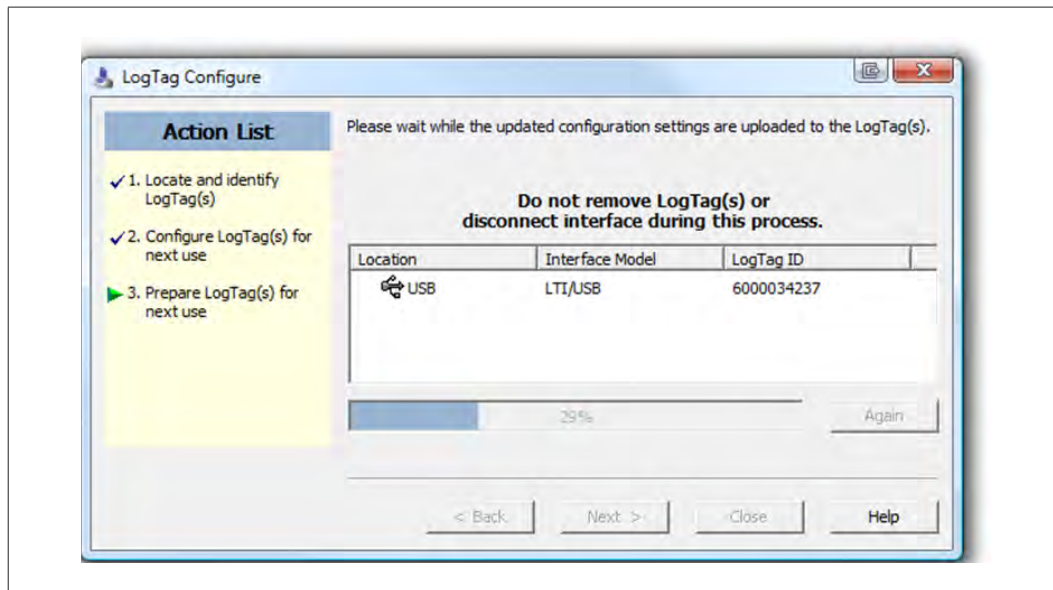
- 7) In the box next to **“Record a reading every”** enter **“20”**, and select **“minutes”**.
- 8) Select **“Record readings so that:”** (the remainder of the fields will be filled automatically.)
- 9) Ensure enough readings are taken to cover the length of the trip. If necessary, increase the number of readings taken.
- 10) Tick **“Enable the OK (Green) indicator”**
- 11) Remove the ticks next to **“Enable the Alert (Red) indicator”** and **“Configure requires a password”**

Figure 3: Configuring the data logger: Steps 4-11



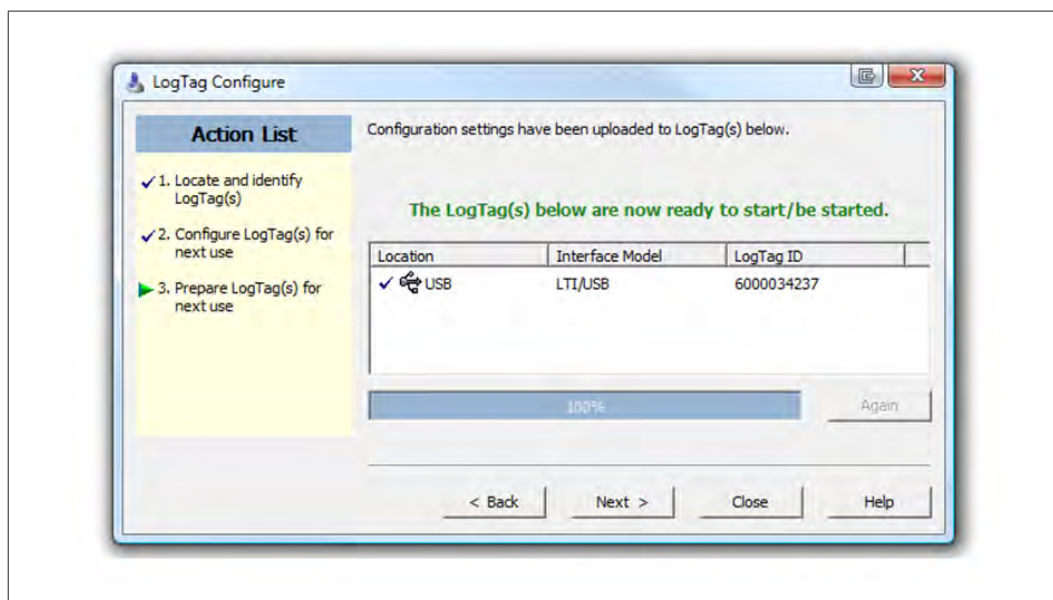
- 12) Once you are satisfied all parameters are set correctly, click on **Next >**. The Configuration upload screen appears.

Figure 4: Configuring the data logger: Step 12



- 13) When the upload is finished, a confirmation screen appears. Only data loggers with a tick have completed configuration and can be used for monitoring. Remove the data logger from the interface and place in the box as described in the Study Protocol. If this data logger is for ambient-temperature monitoring, it should be put in a small box, and labelled with its destination. It should be stored and shipped 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 logger will start logging at the date and time set.

Figure 5: Configuring the data logger: Step 13

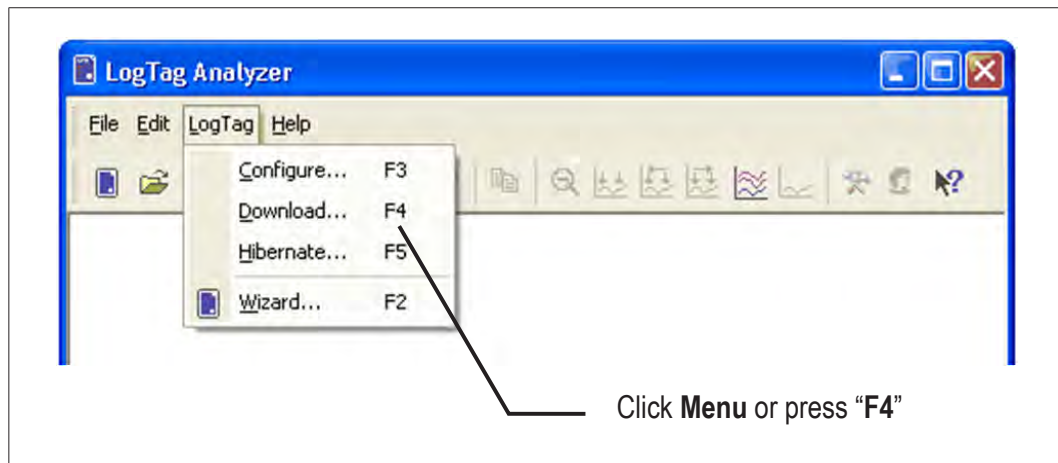


- 14) Fill in the hard (printed) copy *Monitoring Form*.
- 15) Insert the next data logger and press next, continue from step 4 and repeat for all data loggers.

3. Downloading data from the data loggers

- 1) Insert the data logger into the interface and open the **LogTag Analyzer** programme (LTA)⁸.
- 2) Select “LogTag” – “Download” from the menu, or press “F4”.

Figure 6: Downloading data logger: Step 2

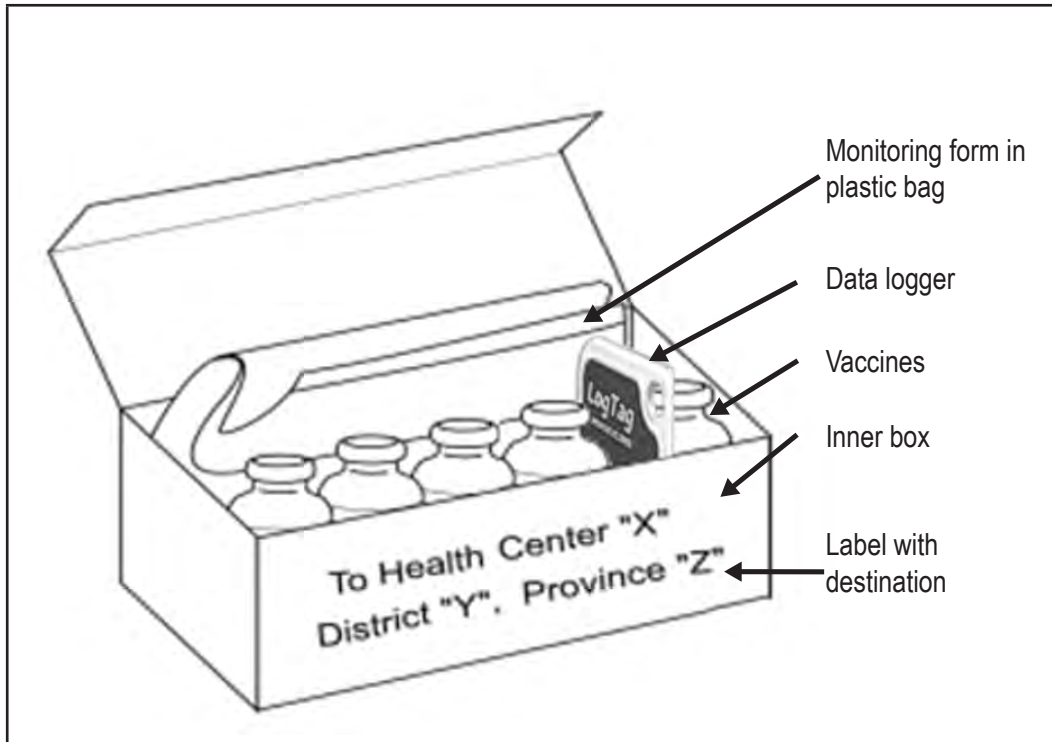


- 3) Once downloaded, LogTag Analyzer automatically saves the file with the filename being the same as the User ID entered in step 4 of the configuration.
- 4) Back-up the file to an external drive, USB key, or on a CD.

⁸ If you start the **LogTag Analyzer** programme with the interface plugged in and then insert the LogTag, downloading will start automatically.

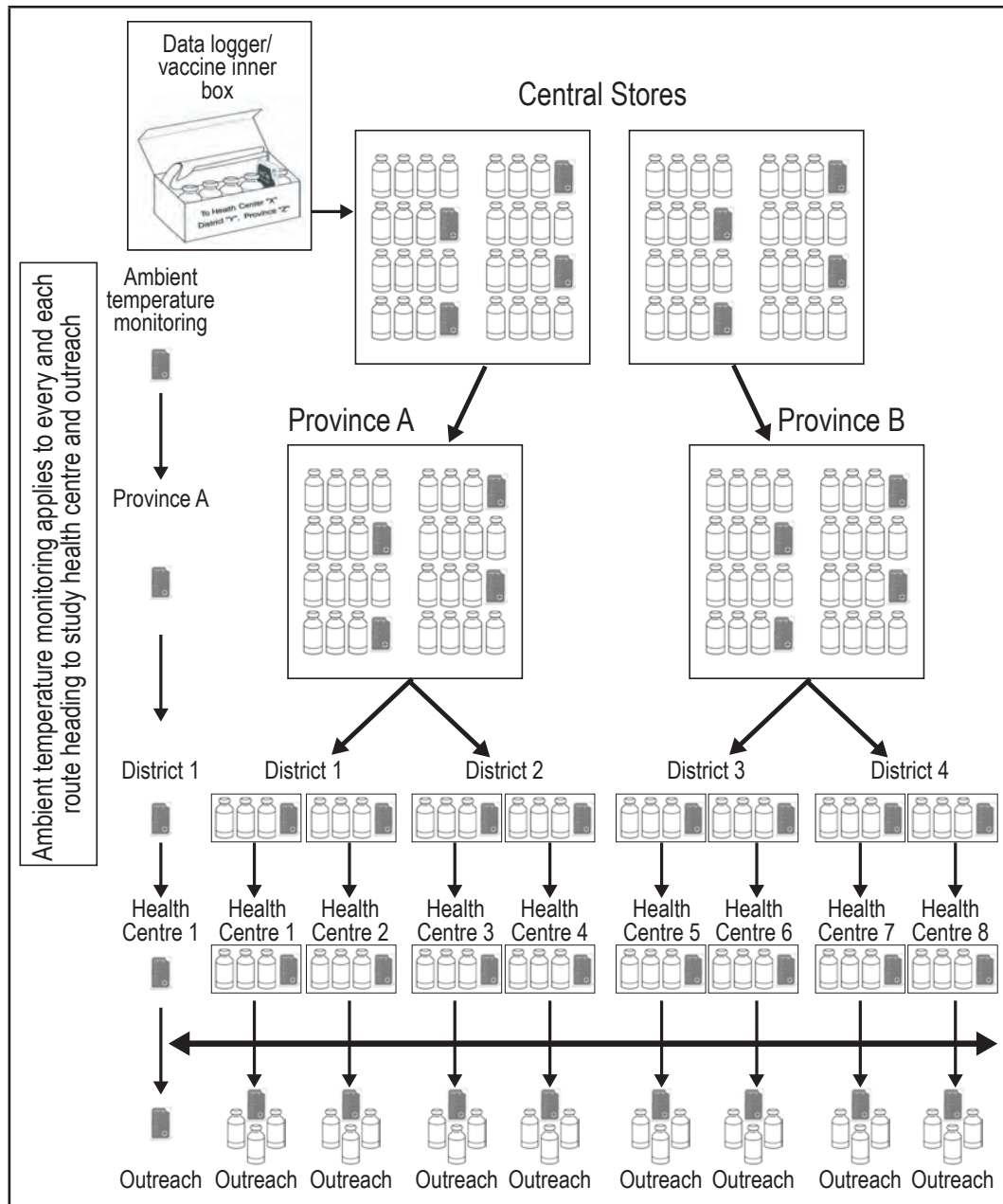
Annex 2:

Data logger packed in inner box



Annex 3:

Cold-chain temperature monitoring



Annex 4:

Monitoring form

Health center destination: _____

Data logger ID# _____

Location

Primary stores C

Province P

District D

Health Center H

Ambient A

Facility Name	Location	IN		OUT	
		Date Received	Time Received	Date Received	Time Received

Shake test at health facility		Date conducted	
Indicate the number of vials that failed the shake test.			

Annex 5:

Cold-chain temperature monitoring

The financial implications of a cold-chain study depend on particular circumstances and salary scales. Costs fall into three categories:

- 1) Initial expenses for materials required
 - LogTag TRIX-8 data logger (16 units)
 - LogTag LTI/USB interface cradle (one cradle is enough for the study; however, the country may choose to purchase more for further use)
 - LogTag Analyzer Software (free of charge)
 - duplication of monitoring forms
 - training materials
- 2) One-time in-country expenditures
 - the cost of translating and/or adapting the study Protocol
 - the cost of translating and/or adapting training materials
 - local transport and per diem for study participants to participate in training
 - data logger collection
 - supervision
- 3) Recurring costs to the programme

Since the study requires the study vaccines to follow routine and standard operations in the country, the amount of staff time spent specifically on the study will be limited, with the exception of one day for training. The amount of time the study coordinator (preferably the immunization programme manager or cold-chain manager) would spend on the study is greater than any other staff involvement. However, identifying the problems in the cold chain and introducing corrective actions are considered to be part of study coordinator's professional responsibility. In this regard, the study itself enables the staff to better perform their jobs and should not be considered as "additional work".

Annex 6:

Example of a time schedule for the study

ACTIVITY	TIME																							
	Month 1				Month 2				Month 3				Month 4				Month 5				Month 6			
	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
1. Preparations																								
a. Protocol development																								
b. Communications with MOH, local staff																								
c. Planning meetings with EPI staff																								
d. Training																								
2. Implementation																								
a. Arrangement of boxes																								
b. Vaccine storage and distribution																								
Storage at primary vaccine store																								
Transport from primary store to provincial store																								
Storage at provincial store																								
Transport from provincial to district store																								
Storage at district store																								
Transport from district store to health centre																								
Storage at health centre refrigerator																								
Outreach																								
c. Data logger collection																								
3. Supervision																								
4. Data entry and analysis																								
5. Report																								

Annex 7:

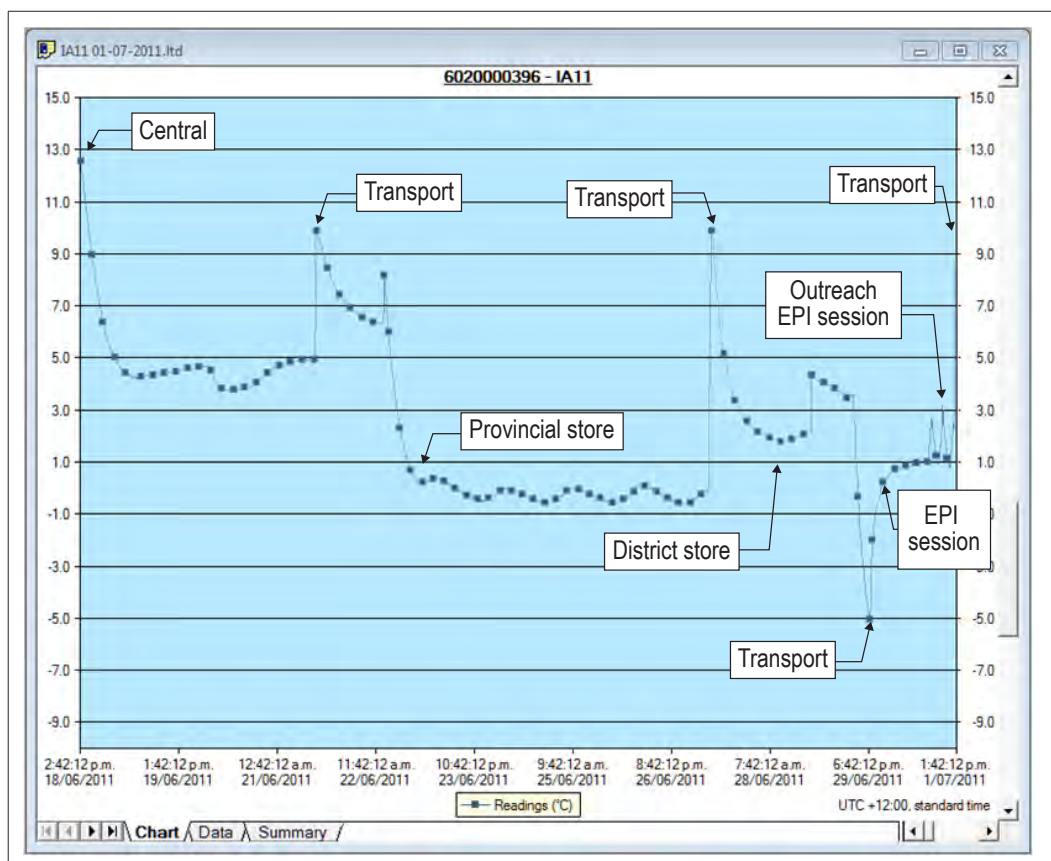
Interview guidelines

Cold-chain personnel can be interviewed individually or in groups. The following questions and topics are designed to help determine their knowledge and attitudes toward freezing in the cold chain.

- Does freezing harm vaccines? Which vaccines?
- How can you tell if a vaccine has been frozen?
- What do you do if you know a vaccine has been frozen?
- Do you think freezing occurs at this point in the cold chain?
- What causes freezing to occur at this point in the cold chain?
- What equipment changes or training could be done to reduce freezing?
- What else could be done to reduce cold-chain freezing?
- Do you have clear guidelines explaining how to reduce freezing and what to do if vaccines are frozen?
- Did you receive training on these topics?

Annex 8:

Sample temperature monitoring graph



Annex 9:

Sample table for minimum and maximum
temperature readings during vaccine transport

Name of province	Name of district	Name of commune	Temp °C	Central store	Transport to province	Province store	Transport to district	District store	Transport to commune	Commune health station	EPI session	Transport to outreach	Outreach EPI session
A	1	a	min	3.1	1.1	2.3	-0.1	2.7	-0.1			2.7	4.3
			max	8.0	9.1	4.6	5.0	9.9	2.7			-	10.6
		b	min	3.1	1.1	1.1	-0.1	3.9	3.1		4.3		
			max	6.2	8.4	3.9	5.0	10.2	6.2		10.6		
	2	c	min	3.1	1.5	2.7	9.9	-1.0	-0.1		-0.1		
			max	8.0	10.6	4.3	10.6	9.5	0.3		1.1		
		d	min	3.1	1.9	2.3	-0.1	-0.6	-	-	3.5	2.3	2.3
			max	7.7	7.3	5.0	2.7	6.9	12.0	12.4	12.4	3.1	-
	3	e	min	4.3	9.1	-3.5	13.8	1.5	9.9	6.2	7.3		
			max	7.7	10.2	8.4	15.3	13.8	11.0	8.8	9.5		
		f	min	3.9	1.9	-3.1	13.1	1.9	4.3	3.9	4.3		
			max	8.0	8.8	5.0	13.8	14.9	9.9	4.6	9.5		
B	4	g	min	3.1	7.7	-3.5	-4.4	-4.0	-6.3		1.9		
			max	7.7	9.9	9.1	5.0	4.6	-0.1		2.3		
		h	min	3.5	6.2	-3.1	-0.1	-0.6	-6.3	-5.8	-0.1	0.7	1.5
			max	7.3	10.6	5.4	8.4	5.0	0.3	-0.1	2.7	1.5	9.1

Annex 10:

Sample table for time and temperature information for shipments to each community health center

Name of province	Name of district	Name of commune	Minimum temp (°C)	Maximum temp (°C)	Percent of time below 0°C (cumulative time below 0°C)
A	1	a	-0.1°C	10.6°C	1.3% (4.0 hrs)
		b	-0.1°C	10.6°C	0.8% (2.5 hrs)
	2	c	-1.0°C	10.6°C	45.5% (6.4 days)
		d	-0.6°C	12.4°C	40.1% (5.6 days)
B	3	e	-3.5°C	15.3°C	11.9% (1.9 days)
		f	-3.1°C	14.9°C	13.1% (2.1 days)
	4	g	-6.3°C	9.9°C	41.9% (4.3 days)
		h	-6.3°C	10.6°C	43.2% (4.8 days)

Annex 11:

How to do the “shake test”

The **shake test learning guide** provides the steps of accepted, standard and correct way of performing a shake test, evaluating the results and suggests on the correct action for different outcomes. It is a decision making tool to decide whether one suspected vaccine vial is damaged by freezing.

This learning guide is designed to be used during the demonstration and coaching sessions of a training program. The trainee (in this case health staff) is also encouraged to use it while practicing by her/himself.

The following video can also be used in learning how to do the shake test:

WHO, Step by step shake test, available at <http://vimeo.com/8389435> (10:07 min)

Shake test is validated by WHO and is found to be 100% specific and 100% sensitive in identifying vaccines that are damaged by freezing^{9, 10}.

Using the learning guide during demonstration

Teaching of a new skill should start with demonstration. A demonstration is basically showing how a skill is performed.

The study coordinator must first of all, make sure that s/he performs the skill precisely as outlined in the learning guide. All the steps are there for a reason, and none should be skipped or modified. The study coordinator must be proficient in performing the shake test. This issue cannot be overemphasized.

A demonstration should be as close to the real thing as possible. Therefore, having real vaccine vials (frozen for control, frozen for test, non-frozen for test) during the training is advised.

The study coordinator distributes the learning guides to health workers prior to demonstration and goes through each step making sure all is clear about the instructions. The study coordinator answers questions about the learning guide.

⁹ Ümit Kartoglu, Nejat Kenan Ozguler, Lara J Wolfson and Wiesław Kurzatkowski, Validation of the shake test for detecting freeze damage to adsorbed vaccines. *Bull World Health Organ* 2010;88: 624–631

¹⁰ WHO, Shake and tell (video), <http://vimeo.com/8381355> (22:17 min)

The next step is to show how to do the shake test. Following the proper demonstration guidelines, the study coordinator demonstrates the shake test by actually doing it. At this point, the participants should be following the study coordinator and their learning guides at the same time. They are free to ask questions at all times during demonstration and coaching.

Using the learning guide during coaching

Coaching is a one-to-one activity between a study coordinator and a health staff on learning to perform a specific skill. During this activity, the health staff performs the shake test, and the study coordinator watches the health staff to provide encouragement, support and feed-back. The health staff uses the learning guide during this session. The study coordinator should emphasize the importance of performing the shake test exactly as it is written on the learning guide.

Using the learning guide during self-practice

A health staff is encouraged to use the learning guide during self-practice. A partner may help the health staff, providing him/her with specific feed-back based on the steps of the learning guide. Self practice with or without a partner is a highly desirable situation which allows the health staff to pace his/her own learning experience, which in turn reduces the anxiety associated with learning a new skill, thus actually facilitating learning.

Using the learning guide during final assessment

This learning guide can be used to assess whether the health staff is in fact, competent to perform a shake test. Using the same tool for assessment and for learning, reduces performance anxiety on behalf of the health staff.

The structure of the learning guide

Performance assessment scale; The scale is used to mark whether each step is performed to a satisfactory level. We expect to see no “1”s to declare the health staff as “competent to perform the shake test” in the final assessment.

“Practice No.” columns: Each numbered column indicates one practice session of the health staff. When practicing with a partner, the partner would write the appropriate number from the assessment scale to each cell in that column. It is assumed that three practices would be sufficient to learn to perform the shake test. If the health staff feels s/he should practice more, s/he should be provided with more blank learning guides.

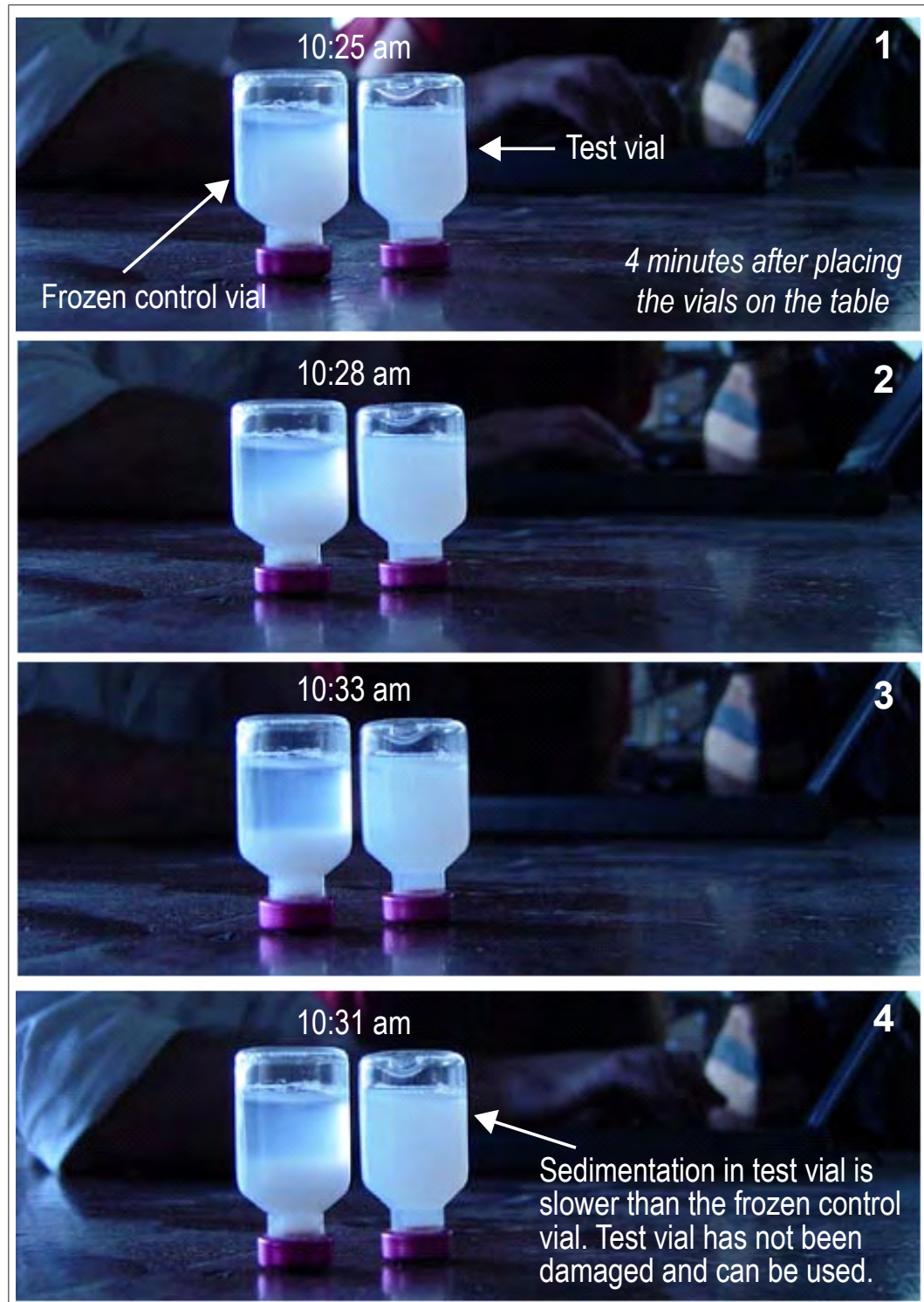
Shake test learning guide

Name of health staff: _____

Performance assessment scale: 1. Insufficient: Health staff performs the shake test incorrectly, or not in the right order or skips it altogether. 2. Competent: Health staff performs the shake test correctly and in the right order but either misses some points or needs to be reminded and encouraged by the study coordinator. 3. Proficient: Health staff performs the shake test correctly, in the right order, and without hesitating.				
NOTES: ■ This protocol must not be altered. There is only one correct way to conduct a Shake Test. ■ The test procedure described below should be repeated with all suspect batches. In the case of international arrivals, the shake test should be conducted on a random sample of vaccine. However, if there is more than one lot in the shipment, the random sample must include a vial taken from each and every lot.		Practice no.		
		1	2	3
1. Take a vial of vaccine of the same type and batch number as the vaccine you want to test, and made by the same manufacturer.				
2. Clearly mark the vial as " FROZEN ".				
3. Freeze the vial in a freezer or the freezing compartment of a refrigerator until the contents are completely solid.				
4. Let it thaw. Do NOT heat it!				
5. Take your " TEST " vial from the batch that you suspect has been frozen.				
6. Hold the " FROZEN " vial and the " TEST " vial together in one hand.				
7. Shake both vials vigorously for 10-15 seconds.				
8. Place both vials on a flat surface side-by-side and start continuous observation of the vials until test is finished. <i>(NOTE: If the vials have large labels, which conceal the vial contents, turn both vials upside down and observe sedimentation in the neck of the vial.)</i>				
9. Use an adequate source of light to compare the sedimentation rates between vials.				
IF:				
10. The TEST vial sediments slower than the FROZEN vial, <div style="text-align: center;">THEN,</div>	10. Sedimentation is similar in both vials <div style="text-align: center;">OR</div> The TEST vial sediments faster than the FROZEN vial <div style="text-align: center;">THEN,</div>			
11. Use the vaccine batch.	11. Vaccine damaged: Notify your supervisor. Set aside all affected vaccine in a container marked " DAMAGED VACCINE FOR DISPOSAL– DO NOT USE ".			
	12. Discard all affected vaccine once you have received permission to do so.			
	13. Fill in the Loss/Adjustment Form.			

The figure below displays the difference between frozen control and (non-frozen) test vial.

Seeing the difference in sedimentation rates during a shake test



The World Health Organization has provided technical support to its Member States in the field of vaccine-preventable diseases since 1975. The office carrying out this function at WHO headquarters is the Department of Immunization, Vaccines and Biologicals (IVB).

IVB's mission is the achievement of a world in which all people at risk are protected against vaccine-preventable diseases. The Department covers a range of activities including research and development, standard-setting, vaccine regulation and quality, vaccine supply and immunization financing, and immunization system strengthening.

These activities are carried out by three technical units: the Initiative for Vaccine Research; the Quality, Safety and Standards team; and the Expanded Programme on Immunization.

The Initiative for Vaccine Research guides, facilitates and provides a vision for worldwide vaccine and immunization technology research and development efforts. It focuses on current and emerging diseases of global public health importance, including pandemic influenza. Its main activities cover: i) research and development of key candidate vaccines; ii) implementation research to promote evidence-based decision-making on the early introduction of new vaccines; and iii) promotion of the development, evaluation and future availability of HIV, tuberculosis and malaria vaccines.

The Quality, Safety and Standards team focuses on supporting the use of vaccines, other biological products and immunization-related equipment that meet current international norms and standards of quality and safety. Activities cover: i) setting norms and standards and establishing reference preparation materials; ii) ensuring the use of quality vaccines and immunization equipment through prequalification activities and strengthening national regulatory authorities; and iii) monitoring, assessing and responding to immunization safety issues of global concern.

The Expanded Programme on Immunization focuses on maximizing access to high quality immunization services, accelerating disease control and linking to other health interventions that can be delivered during immunization contacts. Activities cover: i) immunization systems strengthening, including expansion of immunization services beyond the infant age group; ii) accelerated control of measles and maternal and neonatal tetanus; iii) introduction of new and underutilized vaccines; iv) vaccine supply and immunization financing; and v) disease surveillance and immunization coverage monitoring for tracking global progress.

The Director's Office directs the work of these units through oversight of immunization programme policy, planning, coordination and management. It also mobilizes resources and carries out communication, advocacy and media-related work.

Department of Immunization, Vaccines and Biologicals

Family and Community Health

World Health Organization
20, Avenue Appia
CH-1211 Geneva 27
Switzerland
E-mail: vaccines@who.int
Web site: <http://www.who.int/immunization/en/>