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Improving temperature monitoring in the vaccine cold chain at the periphery: An intervention study using a 30-day electronic refrigerator temperature logger (Fridge-tag®)

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ABSTRACT

This intervention study was conducted in Albania to establish the superiority of the Fridge-tag® (30-day electronic refrigerator temperature logger) against thermometers. Intervention sites used Fridge-tag® and a modified temperature control record sheet, while control sites continued with their routine operation with thermometers. All refrigerators in both groups were equipped with downloadable electronic data loggers to record temperatures for reference. Focus group sessions were conducted with involved staff to discuss temperature monitoring, Fridge-tag® use and its user-friendliness. Significant discrepancies were observed between thermometer readings and the electronic data loggers in control sites, while all alarms from Fridge-tag® were confirmed in the intervention group. Thermometers are not sufficient to monitor temperatures in refrigerators since they miss the great majority of low and high alarms. Fridge-tag® has proven to be an effective tool in providing health workers with the information they need to take the necessary actions when there are refrigerator temperature variations.

1. Introduction

To ensure the optimal potency of vaccines, careful attention is needed in handling practices at the country level. These include storage and transport of vaccines from the primary vaccine store down to the end-user at the health facility, and further down at the outreach sites. The World Health Organization (WHO) recommends that all vaccines should be stored at between +2 °C and +8 °C at all immunization points in the periphery (health centres, health houses, hospitals, and clinics). Liquid formulations of vaccines with aluminium adjuvant containing diphtheria, pertussis, tetanus, hepatitis B, *Haemophilus influenzae* type b, IPV and their combinations should not be frozen[1] [1–3].

Practices exposing vaccines to both high and sub-zero temperatures are widespread in both developed and developing countries at all levels of health systems [4–15]. The most recent systematic literature review of vaccine freezing highlights that accidental freezing is widespread and occurs across all segments of the cold chain [16]. In this review, between 14% and 35% of refrigerators or transport shipments were found to have exposed vaccines to temperatures below zero.

Temperature monitoring in the vaccine cold chain is critical in ensuring that vaccines are kept under optimal cold chain conditions. The general practice for temperature monitoring in vaccine refrigerators at the periphery is to use a thermometer (stem thermometer or bi-metal thermometer). A thermometer, however, only provides a snapshot of the temperature at the point in time when it is checked and cannot be considered as an "appropriate" monitoring tool.[2] When checked and a temperature value of between +2 °C and +8 °C is found, health workers may erroneously conclude that the vaccines are safe since this snapshot reading only provides a value when it is checked and by no means covers the rest of the daytime/nighttime period. Unless a temperature excursion is seen at the time the temperature is checked with a regular thermometer, almost all temperature violations go unnoticed.

To improve temperature monitoring at the periphery, the Performance, Quality and Safety (PQS)[3] project in the Immunization, Vaccines and Biologicals Department has approached temperature monitoring device manufacturers to develop a temperature moni-

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[1] Merriam-Webster Dictionary defines "freezing" as liquid solidification.

[2] Merriam-Webster Dictionary defines "monitoring" as ẗo watch, keep track of, or check usually for a special purposeẅhich includes continuity and/or regularity within its concept.

[3] PQS is a prequalification system of devices and equipment used in immunization services in WHO, that establishes design, performance specifications and verification protocols for devices/equipment.

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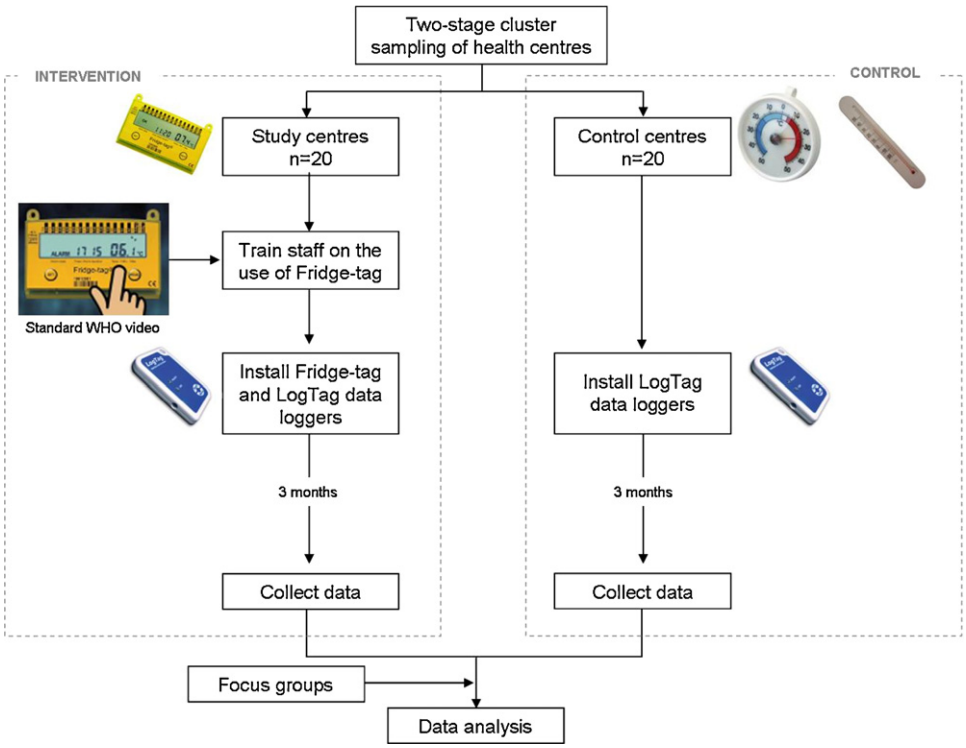

Fig. 1. Study design.

toring device with the following features:

- Capacity to store the last 30-day temperature recordings that can be checked through a history mode and read through an LCD display (not downloadable).
- Preset alarms for high (above +8 °C over 10 h continuously) and low (−0.5 °C and lower for 1 h continuously) temperature exposures.
- Display the highest and lowest temperatures reached as well as their duration compared to preset alarms through the history mode—for details of the performance specifications of the device see WHO/PQS/E06/TR06.1 [17].

Fridge-tag® was the first model prequalified by the WHO—prequalified on 30 September 2007 and revalidated on 5 May 2009 [18].

By the time of the study design, the only other technology available to monitor temperatures in refrigerators was the "min–max thermometer", however, there were no prequalified devices. In addition, the authors were not aware of any use of min–max thermometers in the field. The PQS secretariat approached the temperature monitoring device manufacturers with the intention of phasing out the regular thermometers while introducing the 30-day electronic refrigerator temperature logger. With all these reasons, this study was designed to establish the programmatic value of a 30-day electronic refrigerator temperature logger using Fridge-tag® as an example, as well as assessing this particular device's user-friendliness and its abilities in field conditions.

2. Materials and methods

2.1. Immunization and cold chain system in Albania

Albania's immunization programme is run through 36 districts (second level) and 508 vaccination points (third level) of which 150 are in urban areas and 358 are in rural areas. The Institute of Public Health is responsible for the planning, monitoring and management of the immunization programme at the national level. Epidemiology units in District Public Health Directorates provide guidance, monitoring, supervision and assessment of the immunization services delivered by the primary health care facilities and maternity hospitals. Cold chain equipments for storing vaccines at primary health care facilities are either ice-lined refrigerators or Liebherr-model front opening refrigerators, mostly donated, dating back to 1994. Ice-lined refrigerators are old WHO-listed refrigerators while Liebherr-model refrigerators are not listed in old WHO Performance Information Sheets or in current WHO/PQS database. Temperature monitoring in all refrigerators is done twice daily by checking thermometers and manually recording the temperature on record sheets.

2.2. Study design

This study was designed as an intervention study with the objective of establishing the superiority of the 30-day electronic refrigerator logger against thermometers. Two-stage cluster sampling was used to obtain a representative sample of health care facilities performing immunizations and having a refrigerator. Self-weighting was ensured in such a sample through a choice of regions in which clusters are selected using probability proportional to population size, and by selecting an equal number of sampling units in each cluster. Twenty health centres were selected as "intervention" groups and another 20 health centres were selected as "control" groups (Fig. 1).

Health centre staff from intervention sites were trained on the use of Fridge-tag® through a standard WHO video [19] on how to use the device as well as hands-on practice; no training was provided to the staff from the "control" sites. All refrigerators in the intervention and control sites were equipped with downloadable electronic data loggers as a reference (Trix-8 LogTag® recorder, WHO PQS code E06/06 prequalified on 22 January 2008 and revalidated on 5 May 2009) to record temperatures for 3 months [20].

Intervention sites were asked to monitor temperatures during the study period using Fridge-tag® (Fig. 2) and a modified temperature control record sheet, while control sites continued with their routine operation with thermometers and recording the temperature data on record sheets. At the end of the 3-month data collection period, electronic data loggers and temperature monitoring record sheets were gathered and two focus group sessions were conducted with the involved staff to discuss temperature monitoring, the use of Fridge-tag® and its user-friendliness.

Downloaded data from the electronic data loggers were cross-checked with temperature monitoring record sheets from both groups and further analyses were conducted to document the overlapping and missed information.

The following hypotheses were tested:

- Health workers with Fridge-tag® devices are more confident in temperature monitoring compared to health workers with thermometers.

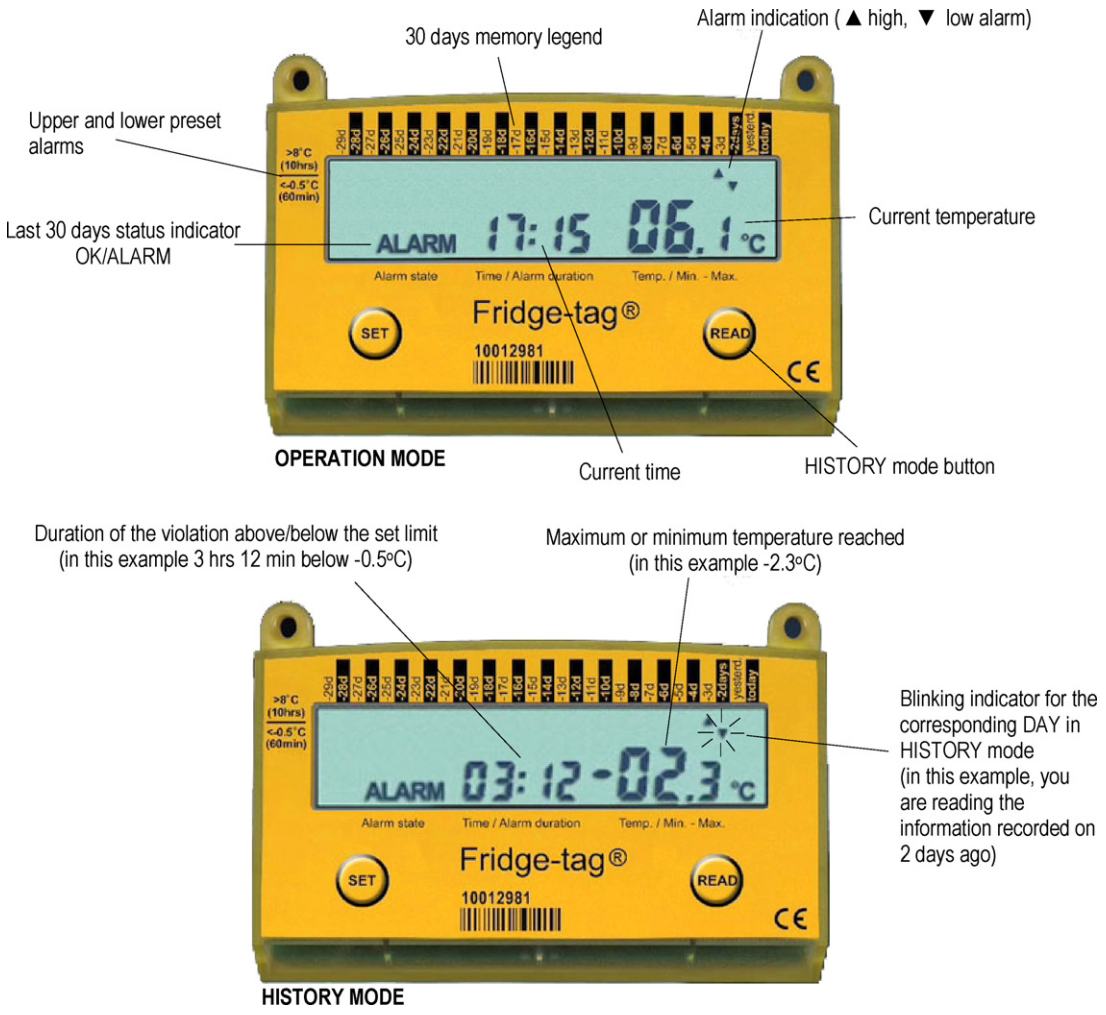

Fig. 2. Fridge-tag® functions.

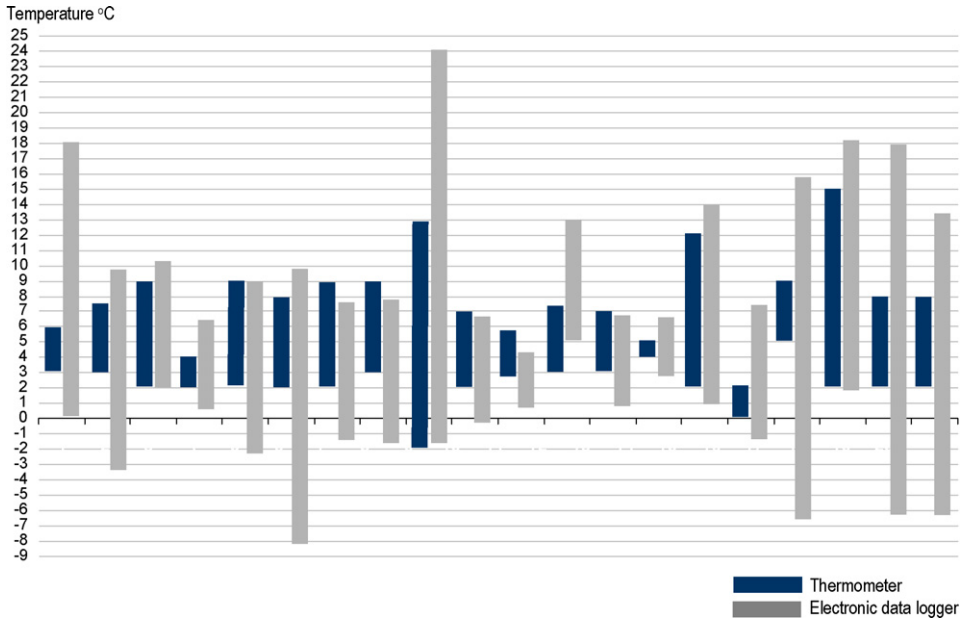

Fig. 3. Comparison of thermometer readings and electronic data logger recordings by centre, control group ($n = 20$).

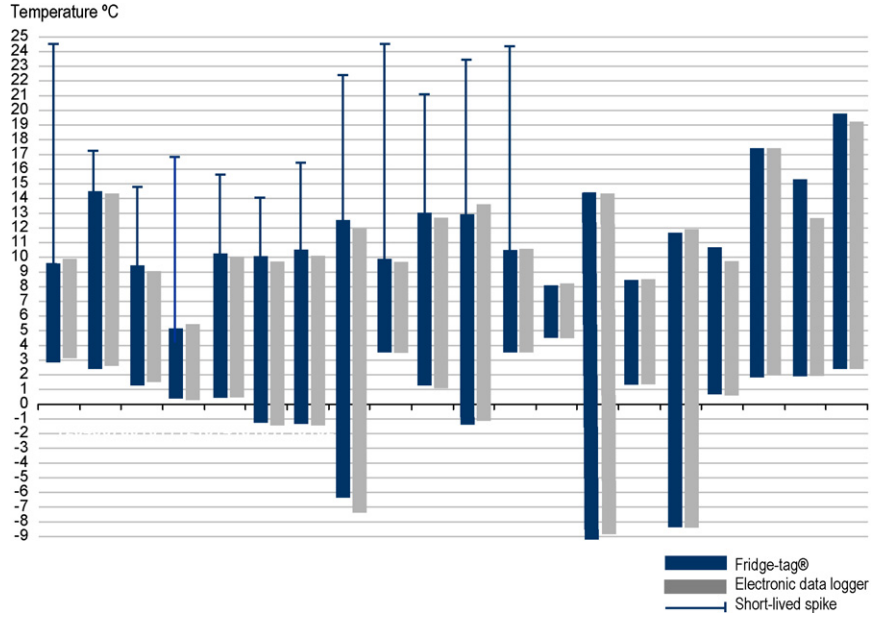

Fig. 4. Comparison of Fridge-tag® readings and electronic data logger recordings by centre, study group ($n = 20$).

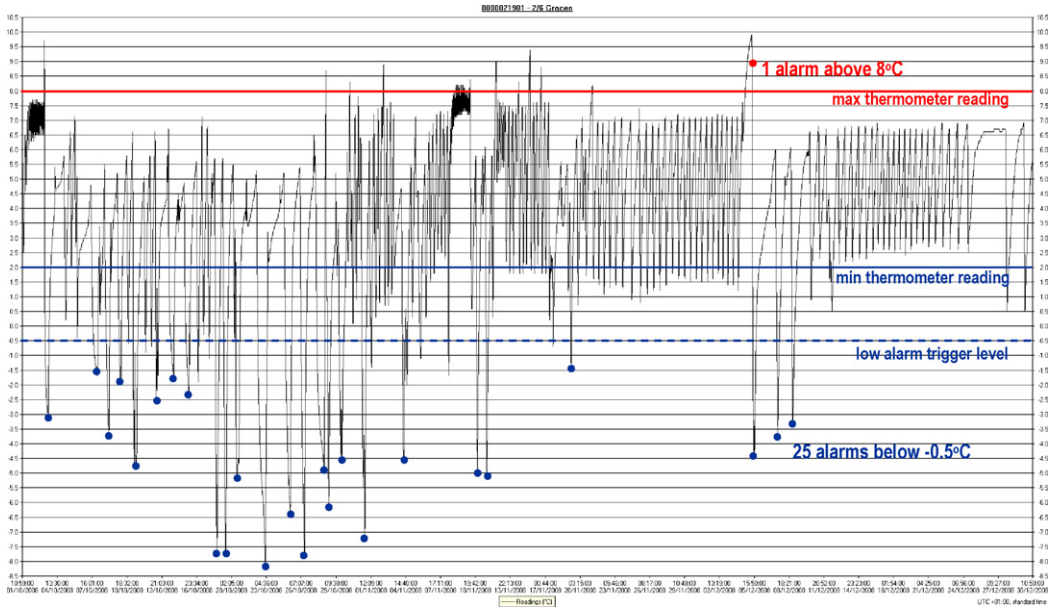

Fig. 5. Comparison of thermometer and electronic data logger recordings, control group (health centre # 2.6).

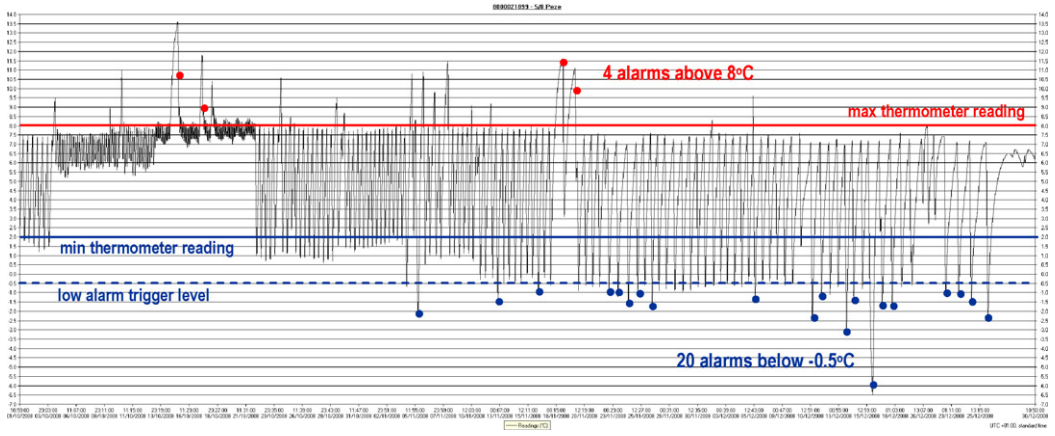

Fig. 6. Comparison of thermometer and electronic data logger recordings, control group (health centre # 5.8).

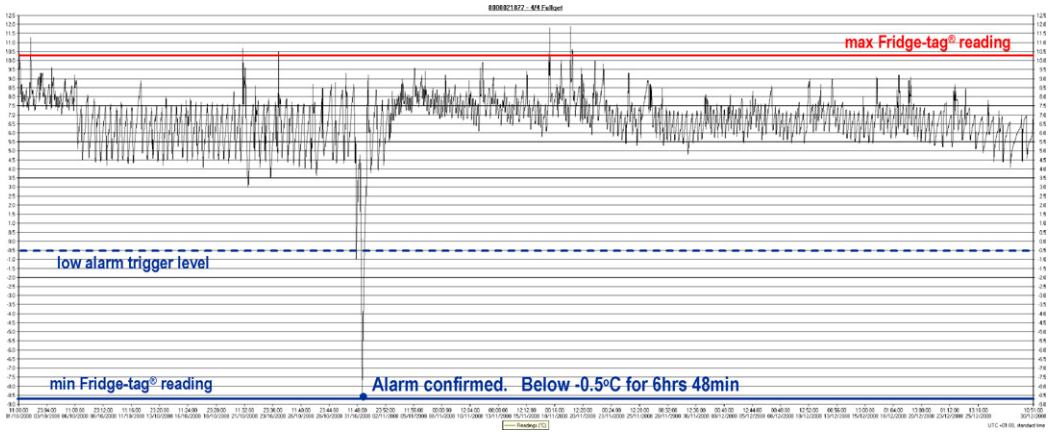

Fig. 7. Comparison of Fridge-tag® and electronic data logger recordings, intervention group (health centre # 4.4).

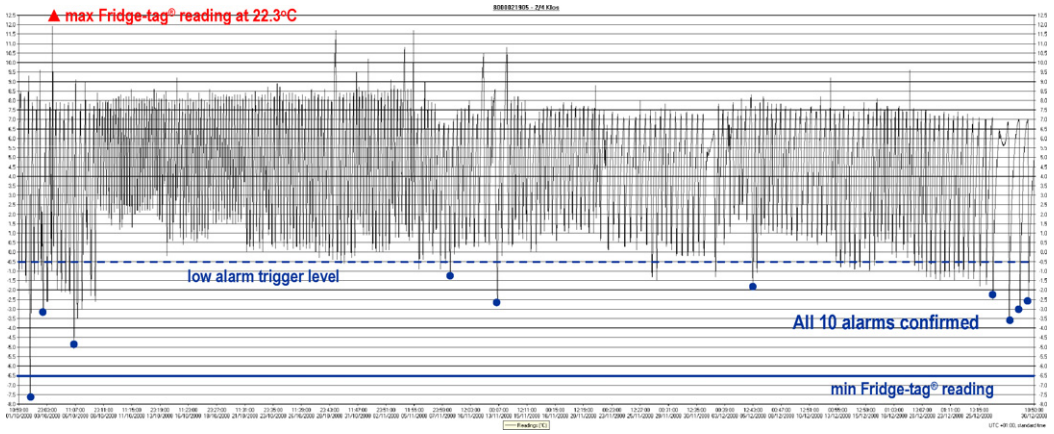

Fig. 8. Comparison of Fridge-tag® and electronic data logger recordings, intervention group (health centre # 2.4).

- Fridge-tag® devices are capable of catching all temperature violations while such go unnoticed with thermometers.

3. Results

The distribution of types of refrigerators in both the study and the control sites were similar. In the study sites, five centres had ice-lined refrigerators and 15 centres had Liebherr-model refrigerators, while in control sites, there were 6 and 14, respectively. Significant discrepancies[4] were observed between the data from thermometer readings and electronic data loggers in the control group. With thermometer readings, only one health centre could document a sub-zero temperature (−2 °C), while all other health centres' measurements ranged from 0 °C to 13 °C. During the same period, electronic data loggers recorded temperatures ranging from −8.2 °C to 24.2 °C. Fig. 3 displays the monthly discrepancies through minimum and maximum temperatures recorded in the control group.

In the study (intervention) group, Fridge-tag® and electronic data logger readings overlapped without any discrepancy in eight cases. As for the remaining 12 cases readings, these overlapped at the lower end but higher temperatures were recorded with Fridge-tag® at the higher end. Although higher temperatures were recorded with Fridge-tag® in 12 cases, only four of these resulted in high temperature alarms, as confirmed by the electronic data logger. Other high recordings were simply spikes (see Section 4 for explanation). When these spikes were ignored, Fridge-tag® readings were in full overlap with the electronic data logger recordings. In health centre # 4.2 after the discovery of a continuous problem with very low temperature, immunization was ceased during which time the refrigerator was replaced; thus this health centre was dropped off the study. Fig. 4 displays the minimum and maximum temperatures recorded in study group by the centre.

The alarm status in the control group based on the data logger readings is shown in Table 1. WHO recommended alarm settings for the Fridge-tag® device were used to illustrate the missed alarms. In the control site, only five health centres' refrigerators were within the recommended temperature range without any alarms. Table 2 displays recorded alarms in the intervention group, all confirmed by the electronic data logger recordings.

The following Figs. 5 and 6 illustrate electronic data logger recordings along with marking lines of minimum and maximum thermometer readings in two selected heath centres (# 2.6 and # 5.8 in the control group) throughout the study period. Based on the WHO recommended alarm settings for the Fridge-tag® device, missed alarms are also indicated.

The following Figs. 7 and 8 illustrate electronic data logger recordings along with marking of Fridge-tag® device readings in two selected health centres (# 4.4 and # 2.4 in the intervention group) throughout the study period. All alarms indicated by the Fridge-tag® device are confirmed by the electronic data logger.

[4] A discrepancy is defined as occurring where the difference between two readings is greater than the sum of accuracy of both devices, e.g., since the accuracy of thermometers is ±1 °C and of data loggers is ±0.5 °C, differences in readings of 1.6 °C were accepted as discrepancy in the control group. Discrepancy was set to be greater than 1.1 °C in the study group since both devices' accuracy was ±0.5 °C.

Table 1
Calculated number of alarms and exposure times according to the data logger readings in the control group ($n = 20$).

Centre	Number of alarms in control group if Fridge-tag® device was used (data from the electronic data logger readings)						Exposure time for ▼ alarm hh:mm		Exposure time for ▲ alarm hh:mm	
	Month 1		Month 2		Month 3					
	Alarm ▼	Alarm ▲	Alarm ▼	Alarm ▲	Alarm ▼	Alarm ▲	Min	Max	Min	Max
1.5	0	0	0	1	0	0			12:34	12:34
1.6	1	0	1	0	2	0	01:48	04:39		
1.7	0	0	0	2	0	1			17:56	19:43
1.8	0	0	0	0	0	0				
2.5	5	0	4	0	0	0	02:08	03:55		
2.6	17	0	5	0	3	1	01:42	02:35	11:27	19:16
2.7	3	0	2	0	0	0	01:47	03:32		
2.8	1	0	3	0	0	0	01:17	04:07		
3.5	0	0	0	0	5[a]	0	01:42	02:12		
3.6	0	0	0	0	0	0				
3.7	0	0	0	0	0	0				
3.8	0	31	0	23	0	0			24:00	24:00
4.5	0	0	0	0	0	0				
4.6	0	0	0	0	0	0				
4.7	0	5[a]	0	8[a]	0	7[a]			11:04	17:43
4.8	1	0	3	0	5	0	02:19	03:31		
5.5	0	5	11	1	0	2	02:07	02:33	12:00	24:00
5.6	0	2	0	3	0	2			11:57	19:22
5.7	4	0	14	0	0	0	02:11	04:14		
5.8	0	2	8	2	12	0	02:33	08:34	11:00	21:34

[a] Readings overlapping with electronic data loggers.

Table 2
Recorded number of alarms confirmed by electronic data logger in the intervention group ($n = 20$).

Centre	Number of Fridge-tag® alarms all confirmed by electronic temperature data logger					
	Month 1		Month 2		Month 3	
	Alarm ▼	Alarm ▲	Alarm ▼	Alarm ▲	Alarm ▼	Alarm ▲
1.1	0	0	0	0	0	0
1.2	0	0	0	5	0	0
1.3	0	0	0	0	0	0
1.4	0	0	0	0	0	0
2.1	0	0	0	0	0	0
2.2	4	0	0	0	0	0
2.3	0	0	0	0	0	0
2.4	3	0	2	0	5	0
3.1	0	0	0	0	0	0
3.2	0	2	0	0	0	0
3.3	3	4	0	0	0	0
3.4	0	0	0	0	0	0
4.1	0	0	0	0	0	0
4.2	27	0	Excluded from the study			
4.3	0	0	0	0	0	0
4.4	1	0	1	0	0	0
5.1	0	0	0	0	0	0
5.2	0	2	0	0	0	0
5.3	0	0	0	0	0	0
5.4	0	0	0	0	0	0

In Fig. 8, the highest reading of Fridge-tag® is recorded as 22.3 °C despite the highest electronic data logger reading was 11.9 °C. Similar higher readings for very short periods of time were observed in 12 study centres.

4. Discussion

In the control group only five health centres had refrigerators without any alarms. In all other control sites, a minimum of one alarm was observed during the study period based on data from the electronic data loggers (the maximum number of alarms was 54 in health centre # 3.8). Only two health centres had confirmed two of the temperature violations at the alarm level (health centres # 3.5 and # 4.7) through the use of thermometers. All other alarms in those two health centres, as well as all the alarms in the other health centres, had been missed. In total, there were 110 low alarms and 98 high alarms were calculated in the control group. No systematic alarm pattern could be observed in the control group; some health centres had alarms in all 3 months, some only at the beginning, and some during the last month.

Large discrepancies were discovered between the thermometer and electronic data logger device recordings at the control sites. These discrepancies varied from 12 °C at the high end to 11.5 °C at the lower end. This is understandable to some extent since a thermometer reading is a “snapshot at a point in time” activity while electronic data logging is “continuous”. However, despite electronic data recordings confirming in one health centre (#3.8) continuously between 9.5 °C and 13 °C for 31 days during the first month, manual recordings through thermometer readings were only between 5 °C and 7.2 °C. This raises questions as to whether the

staff really check the thermometers before recording the reading manually.

In the study group, all Fridge-tag® readings at the lower end were confirmed by the electronic data logger. In many cases, they fully overlapped. In others, there were differences less than 1 °C. Since the accuracy of the both devices is ±0.5 °C, these differences are considered within the accuracy limits, therefore as overlapping. In 12 cases, quite a big difference was observed at the higher end readings. For example, in health centre # 2.4, the highest Fridge-tag® reading was 22.3 °C while the highest electronic data logger reading was 11.9 °C for the same time point. In analysis of the duration of such exposures through the history mode in the Fridge-tag®, in all 12 health centres it was found that these exposure periods were quite short and did not result in any alarm violation. This discrepancy was determined to be caused by an occasional interaction between how a user would read the device and how the device collected and recorded the temperature. The Fridge-tag® device checks the temperature continuously but registers (records) the information in its memory every 10 min. When the user pushes the READ button to see the temperature history, the device does not collect or register any data for 30 s after the READ button is pushed. For example, if a device is taken out of the refrigerator at 9 min, following the last temperature registry, it will have only 1 min to register the temperature after the history function is used. Since the device gets warmer in the hands of the health worker and in the ambient temperature where it is read, the device may not have enough time to re-acclimate itself when it is placed back in the refrigerator and it registers the temperature at 10 min. As a result, a very high temperature, shown as a very short-lived spike, will be recorded by the Fridge-tag®. If these spikes are ignored, a full overlap of recordings is observed in all health centres (Fig. 4). This issue was also mentioned during the focus group discussions with the study site health staff. One health worker indicated the following:

> "You told us it does not record during the history mode. But I have seen very high temperatures and I believe this is due to keeping the device outside".

In total, throughout the study period, there were 46 low alarms and 13 high alarms in the study group. 85% of low alarms and 62% of high alarms appeared during the first month. Since the health staff was aware of these alarms, they took corrective measures as described in the study protocol and managed to reduce or eliminate the alarms in the following months. In one health centre (# 4.2), immunization activities were ceased after the discovery of low temperature problems in the refrigerator. The refrigerator was replaced with a new one after some period. Due to this interruption, this health centre was excluded from the study. When the monthly alarm status is compared between the two groups, the following was observed: a declining number of alarms in the intervention group and no systematic pattern in the control group.

In the study group, in all health centres were supposed to perform a shake test according to WHO protocol when a low temperature alarm was observed, to identify whether vaccines were damaged by freezing. However, due to limited number of vials, health centre staff decided to discard all vials rather than conduct the shake test (the shake test requires one vial of each type to be purposely frozen as a negative control vial) [1,21]. In the control site, there was only one health centre (#3.5) that registered −2 °C during the last month. No shake test was conducted for the same reason and all freeze-sensitive vaccines were discarded. In the control sites, the electronic data loggers showed 10 health centres that had negative temperatures down to −8.2 °C, but, since these conditions were not observed by those taking periodic "snapshots" using thermometers, naturally no shake tests were conducted. It is highly possible that freeze-damaged vaccines were used in some of these health centres since in such low temperatures for up to 8 h 34 min exposure, freeze-sensitive vaccines would have been damaged by freezing.

Health workers who used Fridge-tag® were quite happy with the device and found it to be very easy to use. The following statements were made during the focus group discussions:

> "It is very easy to read. . ."

> "No we were not aware of alarm situation in our refrigerators. Thermometers do not tell this".

> "I wish I have had the fridge tag before".

> "We thought that reading the temperatures twice is a perfect way to check how refrigerator works; now we understand that we have just checked the temperature in two moments during 24 h but nothing regarding the min and max temperatures".

These statements demonstrate that a real mind-shift happened with these health workers regarding temperature control. In the end, they all agreed that thermometers are not the devices that should be used for temperature monitoring in health centre refrigerators.

Health workers in the control sites indicated during the focus group discussions that "they are in control" of temperature monitoring through checking the temperatures twice a day with the help of thermometers:

> "No, no, never below 2 (degrees) and only sometimes when there is no electricity more than 8 (degrees)".

But when the health workers were challenged as to whether this is the best way to monitor temperatures, they started to question the quality of data they receive through thermometers:

> "No, I cannot say I have a good level of temperature control, since I do not know what happened during Sunday, or even the afternoon, when we leave the office".

Health workers then received information on the performance of a new device (Fridge-tag®) and were asked whether they would prefer to have such a device instead of regular thermometers. They all agreed that this would provide them a good level of control and allow them to take measures whenever necessary.

> "Yes it will be great. Then we will see by ourselves if our temperatures are correct or not".

5. Conclusion and recommendations

Temperature monitoring is critical in vaccine cold chain. Health workers handling vaccines at the periphery should have tools to discover problems and, based on the data, take necessary measures. Thermometers (stem or bi-metal) do not provide the necessary level of security and can only provide a spot check rather than truly "continuous" monitoring. It is very unlikely that a health worker catches a cold chain violation using a thermometer, unless the problem continues throughout the day and, by chance, it is observed when the temperature spot check is made. The Fridge-tag® and similar 30-day electronic refrigerator temperature loggers bring a highly significant improvement in temperature monitoring, especially at the health centre level. They allow health workers to see how temperatures changed throughout the daytime/nighttime cycle, including weekends and holidays; so the health worker can determine whether there were any unacceptable temperature exposures. That way, health workers can take informed decisions as corrective measures to reduce and/or eliminate cold chain problems.

This study also provided valuable field-experience data on the Fridge-tag®'s design specifications: the device's algorithm for measuring and recording temperature could sometimes be confounded when the temperatures were being read by the user. Following the study, a series of meetings were held with the manufacturing company Berlinger & Co AG, to further improve the device. A new generation of Fridge-tag® devices is now being developed to delay registry 10 min following use of the history mode.

The authors strongly recommend abandoning the use of thermometers as temperature monitoring devices for vaccine refrigerators and replace them with 30-day electronic refrigerator temperature loggers.

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