Accurate Cold-Chain Temperature Monitoring Using Digital Data Logger Thermometers

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Current Problem

- CDC administers over $3 billion of vaccine to low-socioeconomic families through Vaccines for Children (VFC) program each year
- Storage temperature control is vital to maintaining vaccine potency
  - Storage outside 2 °C to 8 °C range can render vaccines ineffective
  - A meta-analysis published in *Vaccine* estimated **14 to 35%** of delivered vaccines are subjected to inappropriate storage temperatures
- Social and economic costs of improperly stored vaccines
  - Cost of manufacturing and delivering vaccine wasted
  - Vaccine delivery delayed
  - Reported vaccination rates are erroneously high
  - Recipients are not protected
- Better vaccine cold chain management through improved temperature monitoring practices
  - Decrease incidence of waste
  - Improve consumer confidence
  - Increase effective inoculation rates

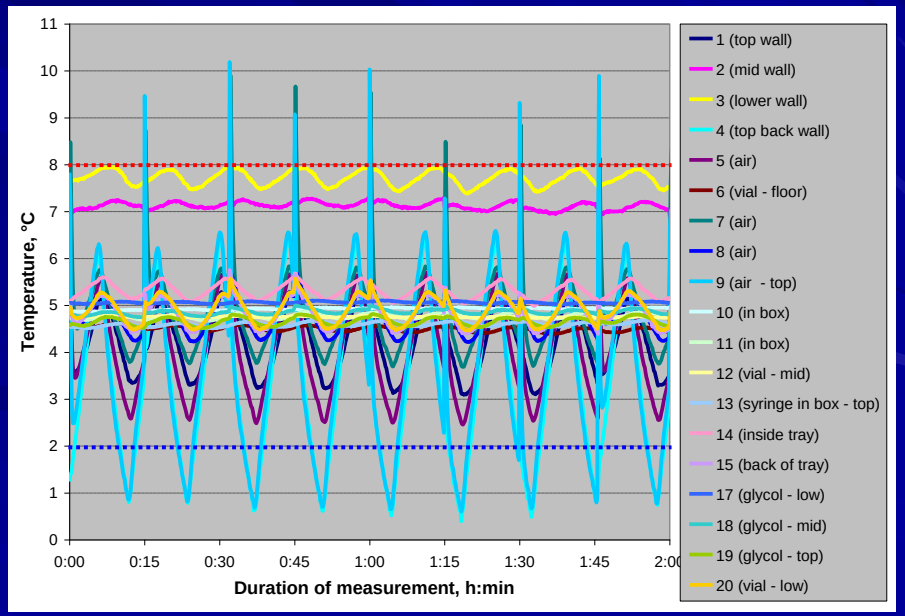
Cold Chain Temperature Monitoring

- **How do you know if stored vaccines are safe and effective?**
  - Track temperature history
- **Refrigerator temperature is NOT a single point measurement**
  - Refrigeration cycle – compressor timing
  - Air circulation patterns – spatial temperature variations
  - Use patterns – door opening, loading density, temperature set point
  - Environmental conditions – room temperature variation, power failures
  - Defrost cycle
  - Thermometer location – what are you measuring?

A refrigerator is ONLY as good as the temperature monitoring system inside

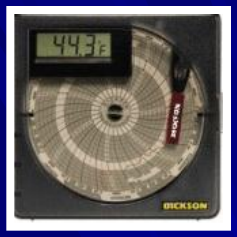
High-tech, pharmaceutical-grade units still affected by variable conditions

Accurate temperature history that reflects actual vial temperatures is **imperative** to effective vaccine management



Cold Chain Temperature Monitoring

Why doesn't the current VFC system work?



F° Check Both Temperatures Twice A Day

Month: _____

Days 1–15 (16-31 continued on other side)

Refrigerator

Staff Initials																														
Day of Month	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15	
Time	am	pm	am	pm	am	pm	am	pm	am	pm	am	pm	am	pm	am	pm	am	pm	am	pm	am	pm	am	pm	am	pm	am	pm	am	pm
Too high* ≥ 49°F																														
48°F																														
47°F																														
46°F																														
45°F																														
44°F																														
43°F																														
42°F																														
41°F																														
Aim for 40°F																														
39°F																														
38°F																														
37°F																														
36°F																														
35°F																														
Too low* 34°F																														
33°F																														
≤ 32°F																														

Freezer

Too high* ≥ 8°F																														
7°F																														
6°F																														
5°F																														
4°F																														
≤ 3°F																														

Take immediate action* if temperature is in the shaded area.

If temperature is above 49° F, write in the current temperature.

If temperature is below 32° F, write in the current temperature.

Take immediate action* if temperature is in the shaded area.

Take immediate action* if temperature is in the shaded area.

If temperature is above 8° F, write in the current temperature.

Instructions for Temperature Log:

Check both temperatures twice a day, each working day of the month. Place an "X" in the boxes that show the temperatures you read in the morning and afternoon; enter your initials and the time in the boxes at the top of the day's column. If your entry is in a shaded area, take immediate action! Use a new form each month and save in a file at month's end for one year.

IMM-682 Fahrenheit (F°) Temperature Log (3/06)

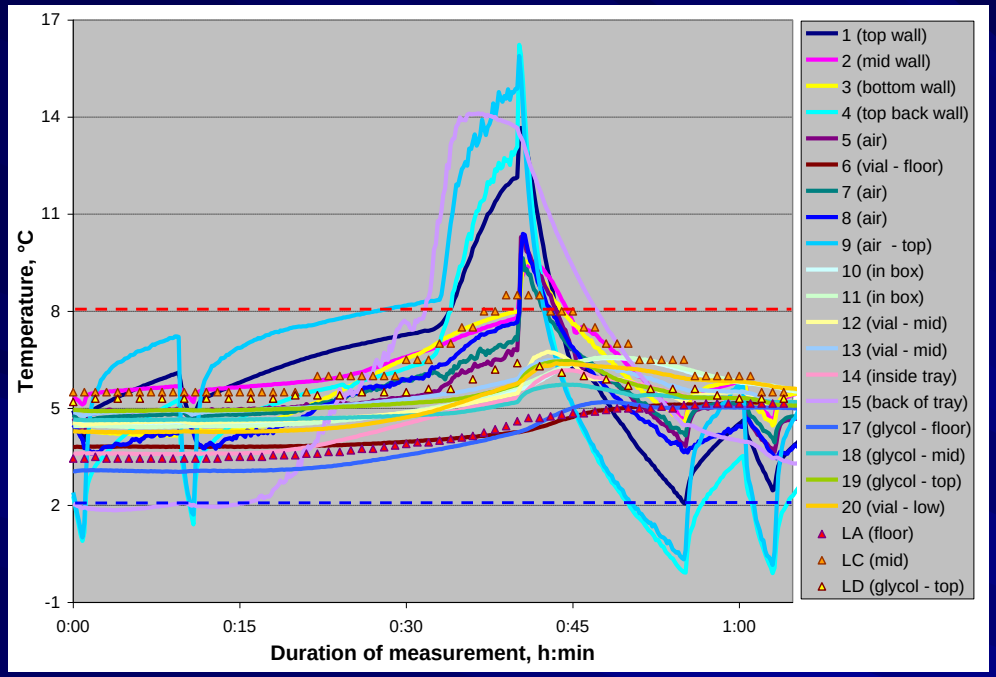
***TAKE IMMEDIATE ACTION if the temperature is too high or too low:**

1. Store the vaccine under proper conditions as quickly as possible.
2. Call your VFC Representative.
3. If he/she is not available, call **VFC Customer Service at 1-877-2GET-VFC (1-877-243-8832)**

VFC Field Representative	LHD Immunization Program
( )	( )

Vaccines for Children Program
California Department of Health Services
850 Marina Bay Parkway
Richmond, CA 94804

Continuous Temperature Monitoring



- Vital to proper vaccine storage
- Current "manual check" system:
  - Possible false alarm if checked during defrost cycle
  - Failure to recognize existence of defrost cycle and take any necessary protective measures
- Freezerless fridge example
  - Cumulative effect of time above 8 °C during multiple defrost cycles?
  - Must evaluate on case-by-case basis
- Monitor placement is very important!

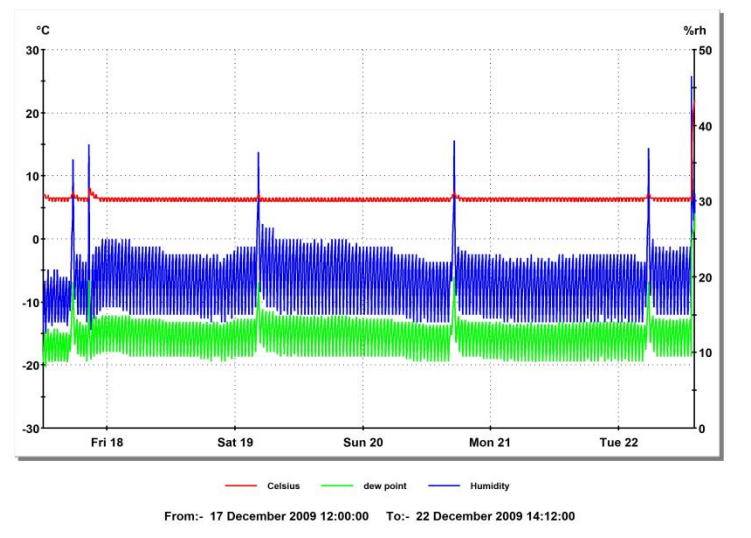
WITHOUT a continuous temperature monitoring system in place..

- Likelihood of undiscovered thermal excursions occurring is **VERY HIGH**

  Examples: overnight power outage, excessive refrigerator cooling following long or frequent periods of door opening, defrost cycle patterns
- Likelihood of administering spoiled, ineffective vaccines to patients is **VERY HIGH**
- By the time temperature deviations are found, may be too late for corrective action
- No way to tell when a problem started, how long it lasted,

…or whether the vaccine is safe!

Continuous Monitoring Solution: Electronic Data Loggers



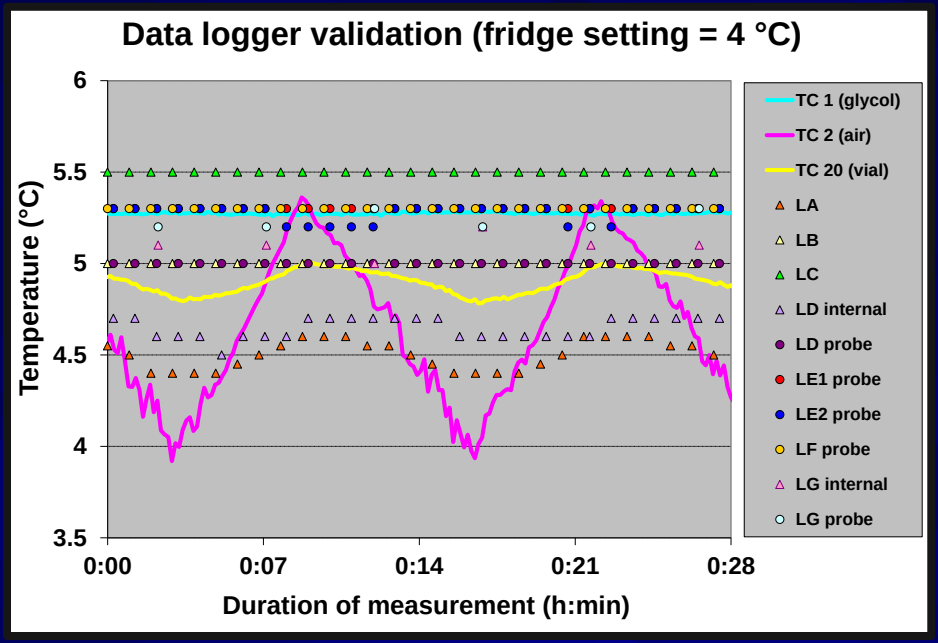
ADVANTAGES

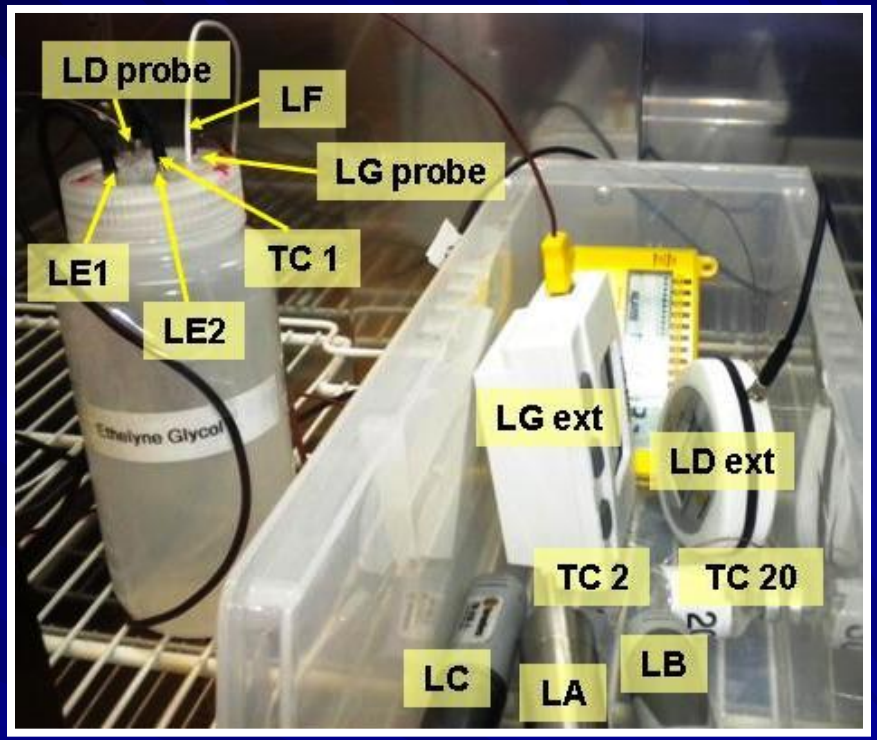
- **Continuous monitoring** - ensures that all thermal excursions are captured, improving confidence in vaccine supply efficacy
- Easy to use
- Quickly analyze results, eliminating time-consuming paperwork
- Archival data stored electronically
- Alarm capabilities, some with email notification mean that problems are revealed (and can be dealt with) immediately
- Wireless models allow for real-time monitoring
- Can be calibrated by end-users at the ice point

DISADVANTAGES

- Data logger use requires computer capability and some training, some field locations are resistant to change

Evaluating Electronic Data Logging Thermometers



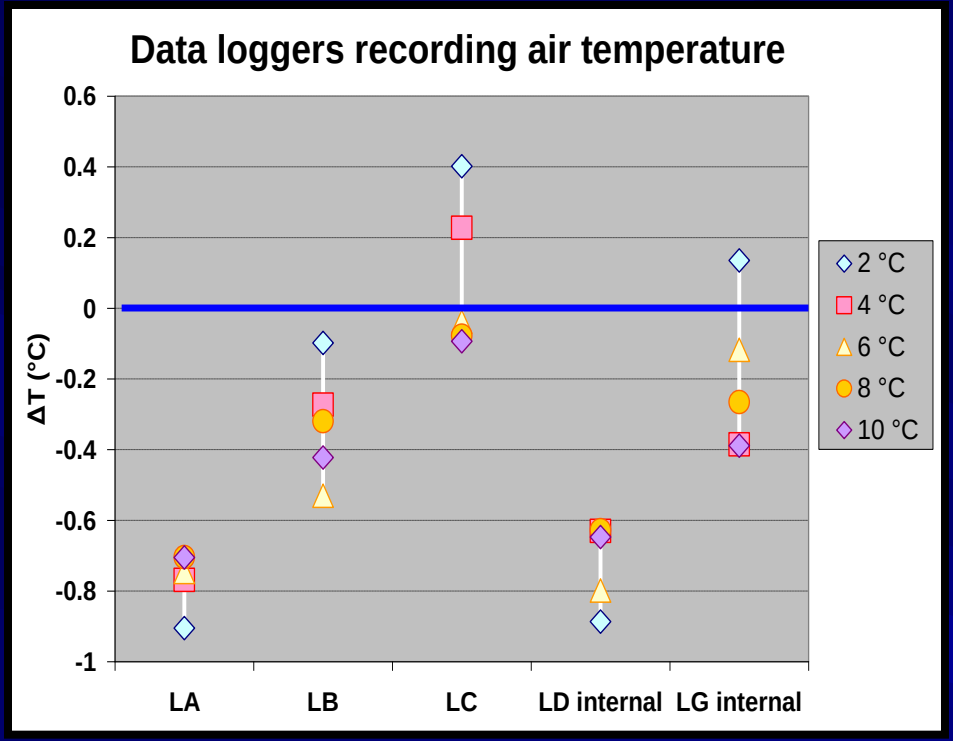


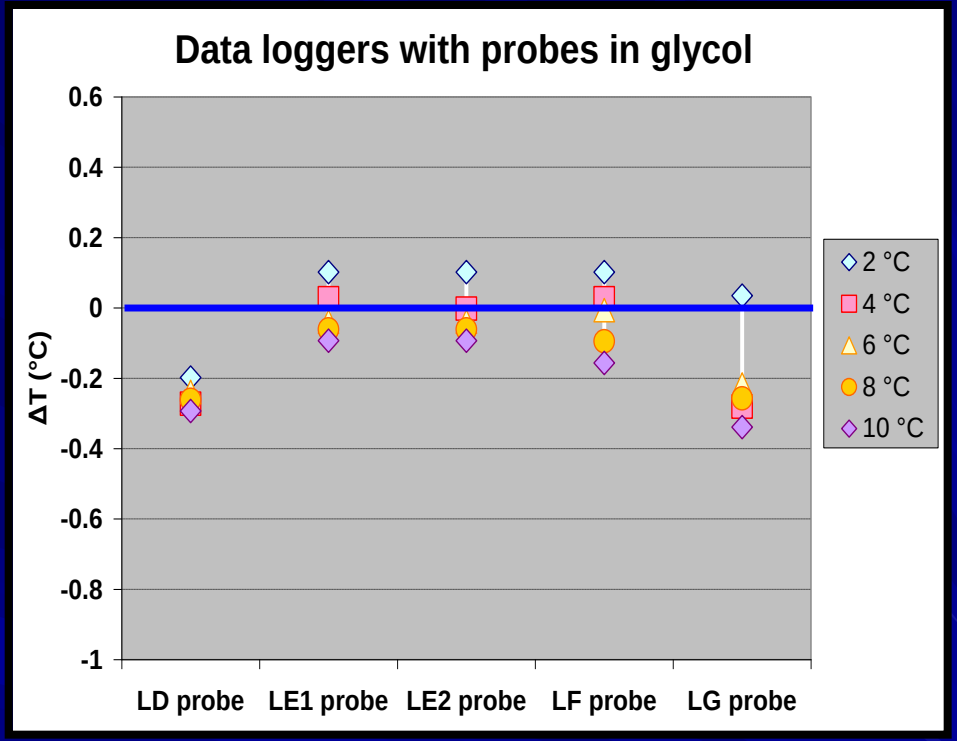
Measurement objectives

- In-depth testing of seven data logger models
  - 3 self-contained units, sensor measures air temperature: LA, LB, LC
  - 2 units with external temperature probes, kept in glycol-filled bottle: LE1 and LE2, LF
  - 2 units with a self-contained air temperature sensor (labeled ext) and a separate probe: LD, LG
- Evaluate out-of-box performance and manufacturer-specified accuracy from 0 °C to 10 °C
  - Shown above: comparison to reference thermocouple (TC 1) at 2 °C, 4 °C, 6 °C, 8 °C, 10 °C
    - Note pink line (air temp. TC) **- refrigerator set point is most likely determined by a similar air temp probe (Tavg = 4.5 °C), we can see that air temp measurements don't correspond to the temperatures of items stored in the refrigerator!**
  - Ice melting point (0 °C)
- Track stability over 19 month period
- Determine proper use so that measurements reflect actual vaccine vial temperatures

Evaluating Electronic Data Logging Thermometers

Deviation from reference thermocouple (blue line, TC 1 in glycol) over range of 2 °C to 10 °C





Reference thermocouple in glycol-filled bottle

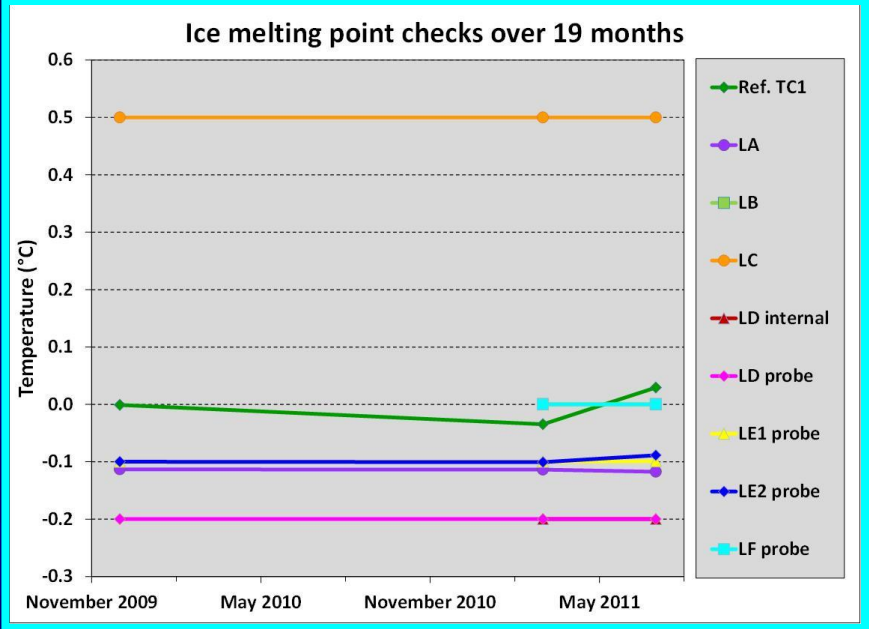
- Glycol approximates thermal mass and properties of liquid vaccine

Average temperatures recorded by data loggers with probes in glycol matched ref TC measurements more closely than loggers recording air temperature

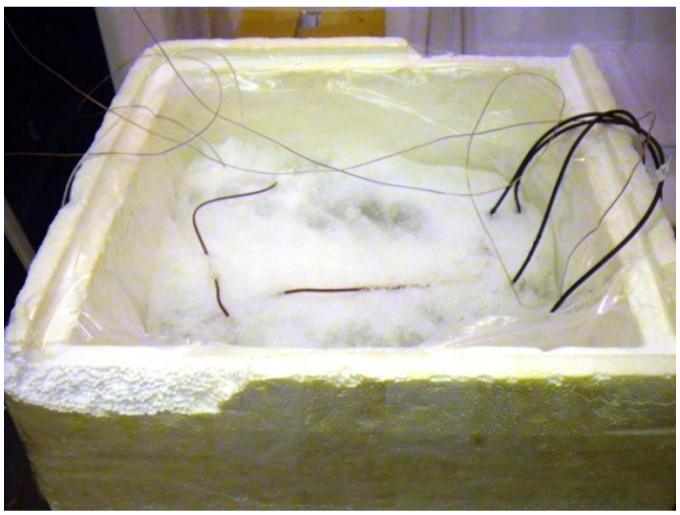
- Air temperature sensors: less thermal mass → more susceptible to small temperature fluctuations, less representative of vaccine temperatures

Tracking Logger Stability Over Time: Drift Test at 0 °C

Ice Melting Point Temperature Readings (°C)					
Sensor Name	Mfc. Spec Accuracy	Trial 1 12/08/09	Trial 2 03/15/11	Trial 3 07/06/11	In Tolerance? (Y/N)
TC1	0.1	0.0	0.0	0.0	Y
TC2	0.1	-	0.0	0.0	Y
TC20	0.1	-	0.0	0.0	Y
LA	0.5	-0.1	-0.1	-0.1	Y
LB	0.5	-	0.0	0.0	Y
LC	0.3	0.5	0.5	0.5	N
LD internal	0.5	-	-0.2	-0.2	Y
LD probe	0.5	-0.2	-0.2	-0.2	Y
LE1 probe	0.5	-0.1	-0.1	-0.1	Y
LE2 probe	0.5	-0.1	-0.1	-0.1	Y
LF probe	0.3	-	0.0	0.0	Y
LG internal	0.4	-	-0.1	-	Y
LG probe	0.4	-	0.4	-	Y



…no measurement drift after 19 months of use!



Data Logger Performance: Manufacturer Specified Accuracy

Loggers with External Probes in Glycol (± °C)			
Sensor Name	Mfc. Specifed Accuracy	Ice Point (T = 0 °C)	Ref. TC Comparison (2 °C to 10 °C)
LD probe	0.5	0.2	0.3
LE1 probe	0.5	0.1	0.1
LE2 probe	0.5	0.1	0.1
LF probe	0.3	0.0	0.2
LG probe	0.4	0.4	0.4

Loggers with Air Temperature Sensors (± °C)			
Sensor Name	Mfc. Specifed Accuracy	Ice Point (T = 0 °C)	Ref. TC Comparison (2 °C to 10 °C)
LA	0.5	0.1	0.9
LB	0.5	0.0	0.5
LC	0.3	0.5	0.5
LD internal	0.5	0.2	0.9
LG internal	0.4	0.1	0.4

- **Loggers with probes in glycol**
  - 5 of 5 are within or better than manufacturer specifications
  - Glycol-filled bottle approximates the thermal mass and properties of liquid vaccine, producing measurements representative of actual vaccine temperatures
  - Easily validate logger performance over the full 0 °C to 10 °C range using a simple ice point check
- **Loggers with air temperature sensors**
  - 3 of 5 are LESS accurate than manufacturer specifications
  - Measuring the wrong thing - air temperature is not representative of liquid vaccine temperatures
  - Ice point check not sufficient to determine validity of logger readings over entire 0 °C to 10 °C range

An ice point check is an easy and effective method for validating thermometer performance, *but it only works if the thermometer is used correctly!*

Selecting a Digital Data Logger Thermometer for Vaccine Temperature Monitoring

Main readout unit (temperature display)

External, detachable temperature probe

CDC International Vaccine Stability Workgroup: Minimum Data Logger Features and Specifications

Detachable temperature probe

- To be kept in liquid-filled bottle
- Cable length > 1 m preferred

Continuous temp monitoring

- At least one reading/15 min

Memory storage : 4000 readings

- ~ 39 days recording at one rdg/15 mins
- Device stops recording when memory is full, reset after data download

Operating range: –20 °C to 40 °C

- (for refrigerated vaccine monitoring)

Uncertainty: ± 0.5 °C

- In the range of –1 °C to 15 °C
- Often listed as device “accuracy”

Resolution: ± 0.1 °C

Battery life: 6 months minimum

Integrated Liquid Crystal Display (LCD) with minimum:

- Last measured temp displayed in °C or °F
- Hi/Lo alarm status indicator

Alarm capabilities

- Factory set, end-user adjustable
- Alarm activation at 2 °C (low) and 8 °C (high)

Download/ archival software

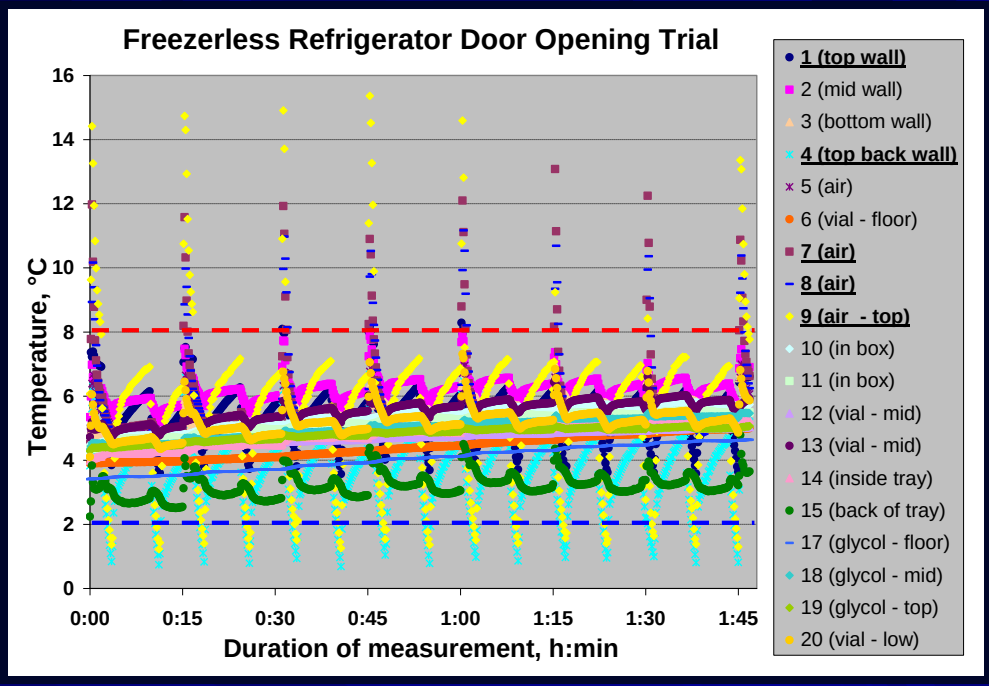
- Download data via standard computer ports (e.g., USB)
- Graphical presentation of date/time/temperature data
- Display alarm configuration details and total time outside high/low thresholds
- Data export capability (e.g., csv, Excel, txt)

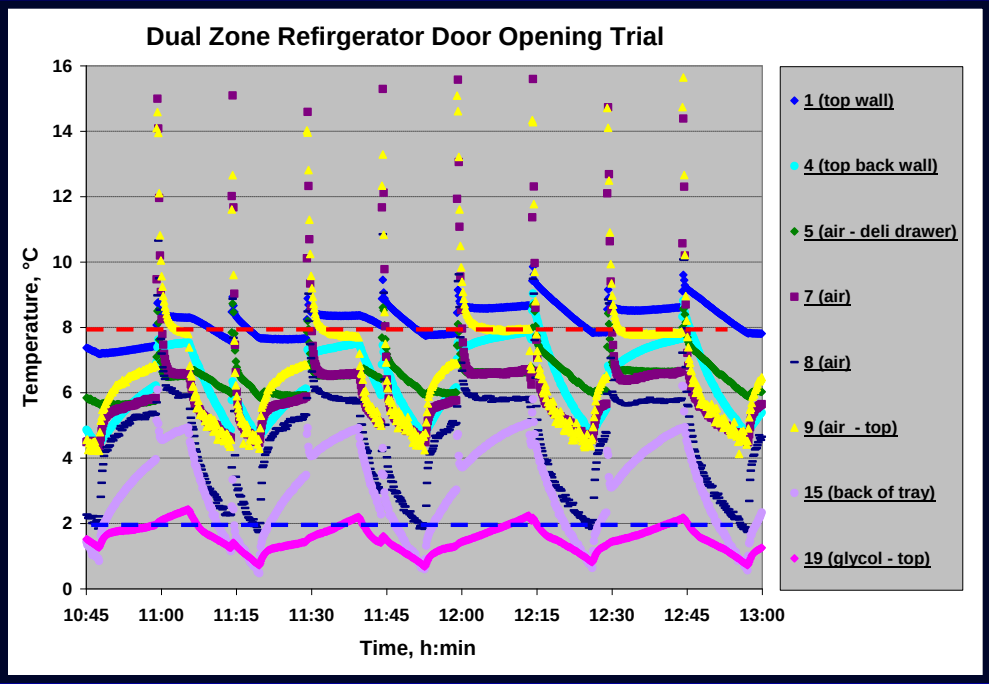
False Alarm Alert: Thermometer Placement Matters!

Sensors in air, attached to walls, or near cooling vents show temperature spikes > 8 °C in all refrigerator types

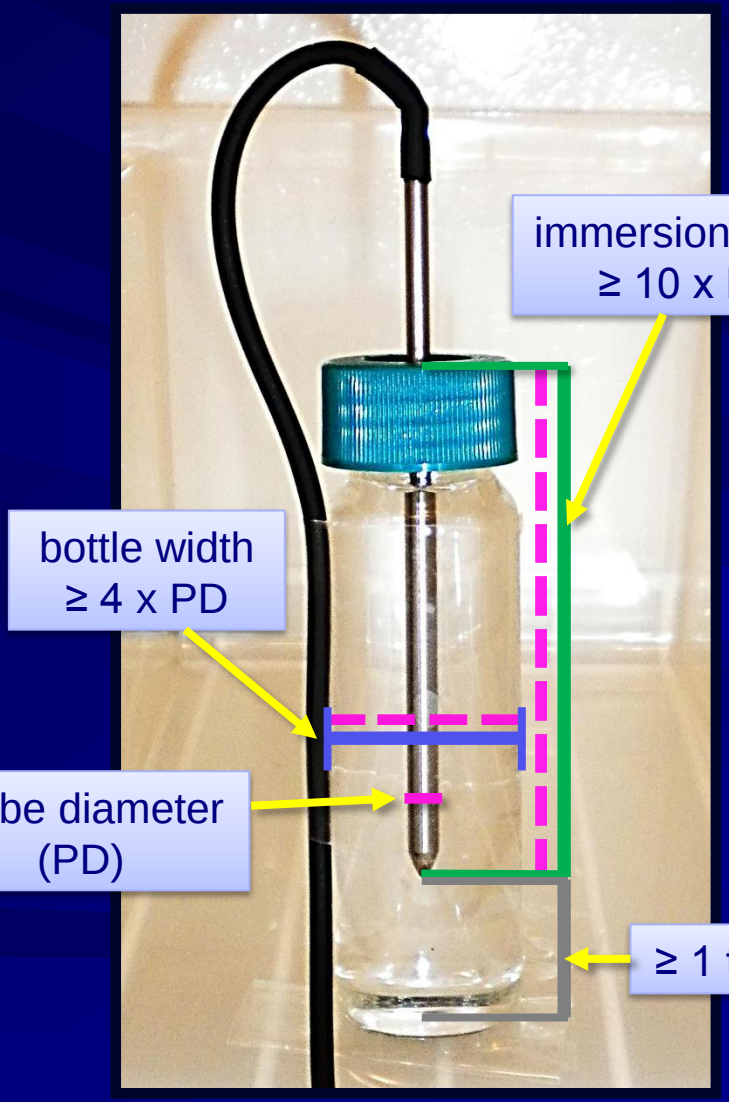
TC #19 (magenta) shows temperature < 2 °C

- Inside glycol-filled bottle, directly on glass shelf under cooling vent
- Repeated door opening results in driving temp down
- Monitor placed in this location NOT a good indicator of stored vaccine temperature!





Data Logger Setup



Select a glass or plastic bottle

- Minimum diameter = 4 x probe diameter
- Minimum height chosen so that
- Immersion depth ≥ 10 x probe diameter,
- Probe tip to bottom distance ≥ 1 to 2 cm
- Sealable lid preferred (e.g. pierceable, rubber septum cap)

Note: If manufacturer supplies a fluid-filled bottle/ vial with data logger, this may be used instead

Completely fill bottle with fluid (e.g., glycol)

Insert logger probe through center of cap

- Position probe tip to achieve depth ≥ 10 x PD
- Make sure tip doesn't touch bottom of bottle
- Make sure entire length of probe is centered within the bottle
- To keep the probe from shifting, fix the cable to the outside of the bottle with tape or cable tie

Data Logger Installation

Attach logger display to outside of refrigerator

Cable is not thick enough to affect refrigerator door seal

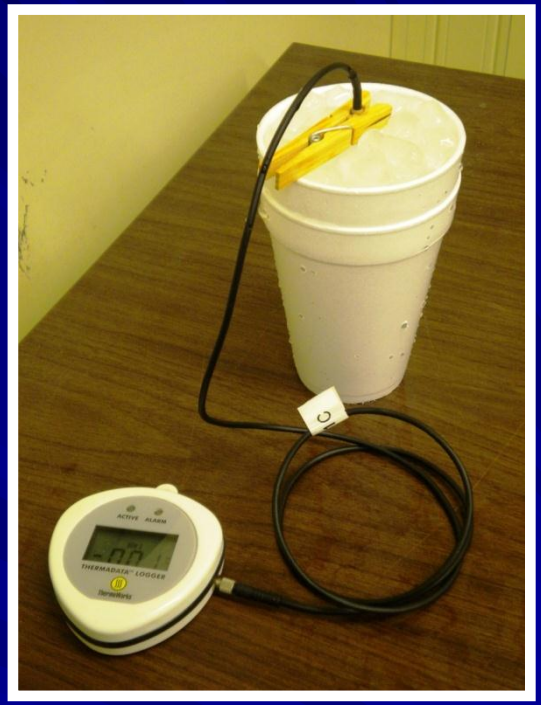
Place logger probe and bottle setup in a tray in the center of the refrigerator. Fix bottle in place with tape or velcro.

Ice Melting Point Validation Method for Establishing Measurement Traceability

NIST-developed ice point method for validation of digital data logger thermometers

- Simple, inexpensive, on-site field validation
- Special equipment – mini ice cube tray, cubes must be no larger than a gumdrop
- Direct comparison to specified reference

***U(k=2)* = ± 0.01 °C**

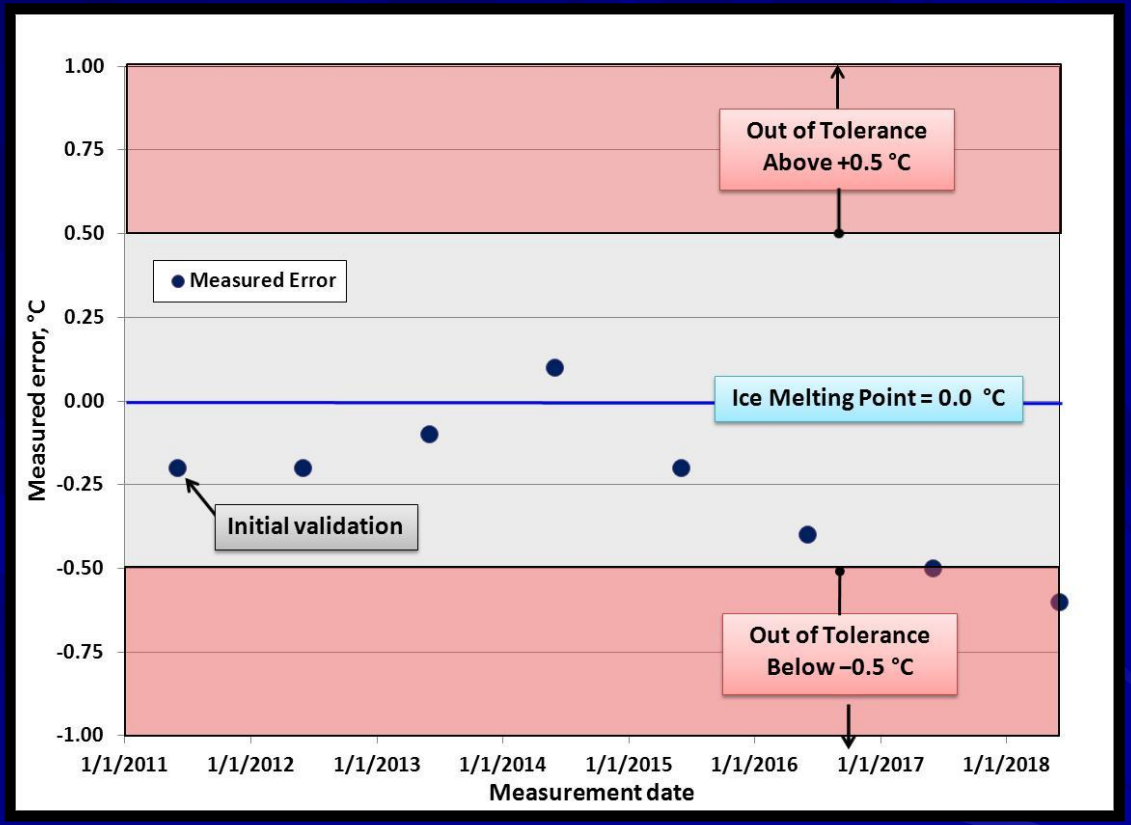


Using Ice Melting Point Validation to Maintain Logger Traceability

THE CONTROL CHART →

Every time the logger undergoes an ice melting point validation, the measured error and measurement date are recorded on a control chart

An up-to-date control chart means that anyone can easily and quickly determine when the last validation occurred, and whether the device was **IN TOLERANCE** or **OUT OF TOLERANCE**



In the example control chart, we can see that a logger was validated at the ice point on an annual basis. From 2011-2017, the logger remained **in tolerance**, with a measured error ≤ ±0.5 °C

The 2018 validation check resulted in an error of 0.6 °C, which is > ±0.5 °C and is **out of tolerance**

Impact and Outlook

- **Study provides the scientific basis for improved CDC vaccine storage and handling policies**
  - VFC Vaccine Storage and Handling Toolkit
  - CDC International Vaccine Stability Workgroup
    - Government, non-profit, and industry collaboration
    - Developing a unified policy and message
  - Distributed to international vaccine community via WHO

- **Widespread improvements in vaccine storage and temperature monitoring practices lead to**
  - Decreased waste
  - Improved consumer confidence
  - Increased effective inoculation rates

Thank You!

Many thanks to the Virginia and DC VFC Programs for their contributions to this study.

Additional thanks to John Stevenson, Tony Richardson, and the Centers for Disease Control for their work in supporting this project.

Appendix

Ice Melting Point Validation Method for Digital Data Logging Thermometers

The cheaper, faster, easier way to establish and maintain thermometer traceability.

What is Traceability?

Measurement traceability is an ***unbroken chain*** of calibrations to a specified reference, where each link in the chain contributes to the total measurement uncertainty.

So why should we care?

Traceability is required to demonstrate that measurements are accurate, reliable, and meaningful, and that they fall within the users' uncertainty needs.

If your measurements (and measuring device) are NOT traceable to a reference or standard, then you have no way of knowing if your measurements are right!

Traceability makes measurements MEANINGFUL.

The Melting Point of Ice

When ice melts, the resulting mixture of ice and water has a temperature of exactly 0.00 °C under normal atmospheric pressure

This is a fundamental, physical property of water

We call the temperature equilibration of ice and water the *ice melting point*

The ice melting point is internationally recognized as a **specified reference measurement standard**

In other words, it's an *intrinsic standard*

How does this fit with my vaccine temperature monitoring needs?

We already know…

- Maintaining the right vaccine storage temperature is critical to ensuring that children receive effective vaccine.
- Continuous temperature monitoring is required to determine if vaccines are safe and effective.
- The only way to know if continuous monitoring measurements are accurate is by establishing traceability.

Users can pay a company to calibrate their thermometers, but without seeing full documentation of the unbroken chain of comparisons to a standard reference, it's hard to be sure that the calibration establishes traceability.

- It's not easy for the average user to determine whether laboratories and companies are meeting the requirements for establishing traceability
- Some companies compound the issue with misleading terminology and claims (e.g., "NIST – traceable")
- This process can ultimately be expensive and time-consuming

The cheaper, faster, and easier way to establish traceability is to DO IT YOURSELF with an ice point validation method that just about anyone can follow.

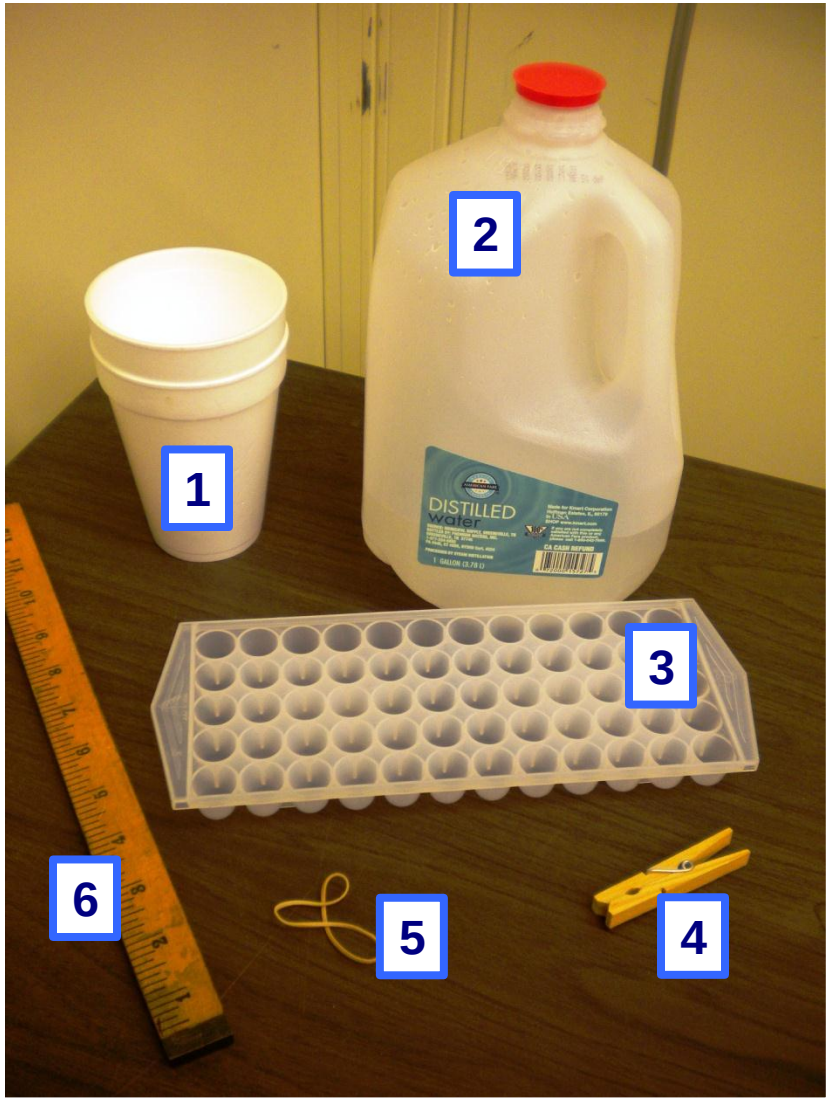
- Measurement uncertainty for this method is ±0.01 °C

Ice Point Validation Method: Materials

To make an ice melting point for validating data logging thermometers, you will need to obtain a few simple materials

1. An insulated container: styrofoam cup (or 2 stacked together), coffee thermos, etc
2. Water: distilled, deionized, or reverse osmosis for uncertainty = ±0.01 °C. Tap water is OK too, and gives uncertainty = ±0.02 °C
3. Mini ice cube tray. It's critical that the tray make cubes no larger than the size of a gumdrop.
4. A clothespin
5. Rubber band
6. Ruler

All of these items can be purchased in major retail stores for under $20



Step 1: Preparing Your Materials

1. Wash your hands, or wear on powder-free gloves. This is to maintain water purity, as salts and oils from our hands can contaminate the ice point (and give you the wrong answer)

2. Rinse off the ice cube tray and then fill with the same water you will be using for the validation (e.g., distilled, deionized, etc). Freeze the tray.

3. Make sure you will have enough ice cubes before you start building the ice melting point – make more than you think you will need (we needed 3 trays full to fill a large styrofoam cup)

4. When you are ready to set up the ice melting point, connect the data logger you wish to validate to your computer and open the logger software to adjust the recording interval. Choose a much higher frequency interval than you would normally use, such as 1 reading / 10 s.

5. If the logger features a computer-only start, start the logger now. For a magnetic key or button push start, just initialize the logger in the software program, and wait to start the logger until after you have the ice melting point set up.

6. Rinse or wipe off your logger probe. This is especially important if it has glycol residue on it. Rinse out your insulated container, too.

7. Lay out your materials and data logger (with probe) on a clean work surface

Step 2: Marking Probe Immersion Depth

When the probe is immersed in the ice point, the probe tip should be at least 1 inch above the bottom of the cup

You can make sure you end up with the right immersion depth later by placing a ruler inside the cup, then lowering your probe to the correct depth

Mark the spot where the top of the probe just sticks above the rim of the cup by wrapping it with a rubber band

This doesn't need to be exact , and it's OK if the probe tip is more than one inch above the bottom of the cup. Just make sure to mark a spot that will give you AT LEAST one inch of clearance.

Step 3: Fill the cup with ice

Empty the ice cube trays into a clean bowl or container – make sure the cubes are no larger than a gumdrop!

Don’t use any cubes that fall on the floor – they’re dirty!

Wearing gloves (or using freshly washed hands), pack the insulated cup with ice cubes

Step 4: Add water

Pour water over the ice in the cup, filling it almost all the way to the top

Wait about one minute before proceeding to the next step (some of the ice cubes will melt)

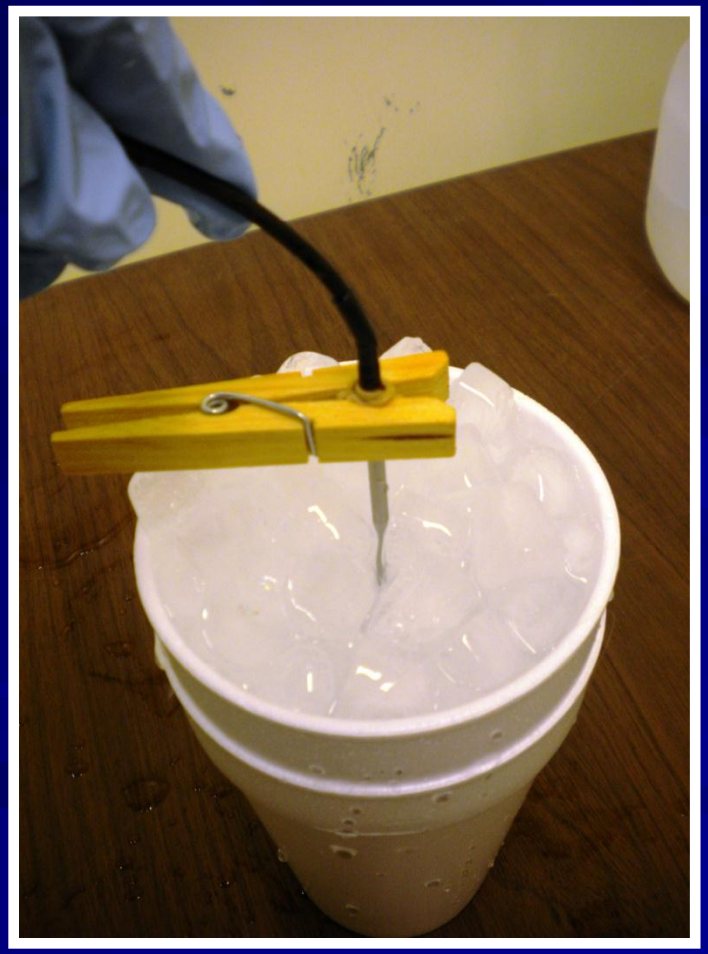
Step 5: Add more ice

Add more ice to fill the cup all the way to the top. Push down on the ice cubes to make sure the ice fills the entire cup all the way to the bottom – there should be not be any floating ice.

Step 6: Insert the data logger probe

Clip the clothespin around the logger probe in the spot that you previous marked with a rubber band

Carefully (gently) insert the probe into the center of the cup and push it straight down until the clothespin is level with the rim of the cup



Make sure the probe is going straight down and that it is NOT tilting or touching the cup

Step 7: Record temperature measurements

After inserting the logger probe, wait ~10 minutes for the device to equilibrate to the temperature of the ice and water, then start the logger using a key or button push

If your logger features a computer start, it should have already been recording – no further action is required

Allow the system to collect data for 30 minutes following equilibration time

After 30 minutes, remove the logger from the ice point setup and download data

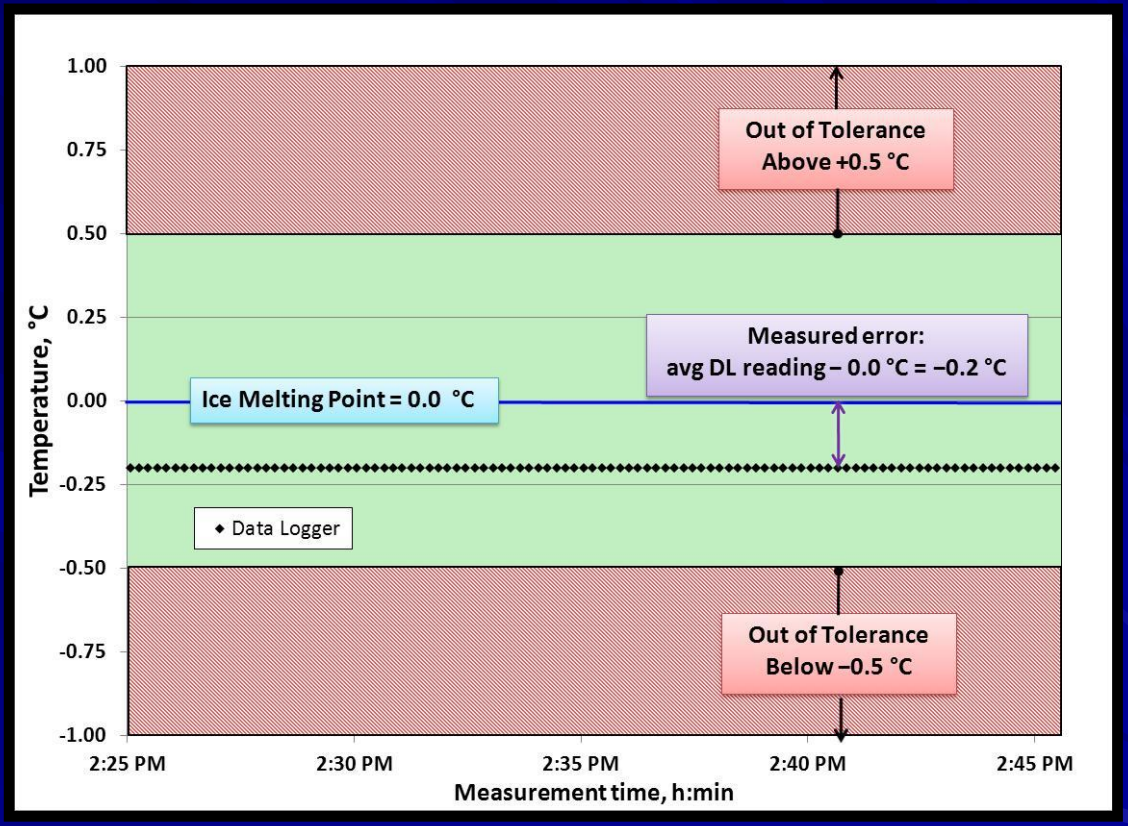
Step 8: Interpreting the results

Depending on when the logger was started and stopped, you may observe a cool-down or warm-up period (equilibration) following insertion into or removal from the ice point.

For validation purposes, we only need to look at the data from the 30 minutes with the probe in the ice point following the equilibration period

If the logger is functioning properly and the ice point was constructed correctly, this selection of data will likely fall in a straight or nearly straight line at a temperature close to 0 °C

The measured error is the difference between the reference ice point temperature (0 °C) and the average data logger temperature over the 30 minutes of post-equilibration measurements



If the measured error falls within the specified accuracy (±0.5 °C), then the device is in tolerance and has been successfully validated at the ice melting point

A measured error > ±0.5 °C indicates that the device is out of tolerance and is NOT acceptable for vaccine temperature monitoring in its current condition

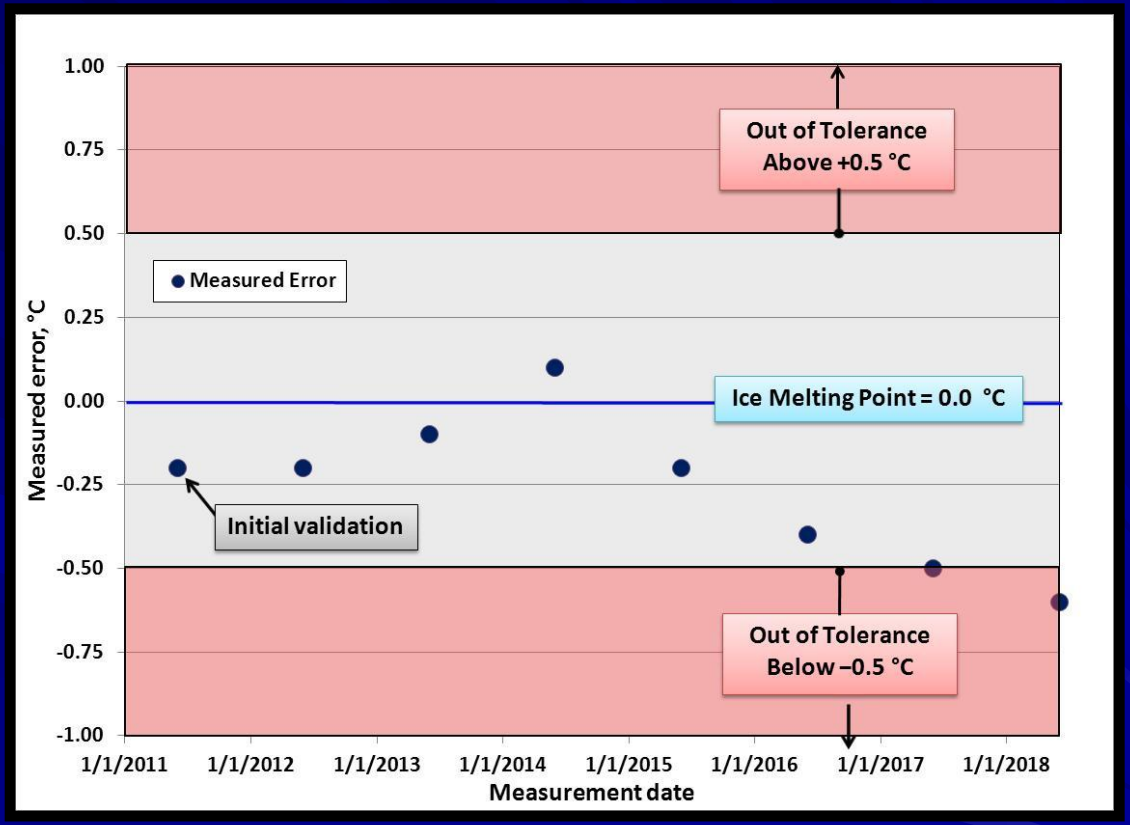
Step 9: Using ice melting point validation to maintain logger traceability

To maintain traceability, we need to keep documentation of logger validation:

THE CONTROL CHART →

Every time the logger undergoes an ice melting point validation, the measured error and measurement date are recorded on a control chart

Keeping an up-to-date control chart means that anyone can easily and quickly determine when the last validation occurred, and whether the device was **IN TOLERANCE** **or** **OUT OF TOLERANCE**



In the example control chart, we can see that a logger was validated at the ice point on an annual basis. From 2011-2017, the logger remained **in tolerance**, with a measured error ≤ ±0.5 °C

The 2018 validation check resulted in an error of 0.6 °C, which is > ±0.5 °C and is **out of tolerance**

How do I know when a data logger needs validation?

- Is the device brand new, or has it just been recalibrated or adjusted by the manufacturer?

  Initial validation MUST be completed BEFORE the device is used to monitor vaccine temperature

- At a minimum, all data loggers used for vaccine temperature monitoring should be measured at the ice melting point on an ANNUAL BASIS, beginning from the initial validation date

- Any logger that produces questionable data or shows signs of measurement drift should also be measured at the ice melting point, REGARDLESS of whether it is due for annual validation

- Any logger that produces an OUT OF TOLERANCE measured error is no longer suitable for vaccine temperature monitoring – remove from service IMMEDIATELY!

- An out of tolerance logger may be returned to the manufacturer for recalibration or repair, or replaced with a new device. Either way, the process starts over from the beginning with a new initial validation.