Thermal Analysis of Refrigeration Systems Used for Vaccine Storage

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Current Problem

- CDC administers ~ $3 billion of vaccine 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 estimates **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

$3 B/yr program X 30% loss due to known thermal excursions = $900 M/yr loss

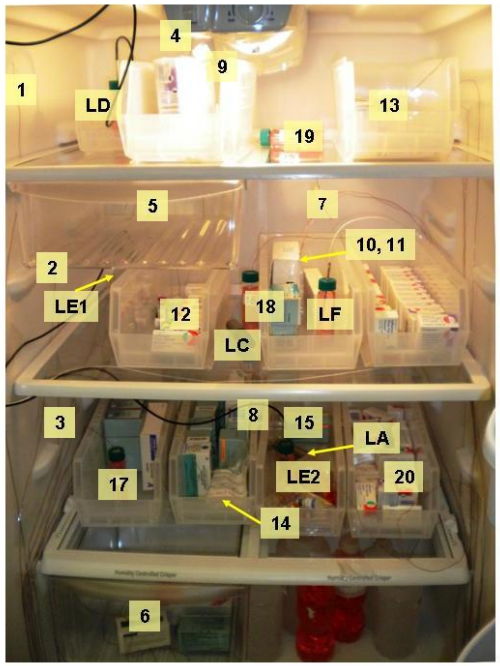
Background and Purpose

- Challenges in ensuring VFC providers follow good vaccine storage and temperature maintenance practices
  - 45,000+ providers, many different storage and temperature monitoring methods
  - Suitability of commercial refrigerators for vaccine storage not well documented
  - Impact of refrigerator loading pattern, normal refrigerator use, environmental temperature fluctuations, …unknown!
  - Inadequate temperature monitoring: improper thermometer placement, possible device inaccuracies, and absence of continuous temperature data collection
- Need for research that matches everyday conditions experienced by vaccine providers
  - Improve storage and handling guidelines and practice

Experimental Method: Measurement System

- **19 thermocouples and 3 to 6 electronic data loggers arranged throughout refrigerators**
  - Calibrated at ice point (0 °C)
  - **Sensors attached to vaccine vials**, walls, inside glycol-filled bottles, and hanging in air
  - Recorded data continuously during trials lasting 15 hours to several days

Device name:	U(k=2), C
Thermocouple measurement system	0.12
Data logger A	0.58
Data logger B	1.41
Data logger C	0.67
Data logger D	0.59
Data logger E	0.59

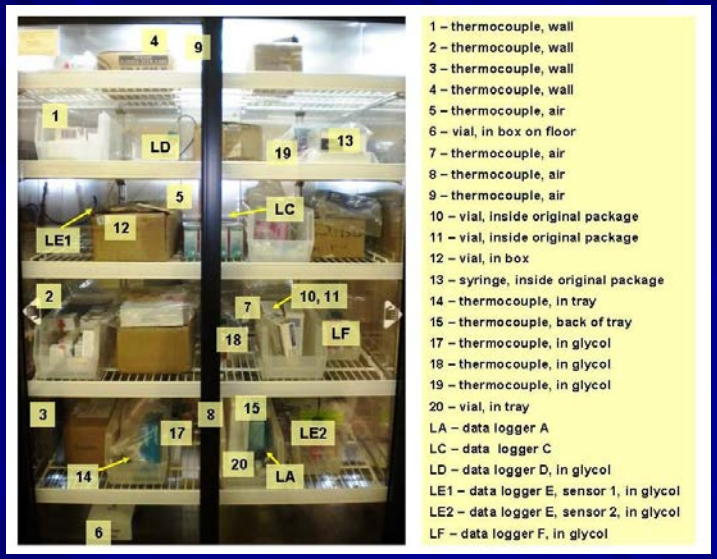


1 – thermocouple, wall
2 – thermocouple, wall
3 – thermocouple, wall
4 – thermocouple, wall
5 – thermocouple, air inside drawer
6 – vial, inside drawer
7 – thermocouple, air
8 – thermocouple, air
9 – thermocouple, air
10 – vial, inside original package
11 – vial, inside original package
12 – vial, in tray
13 – vial, in tray
14 – thermocouple, in tray
15 – thermocouple, back of tray
17 – thermocouple, in glycol
18 – thermocouple, in glycol
19 – thermocouple, in glycol
20 – vial, in tray
LA – data logger A
LC – data logger C
LD – data logger D, in glycol
LE1 – data logger E, sensor 1, in glycol
LE2 – data logger E, sensor 2, in glycol
LF – data logger F, in glycol

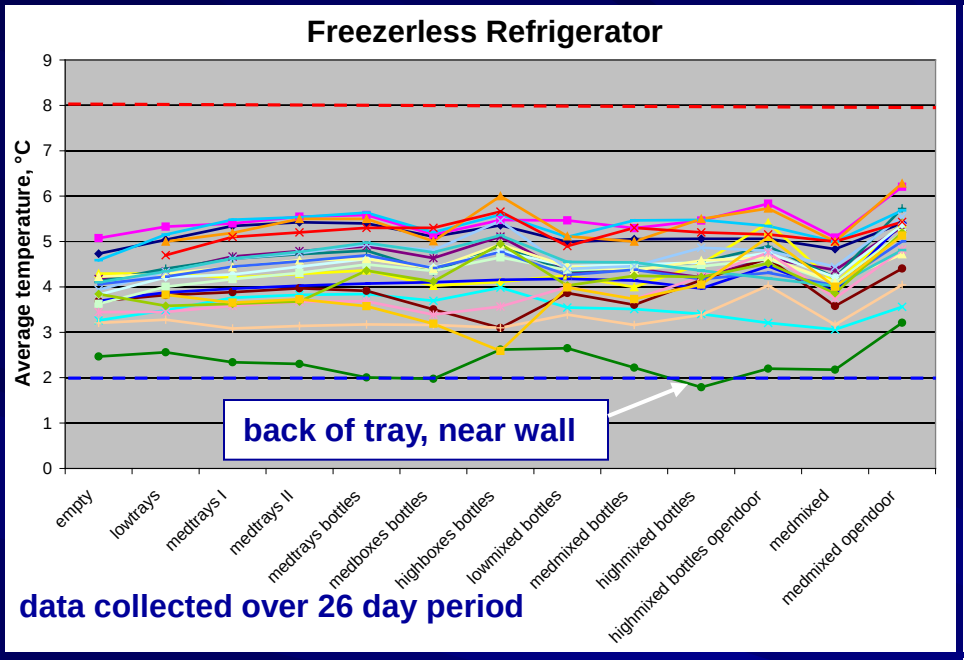
- **Rate of data collection**
  - Thermocouples = 10 s
  - Data loggers = 30 s to 1 min
- **100,000 – 500,000 data points collected during each trial**
  - Complete picture of temperature behavior over time
  - Condense into representative samples and averages to find correlations between tested criteria and temperature trends

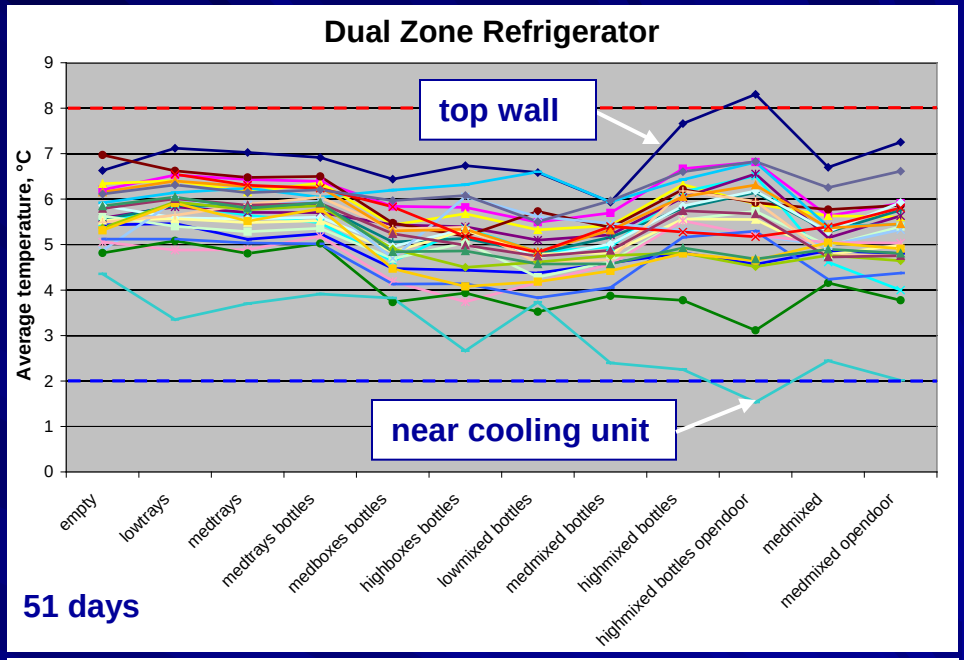
Experimental Method: Tested Criteria

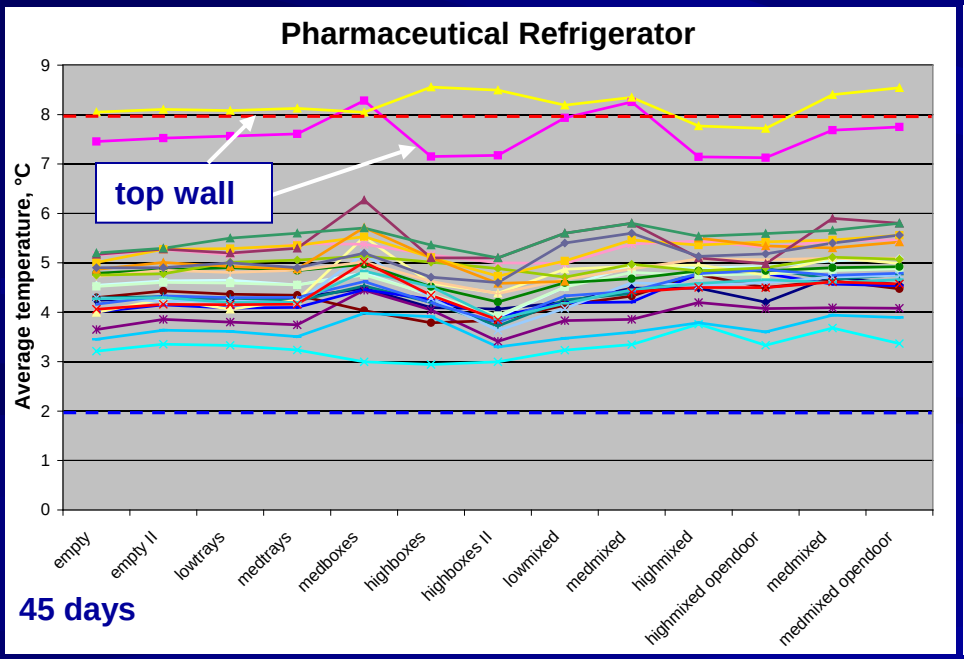
- **4 refrigerator styles**
  - Freezerless, Dormitory-style, Dual Zone Fridge/Freezer, Pharmaceutical grade
- **Varied refrigerator loading patterns**
  - Low, medium, and high density loads
  - Plastic trays, cardboard boxes, and combined trays/boxes storage configurations
  - With and without water bottles (3 - 5% total capacity) in refrigerator door
- **Normal use simulation - open / close refrigerator door**
- **Increased room temperature**
- **Power outage and recovery**

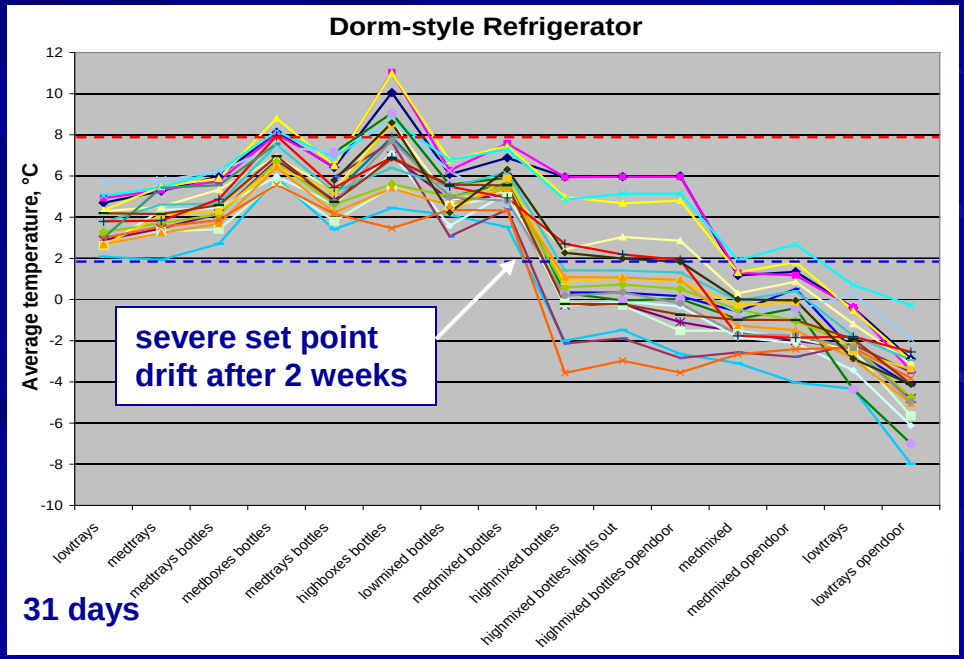


Results: temperature stability of refrigerators





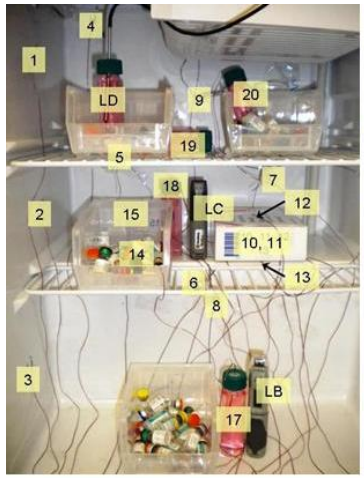




Comparison of Refrigerator Performance in Response to Tested Criteria

I. Loading density

Little or No Impact	Negative Impact on Performance
FREEZERLESS	**DUAL ZONE** • Possible minor increase in location-specific temperature variation for high density loads
PHARMACEUTICAL	**DORM-STYLE** • Noticeable impact on performance due to lack of air circulation • High-density loading patterns increased location-specific temperature variation



Low Density Pack

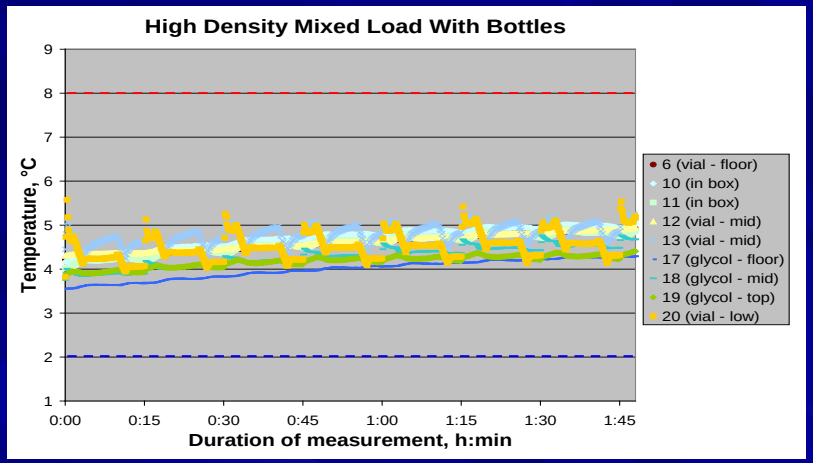
Medium Density Pack

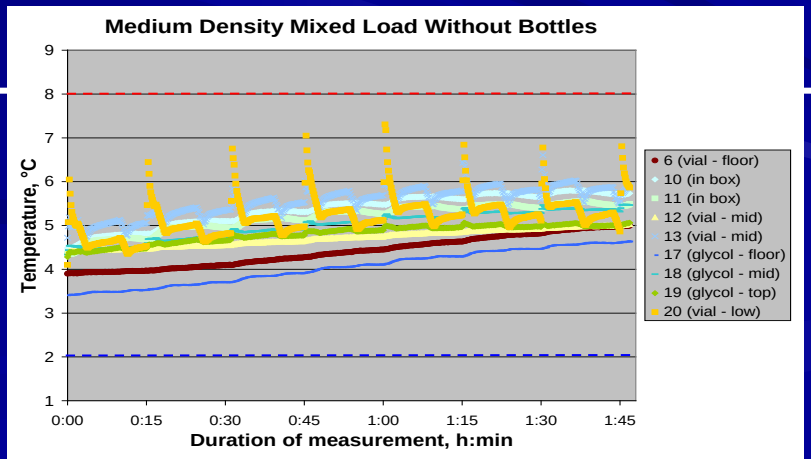
High Density Pack

Density variation pattern in dorm-style fridge

II. Opening/ closing refrigerator door

Little or No Impact	Negative Impact on Performance
PHARMACEUTICAL • Vial temperatures not significantly affected	**DORM-STYLE** • Most sensors record brief temp increases, overall decrease • Exacerbates already poor temperature control
DUAL ZONE • Small increases in vial temps, but remained within 2 °C to 8 °C	
FREEZERLESS • Small increases in vial temps, but remained within 2 °C to 8 °C • Water bottles in door reduced temperature change. Without bottles, temp increased up to 1.2 ˚C higher	





False Alarm Alert: Temperature Monitor Placement Matters!

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

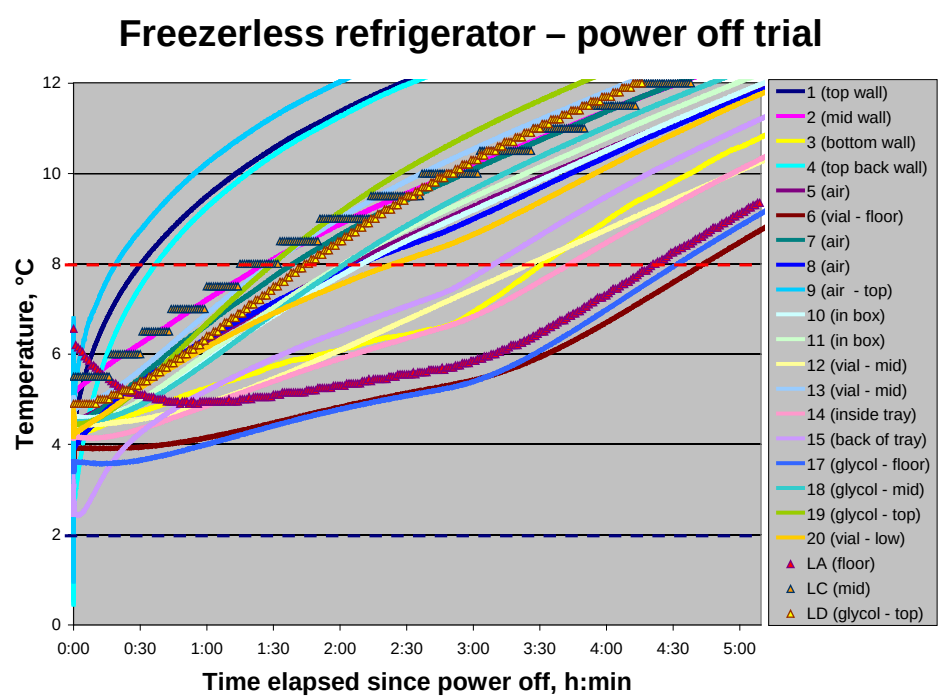
III. Power outage

Refrigerator type	Time after power off until vial temp > 8 °C
FREEZERLESS	1.5 to 4.5 hours
DUAL ZONE	1.25 to 4.75 hours
PHARMACEUTICAL	0.75 to 2.25 hours
DORM-STYLE	0.75 to 3.5 hours

Vials that resisted thermal excursions during an outage the longest were:

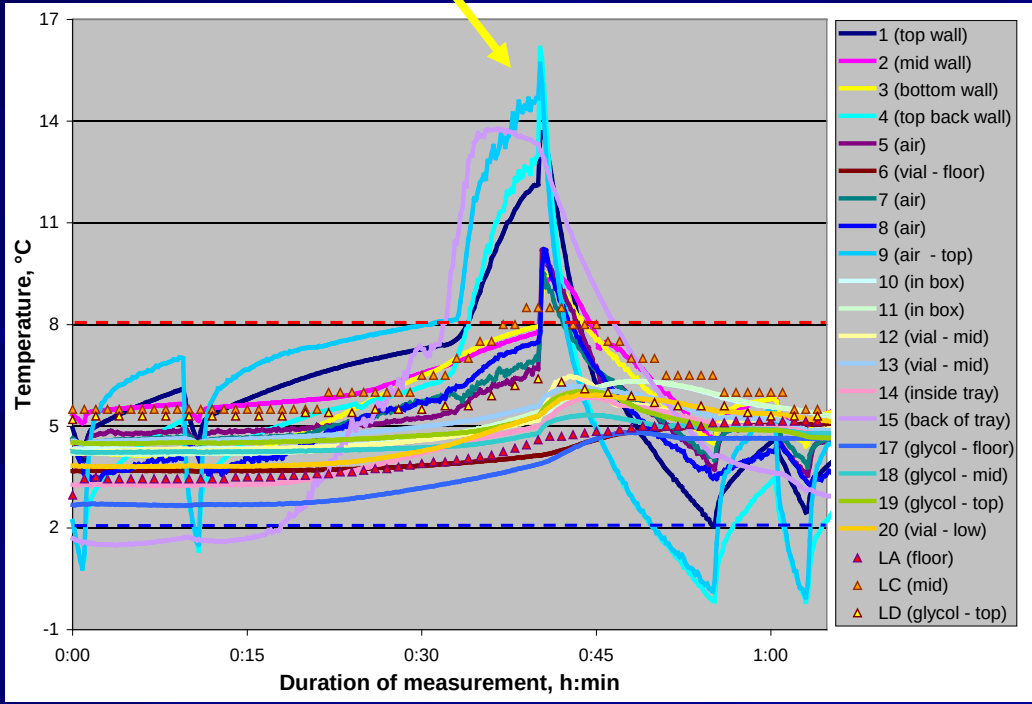
- Contained in boxes, trays, and/or original packaging
- Placed away from the top refrigerator shelf
- In a fridge with a water bottle "temperature ballast"

Allow 6 to 9 hrs for thermal re-equilibration following an outage



IV. Defrost cycle

FREEZERLESS	DORM-STYLE	DUAL ZONE	PHARMACEUTICAL
• Defrost cycle runs every 2-3 days • Vials occasionally exceeded 8 °C for <15 min • Thermometers in air / near walls recorded dramatic temperature spike followed by a drop below 2 °C	• No defrost cycle • Refrigerator interior quickly becomes encased in frost and ice	• Defrost cycle runs at ~30 h intervals • Vial temperatures increased ~0.5 °C, did not exceed 8 °C • Some sensors in air / near walls recorded temperatures > 8 °C for 10-20 min, followed by a drop below 2 °C for <10 min	• No defrost cycle



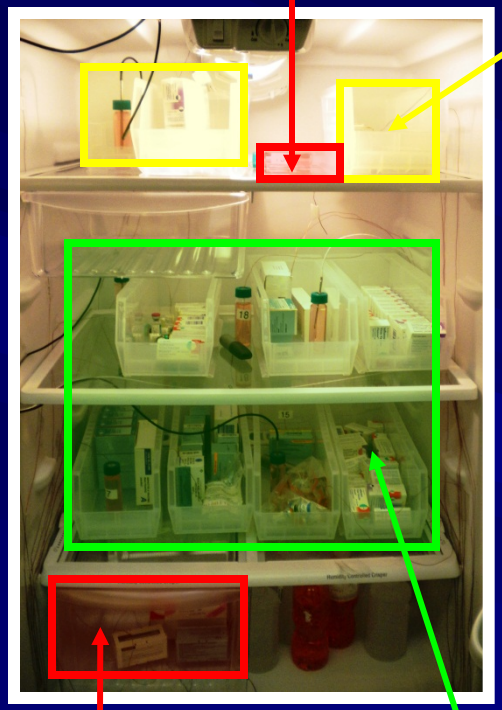
Continuous Temperature Monitoring

- 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?
  - Evaluate on case-by-case basis
- Monitor placement is very important!

Vaccine Vial Storage Methods and Locations

DUAL ZONE

Never place vials directly on glass shelf = 2 - 5 °C colder



No storage in vegetable crisper: thermally isolated + floor level runs cold

PHARMACEUTICAL

Avoid storing on top shelf – near cooling vent. First location to exceed max allowed temp during outages.

Manufacturer recommends no floor storage, but vial TC maintained at 2 – 8 °C throughout testing

FREEZERLESS

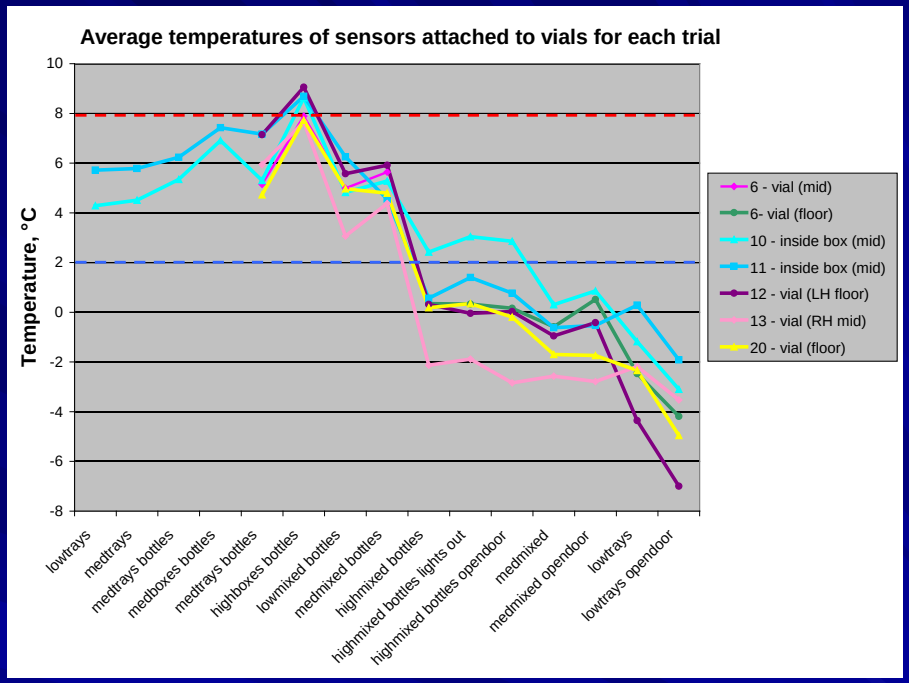
1 – 2 °C colder than main fridge space

Best storage practice – place vaccines in center fridge space, contained in original packaging, cardboard boxes, and/or plastic trays to minimize thermal excursions

Vaccine Vial Storage Methods and Locations

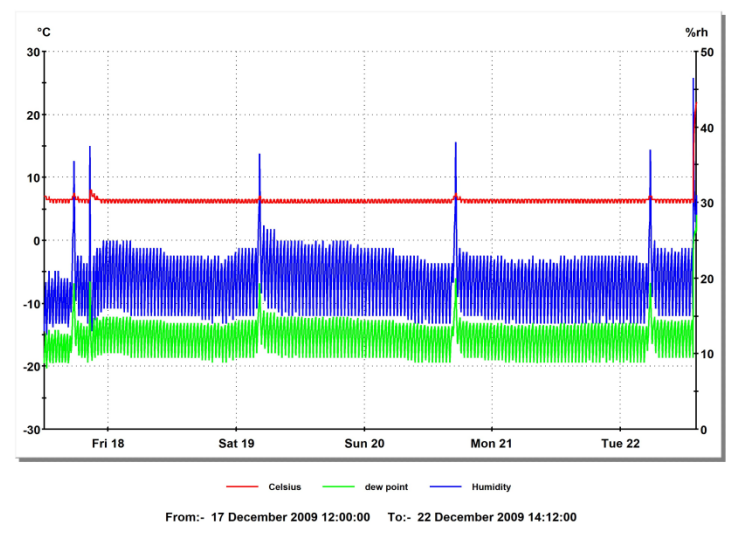
DORM-STYLE REFRIGERATOR

- Consistently unacceptable performance, regardless of vaccine storage location
- Placement on/ near floor, cooling and freezer unit further reduces temperature stability
- No “good” storage area



The dorm-style refrigerator is NOT recommended for vaccine storage under any circumstance!

Vaccine Temperature Monitoring: Electronic Data Loggers



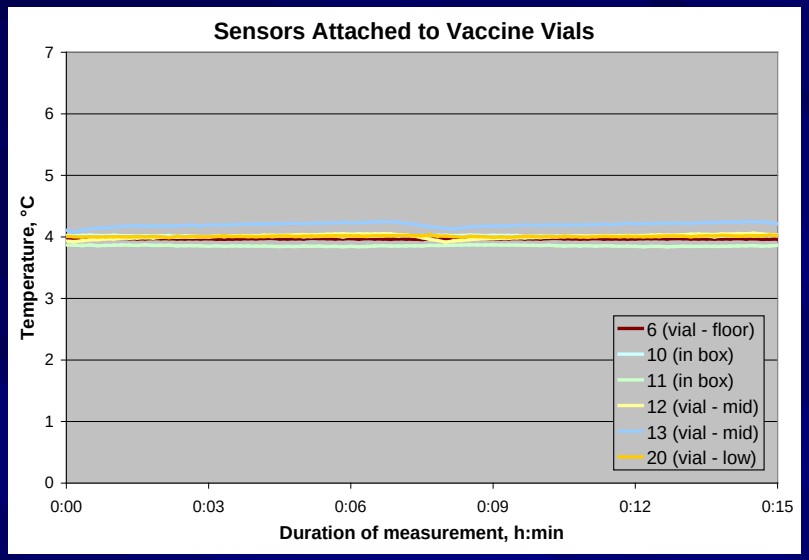
ADVANTAGES

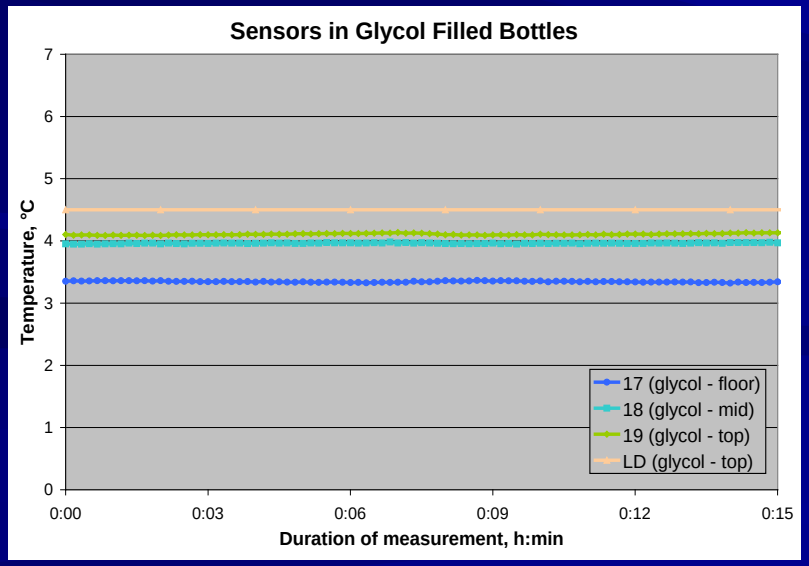
- **Continuous monitoring** - ensures that all thermal excursions are captured, improving confidence in vaccine supply efficacy
- Easy to use
- Quickly analyze results, eliminating time-consuming paperwork
- Archival data stored electronically
- Alarm capabilities, some with email notification mean that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

DISADVANTAGES

- Data logger use requires computer capability and some training

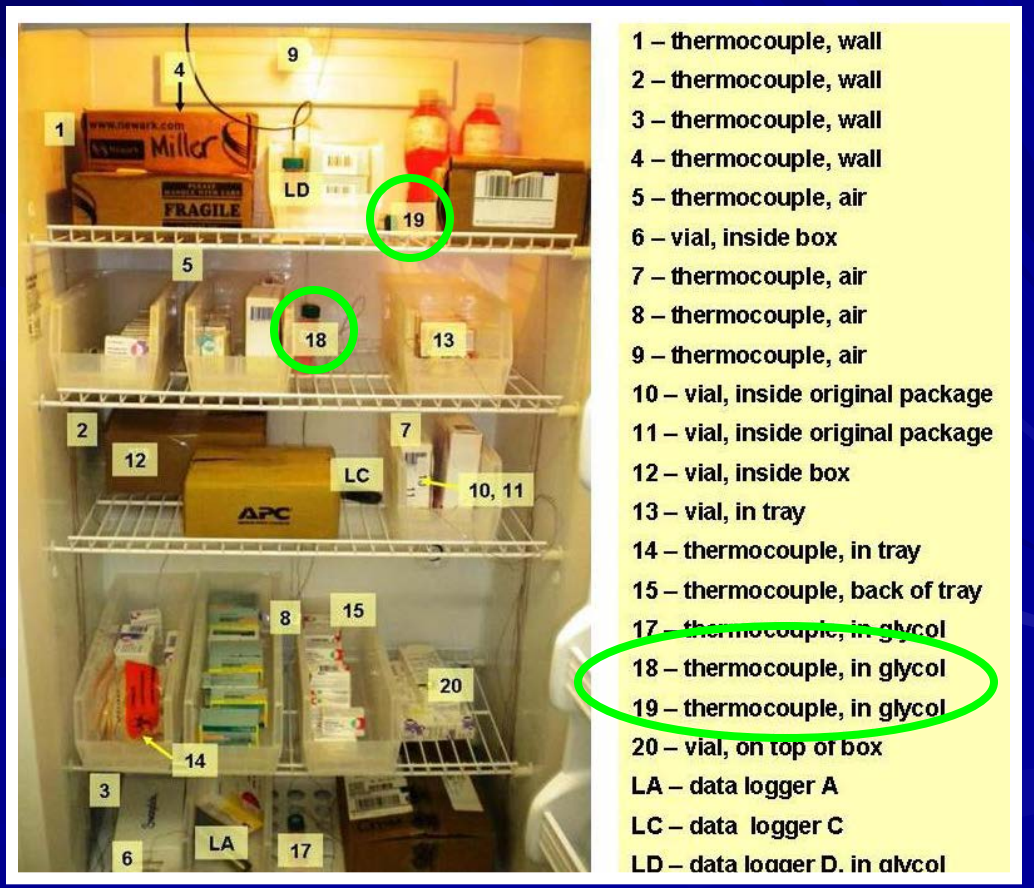
Monitoring Vial Temperature Effectively





Best Location for Temperature Sensors

sensor probe inside glycol-filled bottle, placed in the same locations as vials



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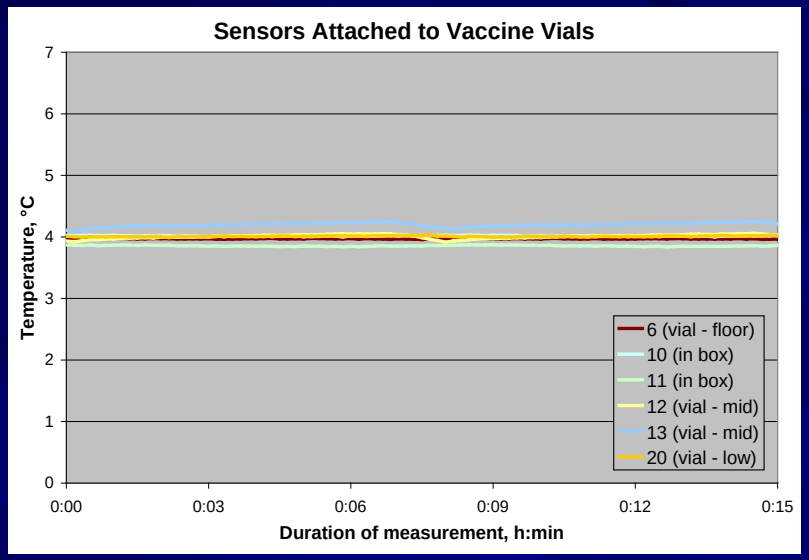
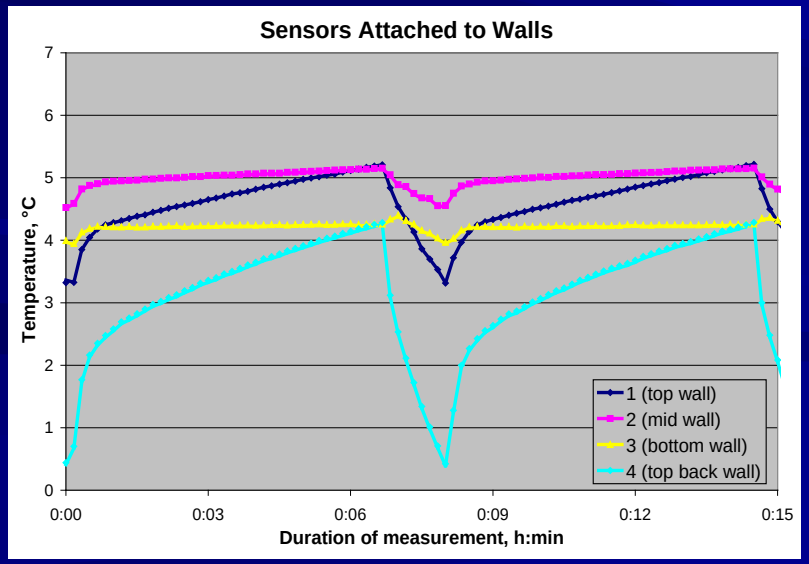


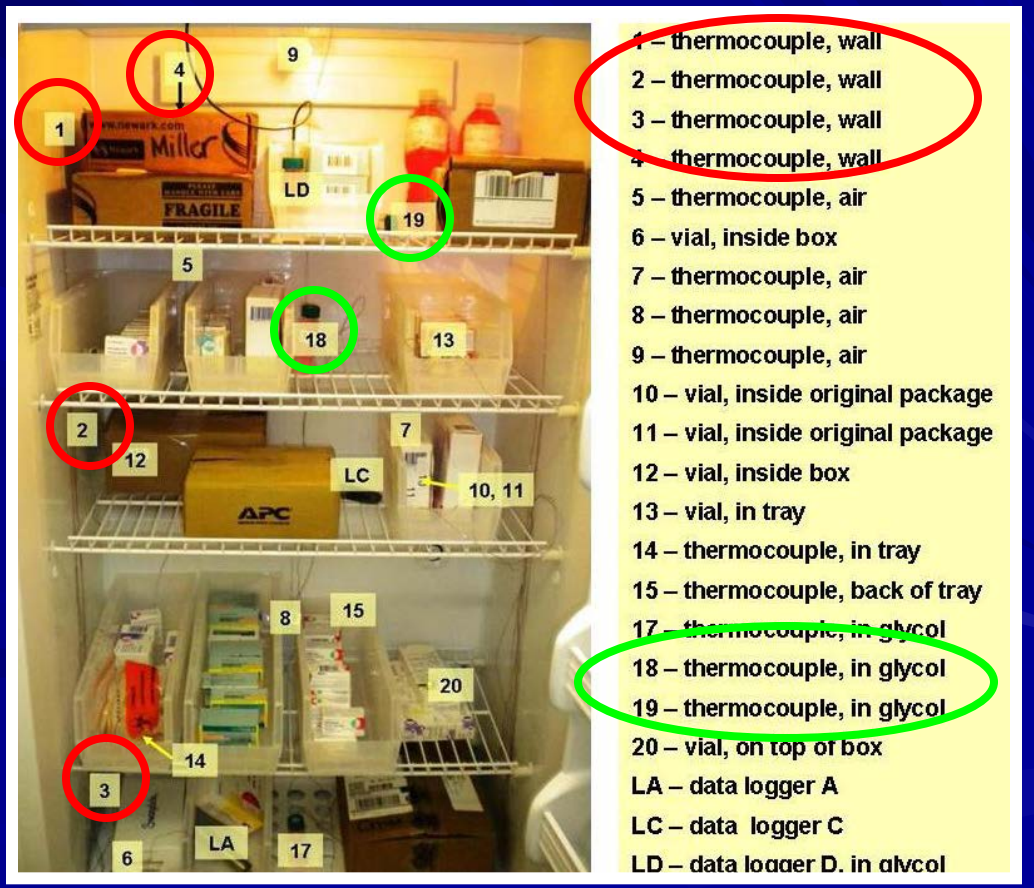
Best Location for Temperature Sensors

sensor probe inside glycol-filled bottle, placed in the same locations as vials

Worst Location for Temperature Sensors

Sensors attached to walls





Summary of Results

- **Freezerless, dual zone, and pharmaceutical type refrigerators are suitable for vaccine storage**
  - Performance unaffected by variations in packing density or type
  - Able to withstand small (2 - 5 °C) environmental temperature fluctuations
  - Water bottle ballast improves temperature stability under non-ideal conditions
  - For best protection against thermal excursions, store vaccine vials in boxes or trays placed in the center of the refrigerator
- **Dorm-style refrigerators should NOT be used for vaccine storage**
  - Severe temperature control drift
  - Lack of air circulation = spatial thermal non-uniformity
  - Susceptible to small room temperature fluctuations
- **Continuous temperature monitoring is an integral part of effective vaccine storage management**
  - Manual checks do not sufficiently capture temperature behavior over time
  - Thermal excursions most likely to occur when nobody is around
  - Widespread implementation of electronic temperature loggers is a simple and inexpensive way to dramatically improve vaccine storage practices
  - Proper placement of temperature monitors is crucial to obtaining meaningful data
  - For best results, sensor placement should match the locations and methods in which vaccine vials are stored