WHITE PAPER

Supporting the Center for Disease Control and Prevention Vaccine Storage Recommendations; an Evaluation of Two Refrigerators

Helmer Scientific, September 2015

Helmer SCIENTIFIC

1.0 Background

Introduction:

In order to protect public health, the Centers for Disease Control and Prevention (CDC) developed recommendations for vaccine handling and storage across the cold chain. Failure to properly manage vaccine inventories can reduce potency, leading to ineffective vaccinations and poor protection against preventable, yet devastating diseases. The CDC released recommendations in 2014 as part of a Vaccine Storage and Handling Toolkit based on studies conducted by the Advisory Committee on Immunization Practices (ACIP), the National Institute of Standards and Technology (NIST), as well as vaccine manufacturer product labeling. These data indicate that the refrigeration and freezer systems used to store vaccines in clinics and hospitals continue to be a major risk point. Using proper cold storage systems that are designed to maintain required temperature ranges, as well as using calibrated temperature monitoring methods, is recommended (1). Following CDC recommendations will help ensure the effectiveness of vaccinations, reduce cost associated with discarded vaccines, as well as reduce the direct and indirect costs of revaccination.

Vaccine Storage Challenges and Risks:

Vaccines require tight temperature storage ranges to ensure potency. Refrigerators are required to maintain temperatures between 35°F and 46°F (2°C and 8°C). Freezers are required to maintain temperatures between -58°F and +5°F (-50°C and -15°C). Mid-range set points are recommended to provide the best safety margin (1). Exposing vaccines to temperatures above or below these ranges for even a few minutes can result in patient safety issues. Exposing refrigerated vaccines to freezing tends to have the greatest risk, as freezing vaccines that contain aluminum adjuvants to increase immune responses can result in a permanent loss of potency (2). Unless the vaccine is visibly frozen at the time of inspection, clinicians cannot use visual checks to accurately determine which vaccines may have been damaged as a result of exposure to improper temperatures.

Indirect costs related to ineffective or repeat vaccinations are extensive but very difficult to measure. One estimate, based on reported cases of ineffective vaccines due to improper storage, is that individual states lose over $3M a year (1). According to a Department of Health and Human Services report, "Vaccines for Children Program - Vulnerabilities in Vaccine Management" released in 2012, 76% of 45 healthcare sites included in a study had vaccines that were exposed to inappropriate temperatures for at least a 5 hour period due to the use of inadequate refrigerators and freezers. These 34 providers had over 9000 Vaccines for Children doses, worth approximately $370,000 (3). The value of vaccines on hand and at risk in a specific facility will vary, but this value may be between $15,000 and $75,000. Healthcare systems that receive government-funded vaccine through programs such as Vaccines for Children (VFC) should be very aware of these financial risks. VFC providers routinely have agreements with State Departments of Health that include financial restitution policies which require providers to replace vaccines deemed non-viable due to provider negligence, including improper storage, on a dose-for-dose basis. These same provider agreements also include terms that allow for compliance site visits and unannounced inspections, further increasing provider risk (4). Based on these direct and indirect cost risks related to improper vaccine storage, the CDC will continue to strengthen vaccine storage guidelines to help control costs and improve public and privately administered vaccinations.

CDC Recommendations for refrigerators and freezer selection:

The CDC has revised guidelines related to selecting appropriate refrigerators and freezers that will be used for sensitive and expensive vaccine storage. These guidelines are in place to help ensure that vaccines are only stored in refrigerators and freezers that maintain temperature consistently across all storage locations (temperature uniformity), and that required temperature ranges are restored quickly after routine door openings (temperature

Exposing vaccines to out-of-range temperatures can result in patient safety issues and a permanent loss of potency.

76% of healthcare sites had vaccines that were exposed to inappropriate temperatures for at least a 5 hour period due to the use of inadequate refrigerators and freezers.

The value of vaccines at risk in a specific facility may be between $15,000 and $75,000.

recovery). According to the CDC Vaccine Storage and Handling Toolkit, healthcare professionals should not use household combination units. These units typically use single compressor systems that are not designed to consistently maintain temperatures in both the freezer and refrigerator compartments. Because these units work by circulating air from the freezer compartment to the refrigerator compartment, vaccines are at high risks of being exposed to freezing temperature, as well as other significant temperature fluctuations by storage location. The CDC also has strict recommendations to discontinue the use of "dormitory" style units. These units usually have a single outer door with the freezer compartment located within the refrigerated area. These types of units have demonstrated unacceptable performance for vaccine storage, regardless of the storage location within the chamber, or the size of the unit. The CDC does not recommend these types of units even for temporary storage (1).

Because of stringent temperature ranges required for proper vaccine storage, the risks to public health if vaccines are exposed to unacceptable temperature ranges, and the limitations of many refrigerators and freezers to meet requirements, the CDC has included guidelines for recommended storage equipment. The CDC recommends the use of stand-alone refrigerator and freezer units or pharmaceutical/medical grade units that meet vaccine storage guidelines (1). Pharmaceutical/medical grade units can utilize special designs best suited to protect vaccines. These design elements may include forced air refrigeration to ensure uniform temperature control throughout the cabinet. Forced air systems allow for more usable space, and decrease risk of user placing vaccines in areas of the refrigerator that do not maintain required temperatures. Pharmaceutical/medical-grade cold storage is also designed to quickly recover to set temperature after door openings. Forced air systems typically utilize specially designed drawers and shelves to enable proper air circulation, which also assist in temperature uniformity and recovery. In addition, pharmaceutical/medical grade refrigeration enables precise temperature control and set points, alarms, and can include built-in temperature monitoring that meets CDC recommendations related to calibration.

2.0 Refrigerator Evaluation

A side-by-side comparison of the Helmer Scientific medical-grade under-counter refrigerator and a competitive under-counter refrigerator and was conducted. This evaluation includes measurement of temperature uniformity across multiple locations in the refrigerator cabinet, temperature recovery after short and extended door openings, and temperature recovery time (pull-down test) from ambient to simulate power loss.

3.0 Methods

All protocols utilized a Helmer Scientific under-counter refrigerator and a competitive under-counter unit. Units had standard shelf configurations, and were not loaded with product. The Helmer Scientific under-counter unit was set to maximum uniformity mode. 15 T style thermocouples were used to measure air temperature at different locations within the chambers to evaluate usable storage space. Thermocouples were placed on all shelves of each test unit and positioned across locations. Probes were placed to capture temperatures from back, front, and middle shelf positions, as well as left side, right side and middle shelf positions. These placements were selected to best match storage locations described in the CDC Vaccine Storage and Handling Toolkit. The temperature was set to 5°C Celsius to match the recommend set-point for refrigerated vaccines as described in the CDC Vaccine Storage and Handling Toolkit (1).

Protocol 1 – Temperature Uniformity:

The Helmer Scientific under-counter refrigerator and a competitive under-counter unit were run for 72 hours to evaluate temperature uniformity within the range of 2°C - 8°C. This 72 hour test did not include any door openings, and simulates temperature uniformity when the refrigerator remains closed for extended periods.

Protocol 2 – Routine Door Openings:

The Helmer Scientific under-counter refrigerator and a compeitive under-counter unit were run for 8 hours to evaluate temperature uniformity within the range of 2°C - 8°C. Doors were opened for 60 seconds every 30 minutes in this 8 hour test to simulate routine door openings.

Protocol 3 – Extended Door Opening:

The Helmer Scientific under-counter refrigerator and a competitive under-counter unit were run for to evaluate temperature uniformity within the range of 2°C - 8°C. Doors were opened for a 15 minute period after reaching set point during this test to simulate an accidental and prolonged door opening.

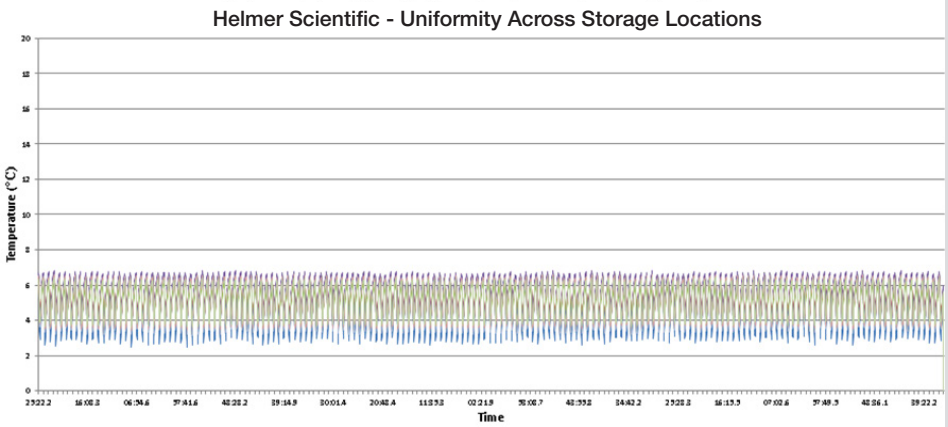
Protocol 4 – Power Loss:

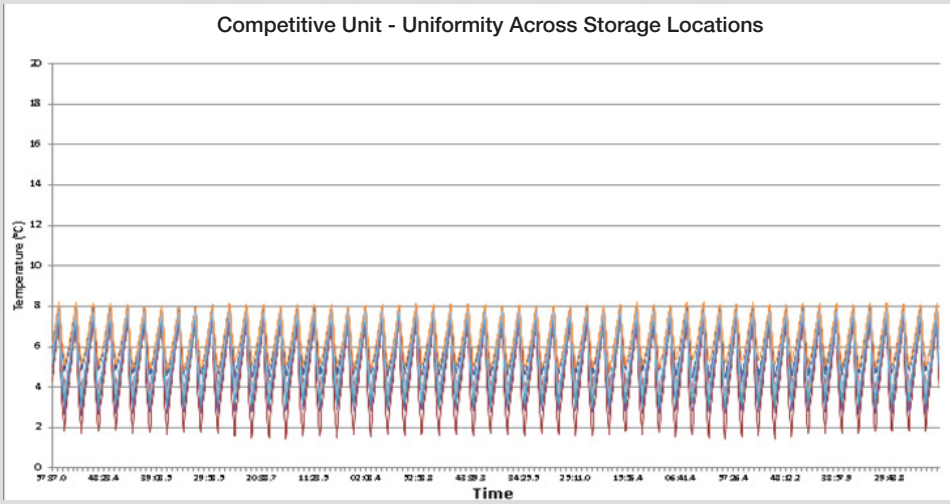
The Helmer Scientific under-counter refrigerator and a competitive under-counter unit were evaluated during a pull-down test. Pull-down tests include powering down units until ambient temperature is reached, then restoring power and measuring time required to reach the set temperature of 5°C.

4.0 Results

Protocol 1 – Temperature Uniformity

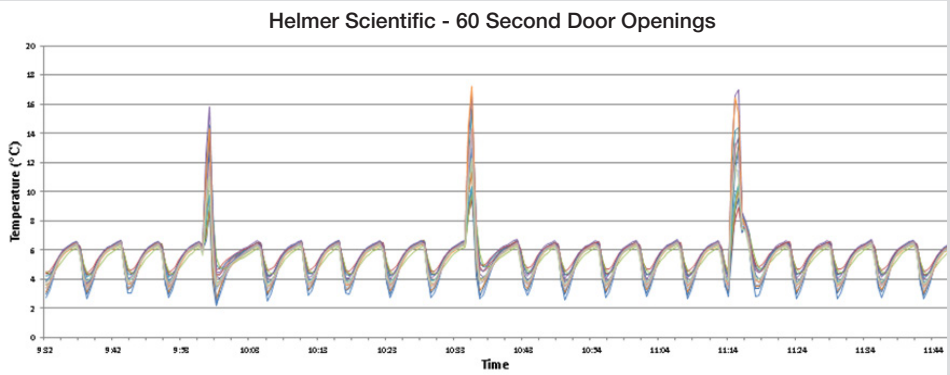
The Helmer Scientific unit maintained air temperatures between 2°C to 8°C across all locations for the entire 8 hour period. The competitive unit exceeded the optimum range of 2°C to 8°C 250 times over the 72 hour period, across all temperature probe locations. The temperature probe located on the middle shelf, front left location of this unit had the most out of range air temperatures with 113 recorded.

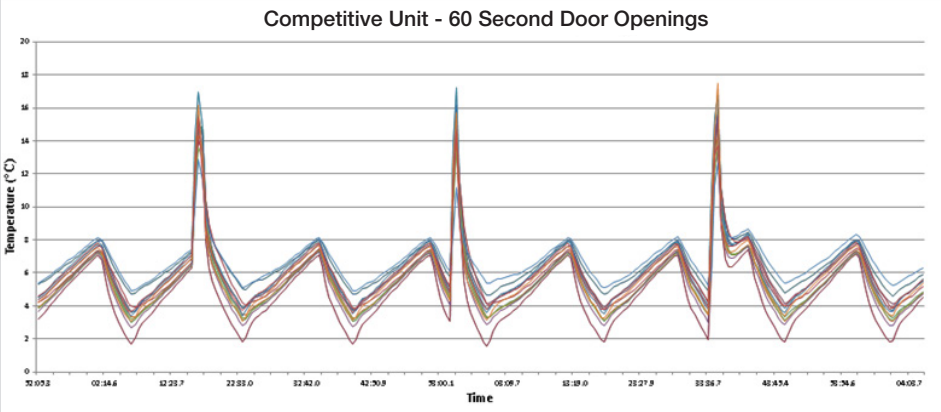




Protocol 2 – Routine Door Openings

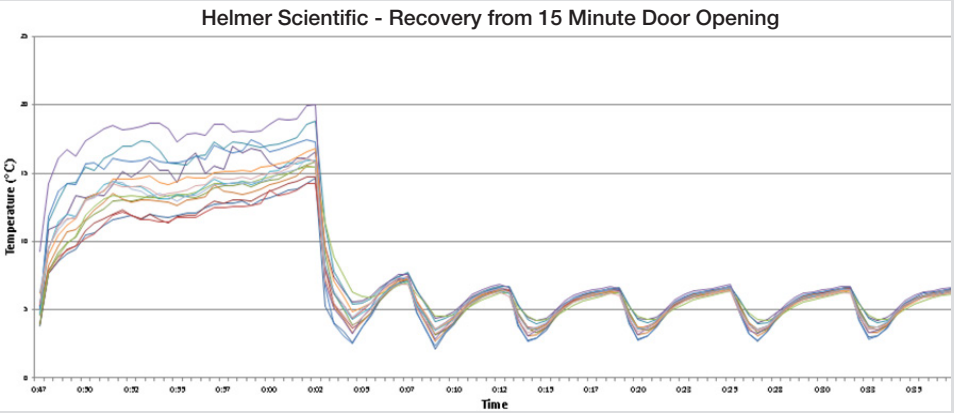
The Helmer Scientific unit required 4 minutes 20 seconds on average to recover from a 60 second door openings. The competitive unit required over 5 minutes to recover temperature from a 60 second door opening.

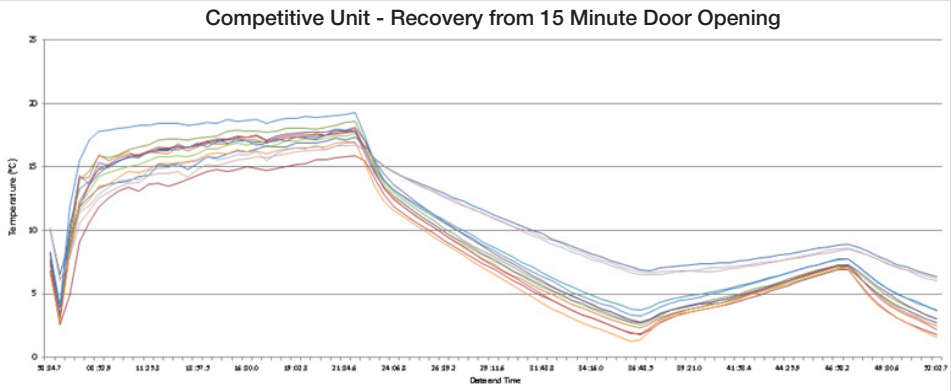




Protocol 3 – Extended Door Opening

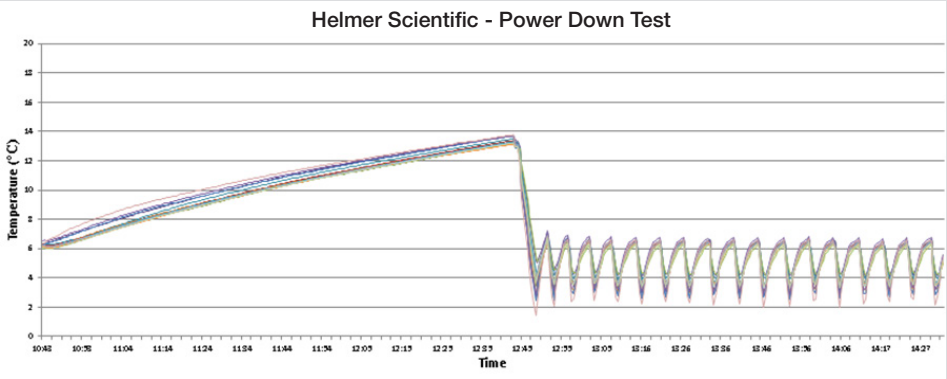
The Helmer Scientific unit required approximately 12 minutes to return to the target temperature range. The competitive unit required approximately 34 minutes on average to return to the target temperature range after having the door open for 15 minutes.

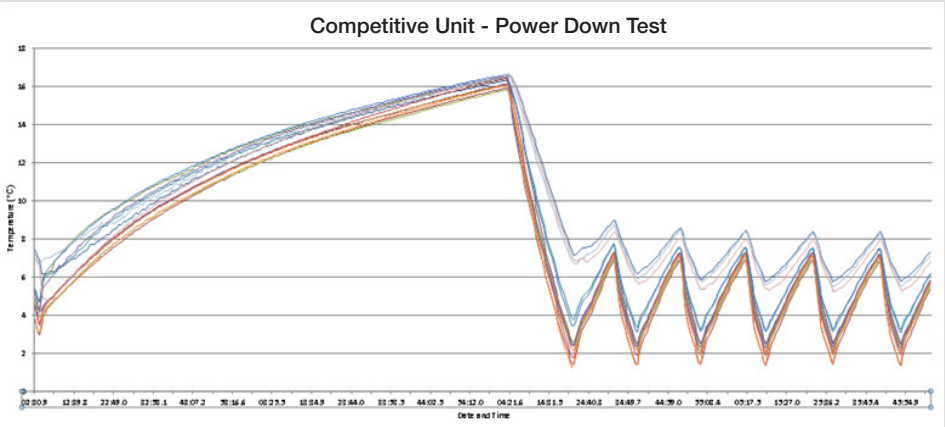




Protocol 4 – Power Loss

The Helmer Scientific unit required 1 hour 4 minutes to reach the set-point (from ambient). Although power was removed from the Helmer Scientific unit, the on-board controls and temperature monitor continued to maintain functionality due to a built-in back-up battery. The competitive unit required 1 hour and 20 minutes order to reach the temperature set-point (from ambient) in the event of a simulated power failure.





5.0 Discussion

The CDC determined that healthcare providers needed stronger recommendations related to vaccine storage to support public health and public safety. These recommendations recognize that there are differences between cold storage options that affect the quality of vaccine storage and the efficacy of vaccinations, as well as the ability to prevent expensive vaccine waste due to exposure to inappropriate and unsafe temperatures. This evaluation has demonstrated that there are differences between refrigerator models in their ability to maintain uniform temperatures, recover from door openings, and recover from power loss.

For uniformity, the Helmer Scientific under-counter unit maintained appropriate air temperatures across storage locations at all times during the study. During the same temperature uniformity protocol, the competitive unit had storage locations that routinely approached the top or bottom of the recommended range for vaccine storage. In addition, temperature probes inside the competitive unit recorded temperatures out of range across locations 250 times, with the middle shelf, front left location accounting for 113 of these out of range events. Although it is possible to recommend that specific storage areas are not used, there is risk that users will make errors and place vaccines in all areas of a refrigerator even with training, so tight uniformity across locations provides additional fail-safes for vaccine storage. Tight temperature uniformity across chamber locations will provide more appropriate usable space for storage.

Temperature recovery studies also showed that there were differences between the Helmer Scientific and competitive units. In both a simulation to mimic "routine" openings, and a simulation to mimic extended or accidental openings, the Helmer Scientific under-counter unit returned to the desired temperature range faster than the competitive unit. Applying these findings to a clinical setting would indicate that refrigerated vaccines would be stored at temperatures outside the CDC recommendations for less time than a competitive unit under a number of different scenarios. The pull-down power failure test was consistent with these results; the Helmer Scientific unit pulled down temperature from ambient to target range faster than the competitive unit. This means that in the case of a power failure event, contents of the Helmer Scientific unit would be exposed to out of range air temperatures for less time. In addition, because the Helmer Scientific unit (iSeries controller) also uses a built-in temperature monitor and alarm system with an internal back-up battery, the Helmer Scientific unit is designed to provide invaluable data about temperature during power outages. This data is critical for Immunization Program administrators and for vaccine manufactures to help determine if vaccines need to be discarded due to improper storage.

CDC recommends only using stand-alone or pharmaceutical/purpose-built units for vaccine storage. This evaluation demonstrated that not all refrigerators have equal performance to maintain required temperatures for vaccines, and that healthcare providers and administrators need to understand the performance of their selected cold-storage system, and its ability to safely maintain temperature to protect vaccines.

Summary comparisons between Helmer Scientific and CliniCool units

Test	Helmer Scientific	Competitive Unit
Uniformity - Data points out of range	0	250
60 sec Door Openings - Recovery time	4.33 minutes	5.08 minutes
15 min Door Opening - Revocery time	12 minutes	34 minutes
Pull-down Test - Recovery time	64 minutes	80 minutes

6.0 Conclusion

The CDC Vaccine Storage and Handling Toolkit makes important recommendations to help protect the efficacy and efficiency of vaccination programs. The use of the Helmer Scientific under-counter pharmaceutical/medical-grade refrigerator will assist healthcare facilities in meeting these requirements by maintaining the tight temperature ranges required for vaccine storage under a number of different situations. Data generated during this evaluation supports the performance claims of the Helmer Scientific under-counter refrigerator.

7.0 References

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2. Journal of Pharmaceutical Science. Vaccines with Aluminum-Containing Adjuvants: Optimizing Vaccine Efficacy and Thermal Stability. August, 2010. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3201794/
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