ACHSM Asia-Pacific Journal of Health Management

RESEARCH ARTICLE

EVALUATING AN AUTOMATED TEMPERATURE-MONITORING SYSTEM IN MEDICINE AND VACCINE STORAGE FACILITIES OF A HOSPITAL NETWORK

Mazdak Zamani, Paul Wembridge

Eastern Health Pharmacy Department, Melbourne, Victoria, Australia

Correspondence: mazdak.zamani@easternhealth.org.au

ABSTRACT

OBJECTIVE

The aims of this study were to evaluate the effectiveness of a new automated continuous temperature monitoring system in detecting temperature excursions and describe the challenges of implementing such a system.

DESIGN

This study is an observational before-and-after audit comparing temperature excursions detected in the three months before and three months after the implementation of the new monitoring system at Eastern Health. Inclusion criteria consisted of all medicine and vaccine storage facilities monitored by the new automated temperature monitoring system. Four sites not connected to the new monitoring system were excluded.

SETTING

Eastern Health is a large tertiary metropolitan health service in Melbourne, Australia. It operates from 21 locations including seven teaching hospitals, with medicines and vaccines stored in 124 refrigerators, 6 freezers and 101 ambient room temperature storage locations.

MAIN OUTCOME MEASURES

An analysis of post-implementation data identified a potential association between refrigerator brands and temperature excursion rate.

RESULTS

There was a large increase in the number of temperature excursions detected post-implementation of the new automated monitoring system. 28,746, 24 and 8,966 temperature excursions were detected post-implementation compared to 344, 0 and 0 pre-implementation in refrigerators, freezers and ambient locations, respectively. The majority of temperature excursions detected in medicine and vaccine fridges were below +2°C (98.4%). One brand of refrigerators was linked to 27,231 (94.7%) excursions ($p<0.001$).

CONCLUSIONS

The new temperature monitoring system detects higher number of excursions which provides better visibility of performance, identifies areas of non-compliance, and guides and evaluates solutions. This study recommends that freezers and ambient storage locations are monitored as robustly as refrigerators, temperature monitoring devices are placed in close proximity to pharmaceuticals, and that healthcare organisations avoid purchasing unreliable medicine and vaccine refrigerators. Finally, this study suggests the development of a National Medicine Storage Guideline.

KEYWORDS

Medicine, medication, vaccine, excursion, automated, temperature, monitoring.

INTRODUCTION

Correct storage temperature of medicines and vaccines ensures their effectiveness and safety. Besides clinical risks to individual patients, inappropriate storage of medicines and vaccines imposes considerable financial wastage and creates potential public health risks such as the outbreak of measles in the Federated States of Micronesia in 2014. [1-3] The National Safety and Quality Health Service Standards require Australian hospitals to implement systems that continuously monitor and preserve the integrity of temperature-sensitive medicines and vaccines.[4]

In October 2020, Eastern Health implemented a centralised automated temperature monitoring system in its medicine storage facilities. Eastern Health is geographically the largest metropolitan health service in Melbourne, Victoria, Australia. It operates from 65 sites across 21 locations including seven teaching hospitals, four nursing homes, and multiple community health and mental health services. Eastern Health has over 10,000 staff and volunteers, 1,500 beds and provides over 1.3 million episodes of patient care per annum.[5] At Eastern Health, medicines and vaccines are stored in 124 refrigerators, six freezers and 101 ambient room temperature storage locations including seven pharmacy departments and 94 medicine rooms and cabinets. Prior to implementing the new monitoring system, the temperate monitoring of refrigerators and freezers was conducted through a combination of manual and automated monitoring systems. The ambient room temperature was only monitored in the seven pharmacy departments. Eastern Health has a clear process for managing temperature excursions, when they are identified, to ensure patient safety is not compromised.

The primary aim of this study was to evaluate the effectiveness of the new centralised automated temperature monitoring system in detecting temperature excursions. The secondary aim was to describe the main challenges of implementing this new system and how they were addressed.

METHODS

This study is an observational before-and-after audit. It compares the temperature excursions detected three months before and three months after the implementation of a new centralised continuous temperature monitoring system, Invisible Systems™ (Manchester, England). The pre-implementation study phase was from 1 July 2020 until 30 September 2020 and the post-implementation from 1 October 2020 until 31 December 2020. Pre-implementation data was retrospectively collected by reviewing paper temperature monitoring records and electronic reports from the previous temperature monitoring systems. Post-implementation data was extracted from Invisible Systems™ online portal.

Inclusion criteria consisted of all medicine and vaccine storage facilities monitored by the calibrated and certified Invisible Systems™. Information about the temperature monitoring sensors and their specifications is available from the manufacturer's website (www.invisible-systems.com). Four medicine and vaccine storage facilities not yet connected to the new system were excluded. The ward medicine trolleys, resuscitation trolleys, anaesthetic trolleys, and patient bedside drawers were considered out of scope.

Age, brand and size of refrigerators were manually audited. Air temperature control mechanisms in ambient storage locations were manually audited. Data was compared and analysed using R (version 3.5.2). Mann-Whitney U test was used to compare the temperature excursion rates of different brands of refrigerators. Fisher's exact test was used to compare different room temperature control mechanisms in ambient storage locations.

The storage temperature range for refrigerators was defined as between +2°C and +8°C (5±3°C).[6,7] Ambient room temperature was defined as below +25°C.[7] The acceptable temperature range for freezers were defined as below -15°C or -70°C depending on the type, function and products stored in that freezer. One temperature excursion was defined as a single occasion of temperature deviating outside the recommended range until it returned within the range, regardless of the length of time it remained outside the range.

RESULTS

The number of temperature excursions in medicine and vaccine storage facilities pre- and post-implementation of the new automated temperature monitoring system are shown in table 1. There were large increases in the number of temperature excursions detected by the new monitoring system compared to the previously recorded data. The

majority of post-implementation temperature excursions in the refrigerators were below +2°C.

TABLE 1. TEMPERATURE EXCURSIONS DETECTED PRE- AND POST-IMPLEMENTATION OF AN AUTOMATED TEMPERATURE MONITORING SYSTEM

	PRE	POST
Refrigerators (+2°C to +8°C)		
Number of refrigerators monitored	116	120
Total number of temperature excursions detected	344	28746
Temperature excursions above +8°C	263	459
Temperature excursions below +2°C	81	28287
Temperature excursions at or below 0°C	0	604
Refrigerators without any temperature excursion (%)	74 (64%)	67 (56%)
Freezers (<-15°C or <-70°C)		
Number of -20°C freezers monitored	5	5
Number of -80°C ultra-low freezers monitored	0	1
Temperature excursions above -15°C	0	23
Temperature excursions above -70°C	0	1
Total number of temperature excursions detected	0	24
Temperature excursions at or above 0°C	0	0
Freezers without any temperature excursion	5	2
Ambient room temperature (<+25°C)		
Number of ambient storage locations monitored	7	97
Total number of temperature excursions above +25°C	0	8966
Temperature excursions above +30°C	0	7
Storage locations without any temperature excursion	7	41

Table 2 shows the specifications and characteristics of the refrigerators. An analysis of the characteristics data against the post-implementation temperature excursions identified a potential correlation with the brand of refrigerators (Table 3). Direct comparison between refrigerator brands using Mann-Whitney U test confirmed statistically significant differences in the mean number of excursions per refrigerator between brand A and brands B (P<0.001), C (P<0.001), D (P<0.001) and E (P=0.04). Additionally, brand A was found to have significantly more temperature excursions per refrigerator than all other brands combined (P<0.001). The number of excursions per refrigerator did not differ significantly between brand A and domestic refrigerators (P=0.72). Other brands (n=16) included those with four or less units installed at Eastern Health were treated as one group in this analysis. The majority of brand A refrigerators were 5-10 years old (n=42), serviced every six months (n=31) and connected to the back-to-base Building Management System (BMS) (n=30). No other potential correlations between the characteristics data and post-implementation temperature excursions were identified.

Table 4 illustrates refrigerator temperature excursions per month as the faulty refrigerators were identified, adjusted, repaired or replaced. 2021 data is displayed in table 4 but not included in data analysis.

TABLE 2. EASTERN HEALTH MEDICINE AND VACCINE REFRIGERATOR DEMOGRAPHIC DATA

MEDICINE AND VACCINE REFRIGERATORS (N=120)	NUMBER OF REFRIGERATORS (%)
Type of refrigerators:	
Purpose-built refrigerators	114 (95%)
Domestic refrigerators	6 (5%)
Size of refrigerators:	
Small (<200L)	70 (58.3%)
Medium (300-500L)	30 (25%)
Large (>900L)	20 (16.7%)
Estimated age of refrigerators:	
<5 years	24 (20%)
5-10 years	66 (55%)
>10 years	30 (25%)
Scheduled maintenance/service of refrigerators:	
Every 3 months	8 (6.7%)
Every 6 months	34 (28.3%)
Every 12 months	2 (1.7%)
Unknown or None	76 (63.3%)
Method of temperature monitoring pre-intervention:	
Manual paper chart (± data logger)	65 (54.2%)
Building Management System	42 (35%)
Comark™ automated monitoring system	9 (7.5%)
Omnicell™ automated dispensing system	2 (1.7%)
Audible alarm and data logger	2 (1.7%)

TABLE 3. COMPARISON OF POST-IMPLEMENTATION TEMPERATURE EXCURSIONS AGAINST REFRIGERATOR BRANDS

BRANDS OF MEDICINE AND VACCINE REFRIGERATORS (N=120)	BRAND A	BRAND B	BRAND C	BRAND D	BRAND E	BRAND – OTHER	DOMESTIC REFRIGERATORS
Number of refrigerators installed	45	20	18	10	5	16	6
Percentage of all refrigerators installed	37.5%	16.7%	15%	8.3%	4.2%	13.3%	5%
Number of temperature excursions post-implementation	27,231	197	13	2	7	572	724
Temperature excursions above +8°C	85	196	13	2	2	13	148
Temperature excursions below +2°C	27,146	1	0	0	5	559	576

Temperature excursions at or below 0°C	507	1	0	0	0	0	96
Percentage of all temperature excursions (n=28746)	94.73%	0.69%	0.05%	0.01%	0.02%	1.99%	2.52%
Mean temperature excursions per refrigerator of this brand	605.1	9.8	0.7	0.2	1.4	35.7	120.7

TABLE 4. NUMBER OF TEMPERATURE EXCURSIONS DETECTED EACH MONTH IN THE MEDICINE AND VACCINE REFRIGERATORS

REFRIGERATOR TEMPERATURE EXCURSIONS	≤0°C	<+2°C	>+8°C	TOTAL
Pre-implementation				
July 2020	0	0	95	95
August 2020	0	77	86	163
September 2020	0	4	82	86
Post-implementation				
October 2020	508	24100	328	24428
November 2020	89	1936	72	2008
December 2020	7	2251	59	2310
Follow-up data (not analysed)				
January 2021	1	69	91	160
February 2021	0	219	55	274
March 2021	2	102	95	197

Out of six medicine and vaccine freezers, one recorded 21 excursions, three had one excursion each and two had no excursions post-implementation. No further data was collected or analysed for freezers.

The ambient room temperature storage locations were audited to determine the possibility of adjusting air temperature independently from the surrounding areas. An analysis of room temperature excursions against the audit results did not identify any possible correlation (table 5). Further analyses of ambient temperature excursions against other variables such as the number, size and brand of medicine and vaccine refrigerators in each location did not suggest any potential correlations either.

TABLE 5. AUDIT OF ROOM TEMPERATURE CONTROL IN THE MEDICINE AND VACCINE AMBIENT STORAGE FACILITIES

AMBIENT STORAGE AIR TEMPERATURE CONTROL (N=97)	TOTAL NUMBER OF LOCATIONS	LOCATIONS WITHOUT EXCURSIONS	COMPARISON
A. Locations *with* air-conditioned air supply but *without* independent temperature control	66 (68%)	29 (43.9%)	A versus B (P=0.62)
B. Locations *with* air-conditioned air supply and *with* independent temperature control	22 (22.7%)	8 (36.4%)	B versus C (P=0.70)
C. Locations *without* air-conditioned air supply	9 (9.3%)	4 (44.4%)	C versus A+B (P=1.00)

DISCUSSION

Following the installation of an automated continuous temperature monitoring system at a large hospital network, the number of temperature excursions detected in medicine and vaccine refrigerators, freezers and ambient storage locations increased.

Temperature excursions of refrigerated medicines and vaccines are common in hospitals and health service managers are not necessarily aware of them.[8,9] Even though exposure to extreme temperatures including heat and freezing does not cause the formation of toxic substances, it may reduce the potency of medicines and vaccines.[10,11] Vaccines and some medicines such as insulins and monoclonal antibodies are complex biological molecules and denature if frozen.[12-14] Ineffective medicines can harm patients by failing to deliver therapeutic effects.[15] Similarly, ineffective vaccines can harm individuals and pose serious public health risks.[3] The inconvenience of revaccination, potential lawsuits and financial wastage are some of the other adverse outcomes of inappropriate storage.[10] Despite advances in the vaccine supply chain, temperature excursions are still common in Australian health system and result in an estimated $16 million dollars wastage per annum.[2]

Refrigerators

This study has highlighted that a large number of temperature excursions in medicine and vaccine refrigerators go undetected when using the conventional monitoring methods. The main difference between the new temperature monitoring system and previous methods used at Eastern Health was the source of temperature data. Pre-implementation, temperature data was obtained either manually once or twice daily from the refrigerator digital thermometers or electronically through BMS. Both methods rely on the built-in refrigerator thermostats to provide the temperature data. This created the biggest challenge of implementing the new temperature monitoring system as it was reporting different readings to those measured by the refrigerator thermostats and staff were questioning its accuracy. This finding was, however, consistent with published literature. Kartoğlu, Nelaj and Maire found the temperature data provided by built-in refrigerator thermometers to be inaccurate and suggested abandoning their use.[16] After numerous tests with calibrated thermometers and digital data loggers, three possible reasons for the temperature discrepancies were suggested.

Firstly, internal refrigerator thermometers are generally installed on top of the refrigerator cabinets for manufacturing convenience. The location of thermometer probe is critical as temperature can vary considerably in different parts of a refrigerator cabinet. In Australia, purpose-built medicine and vaccine refrigerators are required to maintain a stable, uniform and controlled temperature between +2°C and +8°C, close to +5°C.[6] However, local guidelines do not elaborate on the location of built-in refrigerator thermometers although they recommend temperature mapping to identify cold spots.[6,7] Furthermore, the local guidelines provide conflicting information about the location of external data loggers. They recommend both placing digital data loggers in the middle of medicines and vaccines and co-locating them with inbuilt minimum/maximum thermometers to "prevent different readings".[6,7] As a result, the back-to-base BMS probes in the 42 BMS-connected refrigerators at Eastern Health were co-located with the inbuilt thermometers. Conversely, international guidelines recommend placing digital data loggers in the centre of refrigerators and in close proximity to medicines and vaccines. [17,18]

Secondly, observation from this study suggests that some brands of purpose-built refrigerators are more successful in achieving a stable and uniform temperature through more effective air circulation and cooling system design. The analysis of temperature excursion data against different brands of refrigerators identified one brand of purpose-built refrigerators to have the highest rate of temperature excursions, followed by domestic refrigerators. Thirdly, inbuilt thermometers are typically exposed to air temperature. Thus, they record rapid fluctuations in temperature, for instance, when the refrigerator door is opened briefly. On the other hand, the new monitoring system uses validated lagged or buffered temperature probes which are placed inside solid thermal blocks to simulate the core temperature of medicines and vaccines, and avoid rapid fluctuations and false alarms.[6]

The challenges related to medicine and vaccine refrigerators were the most difficult to address. Initially, a review of the national and international guidelines was conducted to verify the new monitoring system probes were correctly installed. [6,7,17-19] Relevant stakeholders were consulted and a consensus was reached to place the Invisible Systems™ temperature probes in the centre of refrigerators, in the middle of medicines and vaccines.

Next, the accuracy of the new monitoring system probes were confirmed using calibrated thermometers and digital data loggers. The frequent temperature excursions below +2°C, including subzero readings, were consistent with the literature. Hanson et al [20] conducted a review of 21 published research articles and concluded that cold chain breach of vaccines is an ongoing global issue and exposing refrigerated vaccines to freezing temperatures continues to be a major problem. This review highlighted that many frontline healthcare workers are unaware of the risks associated with exposure to subzero temperatures and their focus has been on preventing exposure to heat. [20,21]

Moreover, the most common brand of refrigerators at Eastern Health was found to have the highest rate of excursions. To ensure appropriate medicine and vaccine refrigerators are purchased at Eastern Health, a group of representatives from the Pharmacy, Nursing, Infrastructure/Maintenance and Procurement Departments convened and recommended a list of criteria for future purchases such as certified purpose-built medicine and vaccine refrigerator, frost-free, double-glazed glass door, self-closing door, audible door ajar alarm, lockable door, low energy consumption and low noise level.

Freezers

More temperature excursions were detected in freezers post-implementation. One freezer recorded 21 temperature excursions which was found to be due to placing unfrozen ice bricks inside the freezer near the temperature probe. This issue was addressed by placing a dedicated container for unfrozen ice bricks inside the freezer, away from the temperature sensor and frozen pharmaceuticals.

The main challenge with the freezer temperature monitoring was that, contrary to refrigerated medicines, there were no national guidelines regarding the frozen storage thresholds and how to manage freezer temperature excursions. [6,7,17-19,22,23]

Ambient room temperature

A large number of temperature excursions were detected in ambient storage locations post-implementation compared to zero in the seven monitored locations pre-implementation. Of the monitored locations pre-implementation, one recorded temperature excursions post implementation. This was due to staff changing the settings of the air conditioning unit for personal comfort. This finding in addition to the analysis of the temperature excursion data in ambient locations with independent air temperature controls has demonstrated that installing local air conditioning units is not a fail-proof solution as the stand-alone air conditioners can be adjusted or turned off by staff. Additionally, it is not practical to remove the air-conditioner controllers as they may be hardwired on the wall or must be readily accessible to turn on the units following interruptions to power supply. We expected to observe higher rates of temperature excursions in medicine rooms with more heat generating sources such as those with more than one refrigerator or with refrigerators that consume more electricity. However, this was not observed which we believe is due to the complex nature of room temperature control and the many variables involved such as room size, temperature and volume of air entering the room, heat generation, source of heat, presence of air vents or exhaust fans and location of temperature sensors.

Similar to freezers, another challenge was the limited number and variability of guidelines and published articles regarding ambient room temperature monitoring for medicines and vaccines.[22,23] For instance, local guidelines only recommend a high threshold of +25°C for ambient room temperature.[7] However, it is important to also have a low threshold as liquid medicines presented in the forms of solution or suspension may crystalize or precipitate if exposed to cold temperatures.[24] Besides, some automated temperature monitoring systems require both high and low thresholds to be programmed. Therefore, +8°C was programmed in the Invisible Systems™ as the minimum room temperature. The lowest temperature recorded post-implementation was +13.7°C.
The World Health Organisation recommends 'controlled room temperature' to be between +15°C and +25°C and 'cool place temperature' between +8°C and +15°C.[22] The United States Pharmacopeia defines 'controlled room temperature' to be between +20°C and +25°C and allows excursions between +15°C and +30°C as long as Mean Kinetic Temperature (MKT) remains below +25°C.[23] These definitions are not currently included in the Australian guidelines and not used at Eastern Health although Invisible Systems™ reports MKT values.

The third challenge has been the difficulty in managing ambient temperature excursions. Unlike refrigerator temperature excursions where the affected stock can be quarantined and moved to another refrigerator until the faulty refrigerator is repaired or replaced, there are larger

amounts of medicines stored in ambient storage facilities and it is not always practical to move them. Moreover, changing the temperature of air supply to medicine rooms often impacts the surrounding areas potentially making it uncomfortably cold for patients and staff.

Strengths and weaknesses

A major strength of this study is the inclusion of three different temperature storage conditions across an entire healthcare network. Another strength is including all temperature excursions detected over three months pre- and three months post-implementation. It suffices to say that the new system is programmed to record the temperature every 5 minutes which means it could record up to 144 excursions per day for one probe if the temperature repeatedly goes in and out of the recommended range. In contrast, the manual monitoring was undertaken once or twice daily. Furthermore, the new monitoring system continued to record temperature excursions while the faulty refrigerators were being assessed, adjusted, repaired or replaced, and the affected medicines and vaccines were quarantined. This data was not excluded as the primary aim of this study was to evaluate the ability of the new monitoring system in detecting temperature excursions. To ensure patient safety, Eastern Health policy requires affected medicines and vaccines to be immediately quarantined until their safety for use is determined; and the faulty equipment is not used for storage of pharmaceuticals until repaired or replaced.

A limitation of this study was the inability to locate 14 pre-intervention monthly manual temperature recording charts. Despite this, a search of Eastern Health incident management system identified no pre-intervention reported temperature excursions for these locations. Another limitation was that we introduced additional four refrigerators and one freezer at the time of the intervention, and commenced monitoring of ambient temperature in 90 locations resulting in mismatch in total storage locations pre- and post-intervention. It is of note that this study was undertaken during winter and spring in Melbourne. It is important to reassess the effect of higher outdoor temperatures over summer on ambient room temperatures.

Implications for practice

Health service managers should ensure this critical yet basic aspect of patient safety is adequately addressed at their organisations.[4] Effective monitoring of medicines and vaccines temperature is the first step in the quality management process. It provides better visibility of performance, highlights areas of risk, and guides and evaluates mitigation strategies. It is recommended that:

- Inbuilt refrigerator thermometers are not solely relied upon to monitor the storage temperature of medicines and vaccines
- Temperature monitoring loggers and sensors are co-located with medicines and vaccines if mapping data is unavailable
- Medicine and vaccine freezers and ambient room temperature storage locations are monitored as robustly as refrigerators
- Health services avoid using unreliable or domestic refrigerators for storage of medicines and vaccines

Unanswered questions and future research

This study has identified some areas for future research and improvement. Firstly, it has been noted there is no National Medicine Storage Guideline in Australia. Secondly, it is recommended to explore the use of MKT in managing temperature excursions with the aim to incorporate in the relevant local guidelines. Thirdly, it is suggested to temperature map different medicine and vaccine refrigerators based on brand, size, type, etc. The findings of this research will guide correct placement of built-in thermometers and temperature monitoring devices and whether more than one sensor is needed for larger refrigerators.

CONCLUSIONS

An automated continuous temperature monitoring system was installed in all medicine and vaccine storage locations at Eastern Health. Comparison of temperature excursions pre- and post-implementation has shown the new system can detect higher numbers of excursions compared to previous temperature monitoring methods. This provides better visibility of performance, identifies areas of non-compliance, and guides and evaluates solutions. Analysis of temperature excursions identified most temperature excursions were in refrigerators and below +2°C. One brand of purpose-built medicine and vaccine refrigerators was flagged to have the highest rate of excursions, followed by the domestic refrigerators. It has been noted that national and international guidelines do not elaborate on the monitoring of freezers and ambient storage to the same extent as refrigerators. Finally, this study recommends the development of a National Medicine Storage Guideline.

ACKNOWLEDGEMENTS

We like to thank Mrs Saly Rashed, Wantirna Health Pharmacy Manager, for assisting with the implementation of the new temperature monitoring system and review of this article. We also like to thank Mr Bruce Leslie, Director of Infrastructure at Eastern Health, for arranging the audit of ambient storage locations and assisting with the implementation of the new temperature monitoring system.

CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article.

ETHICAL APPROVAL

This study did not involve human or animal subjects and therefore did not require ethics approval. The manuscript was reviewed by Eastern Health Pharmacy Practice Research Group.

References

1. Khan MH, Hatanaka K, Sovannarith T, Nivanna N, Casas LC, Yoshida N, et al. Effects of packaging and storage conditions on the quality of amoxicillin-clavulanic acid–an analysis of Cambodian samples. BMC Pharmacol Toxicol. 2013 Dec;14(1):1-7. https://doi.org/10.1186/2050-6511-14-33
2. D'Onise K, Almond S, MacDonald B, Watson M, Scrimgeour S. Have purpose built vaccine refrigerators reduced the cost of vaccine losses in South Australia? Aust N Z J Public Health. 2012 Dec;36(6):572-6. https://doi.org/10.1111/j.1753-6405.2012.00932.x
3. Breakwell L, Moturi E, Helgenberger L, Gopalani SV, Hales C, Lam E, et al. Measles outbreak associated with vaccine failure in adults—Federated States of Micronesia, February–August 2014. Morb Mortal Wkly Rep. 2015 Oct 2;64(38):1088-92. https://doi.org/10.15585/mmwr.mm6438a7
4. Australian Commission on Safety and Quality in Health Care. National Safety and Quality Health Service (NSQHS) Standards: Medication Safety Standard [Internet]. Sydney NSW: Australian Commission on Safety and Quality in Health Care; 2019 [cited 2021 Jan 27]. Available from: https://www.safetyandquality.gov.au/standards/nsqhs-standards/medication-safety-standard
5. Eastern Health. About us [Internet]. Melbourne VIC: Eastern Health; 2020 [cited 2021 Jan 27]. Available from: https://www.easternhealth.org.au/images/Eastern_Health_Quick_Facts_2020.pdf
6. Australian Government Department of Health. National Vaccine Storage Guidelines – Strive for 5, 3rd edition [Internet]. Canberra ACT: Commonwealth of Australia; 2019 [updated 2020 Apr 16; cited 2021 Jan 27]. Available from: https://www.health.gov.au/sites/default/files/documents/2020/04/national-vaccine-storage-guidelines-strive-for-5.pdf
7. Victorian Pharmacy Authority. Victorian Pharmacy Authority Guidelines [Internet]. Melbourne VIC: Victorian Pharmacy Authority Guidelines; 2019 [cited 2021 Jan 27]. Available from: https://www.pharmacy.vic.gov.au/cms_files/VPA%20Guidelines%20effective%201%20November%202019.pdf
8. Dubrava S, Tait PA, Humphris MA. Identification of Potential and Actual Breaches in the Cold Chain within a Tertiary Hospital. J Pharm Pract Res. 2007 Mar;37(1):16-8. https://doi.org/10.1002/j.2055-2335.2007.tb00650.x
9. Levinson DR, General I. Vaccines for children program: vulnerabilities in vaccine management. Department of Health and Human Services: Office of Inspector General. 2012 Jun. Available from: https://www.coldchain-tech.com/images/documents/VaccineForChildrenProgram.pdf
10. Hibbs BF, Miller E, Shi J, Smith K, Lewis P, Shimabukuro TT. Safety of vaccines that have been kept outside of recommended temperatures: reports to the vaccine adverse event reporting system (VAERS), 2008–2012. Vaccine. 2018 Jan 25;36(4):553-8. https://doi.org/10.1016/j.vaccine.2017.11.083
11. Vimalavathini R, Gitanjali B. Effect of temperature on the potency & pharmacological action of insulin. Indian J Med Res. 2009 Aug 1;130(2):166-70. Available from: https://medgreen.com.tw/images/productnews/5d11fd08e6e87558eb51c761d8dc1c67.pdf
12. Carter AW, Heinemann L. Insulin concentration in vials randomly purchased in pharmacies in the United States: considerable loss in the cold supply chain. J Diabetes Sci Technol. 2018 Jul;12(4):839-41. https://doi.org/10.1177/1932296817747292
13. Matthias DM, Robertson J, Garrison MM, Newland S, Nelson C. Freezing temperatures in the vaccine cold chain: a systematic literature review. Vaccine. 2007

May 16;25(20):3980-6. https://doi.org/10.1016/j.vaccine.2007.02.052
14. Lazar KL, Patapoff TW, Sharma VK. Cold denaturation of monoclonal antibodies. MAbs. 2010 Jan 27;2(1):42-52. https://doi.org/10.4161/mabs.2.1.10787
15. Bassat Q, Tanner M, Guerin PJ, Stricker K, Hamed K. Combating poor-quality anti-malarial medicines: a call to action. Malar J. 2016 Dec;15(1):1-2. https://doi.org/10.1186/s12936-016-1357-8
16. Kartoğlu Ü, Nelaj E, Maire D. Improving temperature monitoring in the vaccine cold chain at the periphery: An intervention study using a 30-day electronic refrigerator temperature logger (Fridge-tag®). Vaccine. 2010 May 28;28(24):4065-72. https://doi.org/10.1016/j.vaccine.2010.03.076
17. Hamborsky J, Kroger A, editors. Centers for Disease Control and Prevention (CDC). Epidemiology and prevention of vaccine-preventable diseases, E-Book: The Pink Book – Chapter 5: Vaccine Storage and Handling [Internet]. Washington DC: Public Health Foundation; 2015 Oct 19 [updated 2020 Jul; cited 2021 Jan 27]. Available from: https://www.cdc.gov/vaccines/pubs/pinkbook/vac-storage.html
18. Public Health Agency of Canada. Storage and handling of immunizing agents: Canadian Immunization Guide [Internet]. Ottawa ON: Public Health Agency of Canada; 2015 [updated 2017 Mar; cited 2021 Jan 27]. Available from: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-1-key-immunization-information/page-9-storage-handling-immunizing-agents.html
19. Ramsay M, editor. Immunisation against infectious disease (the green book): Chapter 3 - Storage, distribution and disposal of vaccines [Internet]. London: Public Health England; 2006 [updated 2013 Jun; cited 2021 Jan 27]. Available from https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/223753/Green_Book_Chapter_3_v3_0W.pdf
20. Hanson CM, George AM, Sawadogo A, Schreiber B. Is freezing in the vaccine cold chain an ongoing issue? A literature review. Vaccine. 2017 Apr 19;35(17):2127-33. https://doi.org/10.1016/j.vaccine.2016.09.070
21. Lloyd J, Cheyne J. The origins of the vaccine cold chain and a glimpse of the future. Vaccine. 2017 Apr 19;35(17):2115-20. https://doi.org/10.1016/j.vaccine.2016.11.097
22. World Health Organisation. TRS 1025 - Annex 7: Good storage and distribution practices for medical products [Internet]. Geneva: World Health Organisation; 2020 Apr 20 [cited 2021 Jan 27]. Available from: https://www.who.int/publications/m/item/trs-1025-annex-7-gdp-medical-products
23. United States Pharmacopeia and National Formulary (USP 43-NF 38). Chapter ‹659› Packaging and Storage Requirements [Internet]. Rockville MD: United States Pharmacopeia; 2017 [updated 2020 Dec; cited 2021 Feb 19]. Available from: https://www.uspnf.com/
24. Allegra JR, Brennan J, Lanier V, Lavery R, MacKenzie B. Storage Temperatures of Out of Hospital Medications. Acad Emerg Med. 1999 Nov;6(11):1098-103. https://doi.org/10.1111/j.1553-2712.1999.tb00110.x.