

# Evidence of Vaccine Freezing in the Cold Chain

## Literature Review

### Asia

**Hanjeet K, Lye MS, Sinniah M, Schnur A. Evaluation of cold chain monitoring in Kelantan, Malaysia. *Bull World Health Organ* 1996;74:391-7.**

An analysis of 234 Freeze Watches™ attached to hepatitis B vaccines vials during their transport and storage from the central store in Kuala Lumpur to Kelantan, a state in north-eastern Malaysia, showed significant levels of exposure to freezing temperatures. All but 2 of the 234 Freeze Watches™ had turned purple, which indicated exposure of 99% of the hepatitis B vaccines to temperatures below 0°C.

**Nelson CM, Wibisono H, Purwanto H, Mansyur I, Moniaga V, Widjaya A. Hepatitis B vaccine freezing in the Indonesian cold chain: evidence and solutions. 2002 [unpublished].**

To characterize the frequency of freezing temperatures occurring in the Indonesian vaccine cold chain and to evaluate the feasibility of procedural changes designed to reduce freezing. Freezing temperatures were recorded in 75% of baseline shipments. The highest levels of freezing occurred during transport from province to district (50%), storage in district ice-lined refrigerators (40%), and storage in health center refrigerators (30%).

**Spanner S. The cold chain in Madhya Pradesh. Danida consultancy report. February 2000.**

Twelve ice-lined refrigerators were monitored with data loggers from 1997 to 1999. 62% of the days monitored registered temperatures below -0.5°C; 5% of the days monitored registered less than -3°C; and 0.2% of the days showed temperatures above 10°C. Written temperature logs did not reflect the actual refrigerator temperatures.

### Australasia

**Miller NC and Harris MF. Are childhood immunization programmes in Australia at risk? Investigation of the cold chain in the Northern Territory. *Bull World Health Organ* 1994;72(3):401-8.**

This study in the Northern Territory of Australia evaluated whether vaccines were being exposed to unsafe temperatures. Oral poliomyelitis vaccine (OPV) and recombinant hepatitis-B (HB) vaccine were monitored as dispatched to the government, independent health services, and general practitioner surgeries which routinely administer these vaccines. MonitorMark time/temperature and Coldsides indicator tags were attached to cards for recording the date, location, and temperature exposures each time the vaccines were moved or used. Some 23% of tagged OPV was exposed for 48 hours or more to a temperature >10°C; 47.5% of tagged HB vaccines were exposed to -3°C or less, the majority of them during storage in health facilities or clinics. Exposures were independent of distance from the distribution center, mode of transport, or type of facility.

**Guthridge SL and Miller NC. Cold chain in a hot climate. *Aust N Z J Public Health* 1997;20:657-60.**

Temperatures of vaccine were monitored during transport and storage from a national warehouse to 5 Northern Territory vaccination clinics. The temperature recordings covered 8,369 hours. Cumulative hours of freezing totaled 422.5, cumulative hours above 10°C totaled 103.5. Authors conclude that in the hot climate of the Northern Territory freezing is the greatest threat to vaccine potency. Recommendations from the study include routine use of cold chain indicators, increased vaccine turnover, and storage of vaccines within an operational temperature range of 4°-8°C. Research is recommended to investigate the efficacy of heat-stable vaccines when stored at ambient temperatures and in air-conditioned environments.

**Gold MS, Martin L, Nayda CL, Kempe AE. Electronic temperature monitoring and feedback to correct adverse vaccine storage in general practice [comment]. *Med J Aust* 1999;171:83-4.**

This study evaluated the effect of direct feedback of temperature conditions followed by a telephone educational questionnaire to correct adverse vaccine storage and to determine the consistency of vaccine storage conditions at provider sites over six months. In metropolitan Adelaide 32 general practitioner vaccine providers were evaluated and vaccine refrigerator temperatures were monitored for 14 days using electronic temperature monitors, with repeat monitoring at two and six months. Of the 32 sites, 13 (41%) had suboptimal storage, 12 sites had more than 20% of storage time below 2°C, and 7 of the 32 sites had more than 5% of storage time below 0°C.

**Wawryk A, Mavromatis C, Gold M. Electronic monitoring of vaccine cold chain in a metropolitan area. *BMJ* 1997;315:518.**

Successful immunization strategies depend on the provision of immunogenic vaccines and the correct manufacture and storage of those vaccines. This study measured the temperature of vaccines stored long term in a metropolitan area of Adelaide, Australia, using electronic data loggers to determine how long vaccines had been exposed to temperatures <0°C. Forty sites were monitored for a median 1,983 hours. Vaccines were exposed to unacceptable cold in 21 sites, being exposed to temperatures <-1°C for a median cumulative time of 39 hours. In 9 sites vaccines were exposed to temperatures <-4°C for a median of 15 hours. In 4 sites vaccines were exposed to unacceptable heat (>8°C) for a median time of 341 (317-529) hours. In 3 sites the temperature exceeded 22°C for a median 0.4 (0.4-0.8) hours.

**Jeremijenko A, Kelly H, Sibthorpe B, Attewell R. Improving vaccine storage in general practice refrigerators. *BMJ* 1996;312:1651-2.**

This paper evaluated the impact of educating a responsible staff member about correct vaccine storage conditions in western Australia. A significant improvement was noted in vaccine storage conditions. Also noted in this paper is that of the 30 unacceptable refrigerator recordings (outside 2°-8°C), 26 of these recorded more than 1 hour below 0.5°C.

**Hazelton K, Balcomb A, Bowd K, Hazelton-Parsons D, Liddle J. The immunisation cold chain. Why is it so hard to get right? *Aust Fam Physician* 2002 31(10):939-42.**

This study demonstrated that a designated person for vaccine storage is an important factor in safe vaccine storage. Installation of commercial thermostats in commonly used domestic refrigerators was found to successfully improve vaccine storage temperatures. An administered mail-out program of temperature data loggers to document the vaccine storage conditions was also evaluated. Authors concluded that current cold chain measures give little confidence that the potency of vaccines can be ensured at all storage sites all the time, and that providers should be concerned about the effectiveness of vaccines. This paper mentioned that the storage of vaccines at less than 0°C cannot be reliably identified by physical freezing of the vaccine, and that it is not necessary for a freeze-sensitive vaccine to achieve an icy state to compromise its potency [unpublished research].

**Beauchamp J and Mansoor O. Temperature and the storage of vaccines. *New Zealand Medical Journal* 1992;April 8:135.**

This letter documents an evaluation of 23 general practices in Wellington, New Zealand, where approximately 50% of all morning readings were outside the 2°-8°C range, many below this range, and the lowest registered temperature being -5°C.

## **Central Asia**

**Bass AG and Battersby A. Vaccine storage in cold climates: Europe to Central Asia [background paper]. March 16-20, 1998; Copenhagen, TechNet 1998.**

A survey of multiple WHO reports documenting extensive freezing in cold climate cold chains. Exemplified by winter freezing of vaccines being a likely cause of the diphtheria epidemic (1998) in the Newly Independent States of the former Soviet Union, authors suggest efforts should be made to improve and protect vaccine during storage and transport. Among the reports cited is a cold chain study in Romania in 1990-91, in which 40% of the freeze monitors had been exposed to freezing. Also cited by authors is a WHO study in Bulgaria in 1990, in which during the winter, 37.6% of 166 Freeze Watch™ burst, indicating sustained temperatures below -4°C occurred. Furthermore, 51% of the Freeze Watch™ indicators burst during transport between the national store and the county store in one of the monitored Bulgarian counties. Authors also cite studies demonstrating the contribution of vaccine transport to the freezing of vaccines in European cold chains conducted in the early 1990s.

**Bass AG. The warm chain: a critical problem for national immunization programs in temperate and colder climates. BASICS, February 1996; Manila, Philippines; TechNet. A Basic Support for Institutionalizing Child Survival Project (BASICS) assignment report.**

This paper addresses the problem of toxoid vaccine freezing as substantiated by a diphtheria outbreaks in vaccinated populations in the former Soviet Union and presents the warm chain system as a possible solution. While the damage to toxoid vaccines caused by freezing events has been well known, little has been done to systematically prevent vaccine freezing in cold climates vaccine storage. Mr. Bass suggests that the management of vaccines in immunization programs has largely focused on preventing heat damage rather than detecting

vaccine freezing. However, winter freezing of vaccines has been identified as a serious operational problem contributing to the diphtheria epidemic in the Newly Independent States of the former Soviet Union. A 1992 WHO report is referenced which found that in Romania, 40% of Freeze Watch™ indicators evaluated were triggered during storage and transport.

**Spanner S and Ickx P. Introduction of time temperature monitors in Kazakstan. BASICS June 1997.**

During electronic monitoring of vaccine storage in Moldova and Kazakstan in 1996, 15 of 21 refrigerators monitored had periods of vaccine storage temperatures colder than 0°C. Most of the freezing events occurred after the ambient temperature fell to below +5°C.

## **Eastern Europe**

**Mercer, D. Ukraine Cold Chain Study 2003 (unpublished report) Program for Appropriate Technology in Health (PATH).**

The Ministry of Health of Ukraine and PATH conducted this study of temperatures in vaccine refrigerators in 2001-2002. 100 immunization facilities in each of two districts were equipped with Freeze Watch™ indicators to assess exposure of vaccines to freezing temperatures. Freezing temperatures were detected in 25% of monitored facilities, equally at central and peripheral facilities. Of the facilities monitored, 5% showed moderate heat exposure, none of it considered damaging. Some concern was noted from the discordant Freeze Watch™ and temperature readings.

**Lugosi L and Battersby A. Transport and storage of vaccines in Hungary: the first cold chain monitor study in Europe. *Bull World Health Organ* 1990;68:431-9.**

With assistance from WHO, the Hungarian Ministry of Health organized two cold chain studies in 1987-88. The first study looked at vaccine transport and storage in the summer months, the second in the winter months. The vaccines (DPT, measles, and BCG), with attached cold chain monitors, were transported from the manufacturers to the child health centers using the normal distribution systems in the country. Evaluation of the results showed significant deviations from acceptable standards. Vaccine transported during summer months was compromised, with 4% of vaccine exposed to excessive heat or cold. During winter months, 38% of vaccine was exposed to below freezing temperatures.

**Battersby A and Turkay F. Storage and transport of vaccines: results and analysis. 1990 WHO/EURO ICP/EPI 010.**

A study in Turkey in 1990 reports freezing in transport and at clinics in which 11.4% of Freeze Watch™ indicators burst.

## **United Kingdom/ United States**

### **Thakker Y, Woods S. Storage of vaccines in the community: weak link in the cold chain?. *BMJ* 1992;304:756-8.**

A survey of general practices and child health clinics in Britain, supported by electronic monitoring of storage temperatures of selected refrigerators, demonstrated weaknesses in the vaccine cold chain. Of the 40 survey respondents, only 16 were aware of the appropriate storage conditions for the vaccines; 8 had minimum and maximum thermometers, but only 1 of these was monitored daily. In 6 of the 8 practices monitored, vaccines were exposed to either subzero temperatures (three refrigerators) or temperatures up to 16°C (three).

### **Woodyard E, Woodyard L. and Alto WA. Vaccine storage in the physician's office: a community study. *J Am Board Fam Pract* 1995;8(2):91-4.**

A survey was conducted of 26 physician offices and the Colorado County Health Department to determine the quality of vaccine storage. A maximum-minimum thermometer was placed in the middle of the storage area for 24 hours, and temperatures were recorded. Of the 27 sites, only two had refrigerator temperatures in which both maximum and minimum temperatures fell within the acceptable range of 2°-8° C. Sixty-three percent fell below minimum, 59% were above maximum, and 93% fell either below or above or both. In the conclusion, authors suggest that a majority of vaccines in the community have been exposed to conditions that could reduce or destroy their potency.

### **Bell KN, Hogue CJ, Manning C, Kendal AP. Risk factors for improper vaccine storage and handling in private provider offices. *Pediatrics* 2001 Jun;107(6):E100**

This article summarizes a population-based survey, including site visits to a random sample of private physicians' offices in Georgia. Each site visit included measurements of refrigerator and freezer temperatures with digital thermometers. While 4.5% of offices visited had refrigerators too warm (9°C or warmer), 14.9% were too cold (1°C or lower).

### **Gazmararian, J.A., et al. Vaccine Storage Practices in Primary Care Physicians Offices. *American Journal of Preventative Medicine*, (2002);23(4)246-253.**

To assess the compliance of primary care physician offices with U.S. Centers for Disease Control and Prevention vaccine storage guidelines, 721 primary physician offices were visited in four cities in the United States baseline data demonstrated that greater than 80% of these offices followed most vaccine storage guidelines. Of the vaccine refrigerators monitored, 83% of temperatures were in the 2-8°C range. Of the out-of-range refrigerators, 89% were too cold (<2°C) and 70% were below freezing. Authors suggest distributing a "tip sheet" with suggestions that offices could follow if temperatures are out of range (e.g. adjust internal controls, check and clean refrigerator coils, use a min-max thermometer to better understand temperature fluctuations).

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