

## Resources for Storing and Delivering Insulin During a Disaster

During a disaster people with diabetes, clinics and hospitals may lose their insulin supplies, their cool storage systems for medicines (such as insulin), their insulin delivery systems (e.g., syringes, pens or insulin pumps), their glucose monitoring systems and tests strips and/or glucose sensors.

This may necessitate the use of insulin that has not been refrigerated as recommended. Experience and several studies show that the use of non-refrigerated insulin is safe during an emergency. Insulin storage options are considered.

People may need to use an alternate insulin than their usual medication, hence insulin swapping information can be helpful.

The reuse (by individuals only) of their own 'single-use' syringes, pen needles and lancets in an emergency is a reasonable option. Safe sharps waste disposal is also important.

Donated glucose-meters during a disaster may be in alternate glucose units, hence conversion charts (mg/dl to mmol/l) can be helpful. Charts to estimate HbA1c levels from continuous glucose monitoring time-in-range (TIR) are also available.

This section provides relevant information, including references and information sheets from diabetes organisations.

## Insulin use during disasters

### *Insulin cool storage*

Common clinical recommendations for insulin-using patients are to store their not-in-use insulin vials in a refrigerator, and that they can keep their insulin vial in use at room temperature (and usually less than 30 degrees C) for up to 28 days, a time during which most people would finish the vial. Injecting cold insulin is more uncomfortable than that of room-temperature insulin. **Insulin should never be frozen, as once thawed it will be inactive.** Insulin that has been stored at room temperature or in hot environments or is out-of-date does not usually become toxic and very gradually loses potency.

It is recognised that many people with diabetes in disadvantaged regions or during disasters do not have access to a refrigerator. Many traditional cool storage methods, which usually rely on evaporative cooling, such as non-glazed clay pots and wet animal skins, are effective at keeping insulin cooler than ambient temperature and to a similar level as commercially available chemical-based reusable cool-packs (e.g., FRIO pack, [www.frioaustralia.com](http://www.frioaustralia.com)). Other similar products can be found on-line.

An excellent research study evaluating the efficiency of traditional storage methods for insulin is:

Ogle GD, Abdullah M, Mason D, Januszewski AS, Besançon S. Insulin storage in hot climates without refrigeration: temperature reduction efficacy of clay pots and other techniques. *Diabetic Medicine* 2016;33(11):1544–1553. doi: 10.1111/dme.13194.

The related abstract follows.

**Insulin storage in hot climates without refrigeration: temperature reduction efficacy of clay pots and other techniques.**

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**AIM:** Insulin loses potency when stored at high temperatures. Various clay pots part-filled with water, and other evaporative cooling devices, are used in less-resourced countries when home refrigeration is unavailable. This study examined the cooling efficacy of such devices.

**METHODS:** Thirteen devices used in Sudan, Ethiopia, Tanzania, Mali, India, Pakistan and Haiti (10 clay pots, a goat skin, a vegetable gourd and a bucket filled with wet sand), and two identical commercially manufactured cooling wallets were compared. Devices were maintained according to local instructions. Internal and ambient temperature and ambient humidity were measured by electronic loggers every 5 min in Khartoum (88 h), and, for the two Malian pots, in Bamako (84 h). Cooling efficacy was assessed by average absolute temperature difference (internal vs. ambient), and % maximal possible evaporative cooling (allowing for humidity).

**RESULTS:** During the study period, mean ambient temperature and humidity were 31.0°C and 32.0% in Khartoum and 32.9°C and 39.8% in Bamako. All devices reduced the temperature ( $P < 0.001$ ) with a mean (SD) reduction from  $2.7 \pm 0.5^\circ\text{C}$  to  $8.3 \pm 1.0^\circ\text{C}$ , depending on the device. When expressed as % maximal cooling, device efficacy ranged from 20.5% to 71.3%. On cluster analysis, the most efficacious devices were the goat skin, two (non-glazed) clay pots (from Ethiopia and Sudan) and the suspended cooling wallet.

**CONCLUSIONS:** Low-cost devices used in less-resourced countries reduce storage temperatures. With more efficacious devices, average temperatures at or close to standard room temperature (20–25°C) can be achieved, even in hot climates. All devices are more efficacious at lower humidity. Further studies are needed on insulin stability to determine when these devices are necessary.

During a disaster power may be lost, for days or more, and refrigerator storage may not be possible.

Options for storing insulin if traditional refrigeration is not available:

- Generator-powered refrigerator
- Battery or solar powered portable refrigerator
- Small USB powered refrigerator (often a 'gadget' to cool a can of soda, powered by a USB cord connected to a laptop or portable battery such as used to recharge a phone or laptop.
- FRIO™ pack (<https://www.frioinsulincoolingcase.com/>). Coming in a range of sizes, FRIO® insulin coolers can keep insulin and other temperature-sensitive medications cool (18–26°C (64.4–78.8°F) for at least 45 hours, even in environment temperatures of 37.8°C (100°F). These chemically activated reusable packs last five times longer than icepacks.
- Portable insulated box or lunch bag with ice bricks or cold (frozen gel) bricks or a bag of frozen vegetables (e.g., peas) from the freezer. The reusable gel bricks usually only remain cool for half to one day after removed from the fridge or freezer, and frozen vegetables would likely last even less time. Ensure insulin is not directly against the ice, brick, or frozen vegetables as it may freeze the insulin, rendering it inactive.
- Traditional cooling methods; e.g., clay pots (Ogle G et al. *Diabetic Medicine* 2016, on previous page)

***In an emergency do not discard or not use insulin that has not been refrigerated unless or until adequate supplies of replacement insulin is available.***

Experience and publications support the use of insulin that has been stored at higher than recommended temperatures during disasters (Grajower et al., *Diabetes Care* 2003;26(9):2665–2666; Kaufman et al., *PloS One* 2021;16(2):e0245372). Both these papers can be downloaded for free via PubMed.

**The USA DDRC advises healthcare professionals as follows re unrefrigerated insulin:**

Insulin storage notes:

- Insulin should be kept away from direct heat and sunlight. DO NOT use insulin that has been frozen.
- Unopened insulin vials and pens should be stored in a refrigerator at 36° F to 46°F and are good until expiration date on the vial or pen.
- Opened vials and pens may be left unrefrigerated at 59°F to 86°F for up to 28 days.
- Insulin loses potency when exposed to extreme temperatures which can result in loss of blood glucose control; however—under emergency conditions—insulin that has been stored above 86°F may be used if necessary. Once properly stored insulin becomes available, insulin that has been exposed to extreme conditions should be discarded.

Similarly, the USA DDRC advises If you lose power and you have unused insulin, don't throw it out! In an emergency, it is usually okay to use expired or non-refrigerated insulin.

Essential is essential for life, especially people with .

**A study by Doctors Without Borders and the University of Geneva shows good stability of insulin in tropical conditions.**

The abstract is on the next page, and some key data are on page after. The full paper can be downloaded from PubMed for free.



**UNIVERSITÉ  
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**MEDECINS SANS FRONTIERES  
ÄRZTE OHNE GRENZEN**

**Insulin can be  
stored out of  
refrigeration even  
in hot settings!**

A team from UNIGE and MSF has shown that a vial of insulin can be stored for 4 weeks after opening and at up to 37°C, without losing efficacy.

## **Heat-stability study of various insulin types in tropical temperature conditions: New insights towards improving diabetes care.**

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Strict storage recommendations for insulin are difficult to follow in hot tropical regions and even more challenging in conflict and humanitarian emergency settings, adding an extra burden to the management of people with diabetes. According to pharmacopeia unopened insulin vials must be stored in a refrigerator (2–8°C), while storage at ambient temperature (25–30°C) is usually permitted for the four-week usage period during treatment.

In the present work we address a critical question towards improving diabetes care in resource-poor settings, namely whether insulin is stable and retains biological activity in tropical temperatures during a four-week treatment period.

To answer this question, temperature fluctuations were measured in Dagahaley refugee camp (Northern Kenya) using log tag recorders. Oscillating temperatures between 25 and 37°C were observed. Insulin heat stability was assessed under these specific temperatures which were precisely reproduced in the laboratory. Different commercialized formulations of insulin were quantified weekly by high performance liquid chromatography and the results showed perfect conformity to pharmacopeia guidelines, thus confirming stability over the assessment period (four weeks). Monitoring the 3D-structure of the tested insulin by circular dichroism confirmed that insulin monomer conformation did not undergo significant modifications. The measure of insulin efficiency on insulin receptor (IR) and Akt phosphorylation in hepatic cells indicated that insulin bioactivity of the samples stored at oscillating temperature during the usage period is identical to that of the samples maintained at 2–8°C.

Taken together, these results indicate that insulin can be stored at such oscillating ambient temperatures for the usual four-week period of use. This enables the barrier of cold storage during use to be removed, thereby opening up the perspective for easier management of diabetes in humanitarian contexts and resource poor settings.

Data from the manuscript, reproduced with permission:

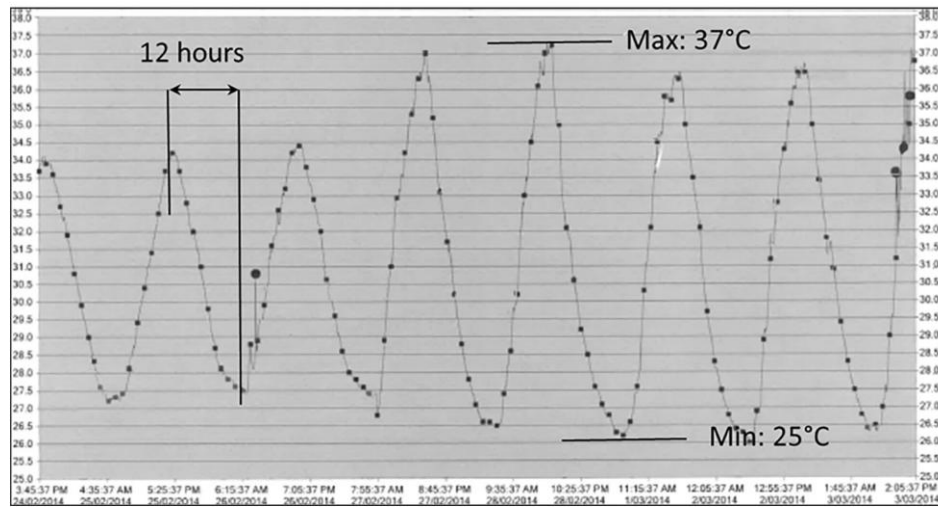


Fig 1. Field ambient temperature measurement over a period of seven days at a patient's home using log tag monitoring (data provided by MSF).

<https://doi.org/10.1371/journal.pone.0245372.g001>

Table 1. Recoveries of insulin at T = 4 and 12 weeks of temperature cycling, expressed as percentages of values measured at T = 0.

Insulin type	T 4 week Recovery [% of T0 value]	T 12 week Recovery [% of T0 value]
Lispro analog	101.7 +/- 5.3	99.4 +/- 0.7
Mixed lispro analog	103.3 +/- 2.5	102.7 +/- 6.1
Glargine analog	98.4 +/- 2.4	99.8 +/- 1.0
Aspart analog	99.7 +/- 1.6	100.2 +/- 0.9
<b>NPH isophane</b>	<b>101.3 +/- 1.3</b>	<b>101.6 +/- 8.9</b>
<b>Rapid</b>	<b>100.1 +/- 0.5</b>	<b>101.3 +/- 2.3</b>
<b>Mixed</b>	<b>100.6 +/- 1.6</b>	<b>101.9 +/- 3.5</b>

(in bold characters: the three human insulins used on the field).

<https://doi.org/10.1371/journal.pone.0245372.t001>

# Thermal stability and storage of human insulin Cochrane Systematic Review

- **Bernd Richter Brenda Bongaerts Maria-Inti Metzendorf** published: 06 November 2023 free at <https://doi.org/10.1002/14651858.CD015385.pub2>

## Abstract

**Background** Health authorities stress the temperature sensitivity of human insulin, advising protection from heat and freezing, with manufacturers suggesting low-temperature storage for intact vials, and once opened, storage at room temperature for four to six weeks, though usage time and maximum temperature recommendations vary. For human insulin, the recommendations of current shelf life in use may range from 10 to 45 days, and the maximum temperature in use varies between 25 °C and 37 °C. Optimal cold-chain management of human insulin from manufacturing until the point of delivery to people with diabetes should always be maintained, and people with diabetes and access to reliable refrigeration should follow manufacturers' recommendations. However, a growing segment of the diabetes-affected global population resides in challenging environments, confronting prolonged exposure to extreme heat due to the climate crisis, all while grappling with limited access to refrigeration.

**Objectives** To analyse the effects of storing human insulin above or below the manufacturers' recommended insulin temperature storage range or advised usage time, or both, after dispensing human insulin to people with diabetes.

**Search methods** We used standard, extensive Cochrane search methods. The latest search date was 12 July 2023.

**Selection criteria** We included clinical and laboratory studies investigating the storage of human insulin above or below manufacturers' recommended temperature storage range, advised usage time, or both.

**Data collection and analysis** We used standard Cochrane methods. We used GRADE to assess the certainty of evidence for the clinical study. Most information emerged from in vitro studies, mainly from pharmaceutical companies. There is no validated risk of bias and certainty of evidence rating for in vitro studies. We thus presented a narrative summary of the results.

**Main results** We included 17 eligible studies (22 articles) and additional information from pharmaceutical companies.

### Pilot clinical study

One pilot clinical study investigated temperature conditions for insulin stored for six weeks in an unglazed clay pot with temperatures ranging between 25 °C and 27 °C. The mean fall in plasma glucose in eight healthy volunteers after clay pot-stored insulin injection was comparable to refrigerator-stored insulin injection (very low-certainty evidence).

### In-vitro studies

Nine, three and four laboratory studies investigated storage conditions for insulin vials, insulin cartridges/pens and prefilled plastic syringes, respectively. The included studies reported numerous methods, laboratory measurements and storage conditions.

Three studies on prefilled syringes investigating insulin potency at 4 °C up to 23 °C for up to 28 days showed no clinically relevant loss of insulin activity.

Nine studies examined unopened vials and cartridges. In studies with no clinically relevant loss of insulin activity for human short-acting insulin (SAI), intermediate-acting insulin (IAI) and mixed insulin (MI) temperatures ranged between 28.9 °C and 37 °C for up to four months. Two studies reported up to 18% loss of insulin activity after one week to 28 days at 37 °C. Four studies examined opened vials and cartridges at up to 37 °C for up to 12 weeks, indicating no clinically relevant reduction in insulin activity. Two studies analysed storage conditions for oscillating temperatures ranging between 25 °C and 37 °C for up to 12 weeks and observed no loss of insulin activity for SAI, IAI and MI. Four studies, two on vials (including one on opened vials), and two on prefilled syringes, investigated sterility and reported no microbial contamination.

### **Data from pharmaceutical companies**

Four manufacturers (BIOTON, Eli Lilly and Company, Novo Nordisk and Sanofi) provided previously unreleased human insulin thermostability data mostly referring to unopened containers (vials, cartridges). We could not include the data from Sanofi because the company announced the permanent discontinuation of the production of human insulins Insuman Rapid, Basal and Comb 25.

BIOTON provided data on SAI after one, three and six months at 25 °C: all investigated parameters were within reference values, and, compared to baseline, loss of insulin activity was 1.1%, 1.0% and 1.7%, respectively.

Eli Lilly and Company provided summary data: at below 25 °C or 30 °C SAI/IAI/MI could be stored for up to 25 days or 12 days, respectively. Thereafter, patient in-use was possible for up to 28 days.

Novo Nordisk provided extensive data: compared to baseline, after three and six months at 25 °C, loss of SAI activity was 1.8% and 3.2% to 3.5%, respectively. Loss of IAI activity was 1.2% to 1.9% after three months and 2.0% to 2.3% after six months. Compared to baseline, after one, two and three months at 37 °C, loss of SAI activity was 2.2% to 2.8%, 5.7% and 8.3% to 8.6%, respectively. Loss IAI activity was 1.4% to 1.8%, 3.0% to 3.8% and 4.7% to 5.3%, respectively. There was no relevant increase in insulin degradation products observed. Up to six months at 25 °C and up to two months at 37 °C high molecular weight proteins were within specifications. Appearance, visible particles or macroscopy, particulate matter, zinc, pH, metacresol and phenol complied with specifications.

There were no data for cold environmental conditions and insulin pumps.

### **Authors' conclusions**

Under difficult living conditions, pharmaceutical companies' data indicate that it is possible to store unopened SAI and IAI vials and cartridges at up to 25 °C for a maximum of six months and at up to 37 °C for a maximum of two months without a clinically relevant loss of insulin potency. Also, oscillating temperatures between 25 °C and 37 °C for up to three months result in no loss of insulin activity for SAI, IAI and MI. In addition, ambient temperature can be lowered by use of simple cooling devices such as clay pots for insulin storage. Clinical studies

on opened and unopened insulin containers should be performed to measure insulin potency and stability after varying storage conditions. Furthermore, more data are needed on MI, insulin pumps, sterility and cold climate conditions.