



**International
Diabetes Federation**
Europe

STORAGE OF INSULIN

IDF EUROPE AWARENESS PAPER



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INTRODUCTION

Some 66 million people live with diabetes in Europe today. One third of them use insulin for lifelong treatment. Insulin is also on the list of WHO essential medicines.

Diabetes is a complex chronic condition with hundreds of variables in play that influence PWDs' glycemic control. It is crucial for PWDs to be able to rule out as many variables as possible which could affect glycemic control. This must include ruling out the possibility that insulin quality and potency are less than optimal (1).

Being able to trust that insulin will work consistently is a key prerequisite to successful treatment, achieving balance for people with diabetes (PWDs) and reaching optimal therapeutic outcomes.

In the light of recent scientific findings, the International Diabetes Federation European Region (IDF Europe) has issued this paper to raise awareness on the topic of safe storage of insulin and to provide recommendations to healthcare professionals (HCPs) and PWDs, as well as IDF Member Associations. As more evidence is emerging on the challenges of storing insulin at home by PWDs, IDF Europe recognizes the need for raising awareness about these overlooked risks, and improving PWDs' education. These recommendations must be practical and go beyond the limited insulin package leaflets.

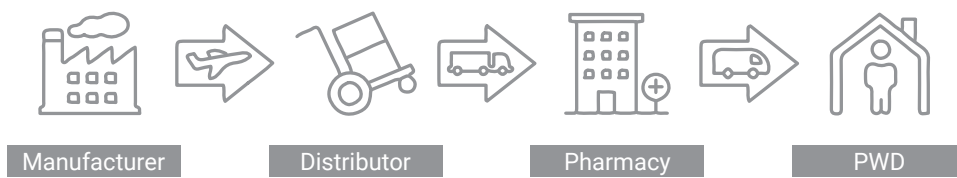
Proper storage improves treatment safety and reduces the stress and burden of living with diabetes. Mitigating the risk of insulin freezing at home will certainly help PWDs achieve the optimal therapeutic outcomes of the treatments that they are prescribed. Raising awareness among PWDs should be done in a positive and constructive manner.

A. Insulin requires strict cold chain standards

Insulin is categorised as a 'cold chain product' because it loses potency when exposed to heat and when frozen. The only way to guarantee its full effectiveness is to store and transport insulin products within a temperature range of 2-8°C as long as it is unopened.

According to Good Distribution Practice guidelines (2), storage conditions including temperature during storage and transit should be continuously monitored until the end of the cold supply chain to assure the quality of the drug.

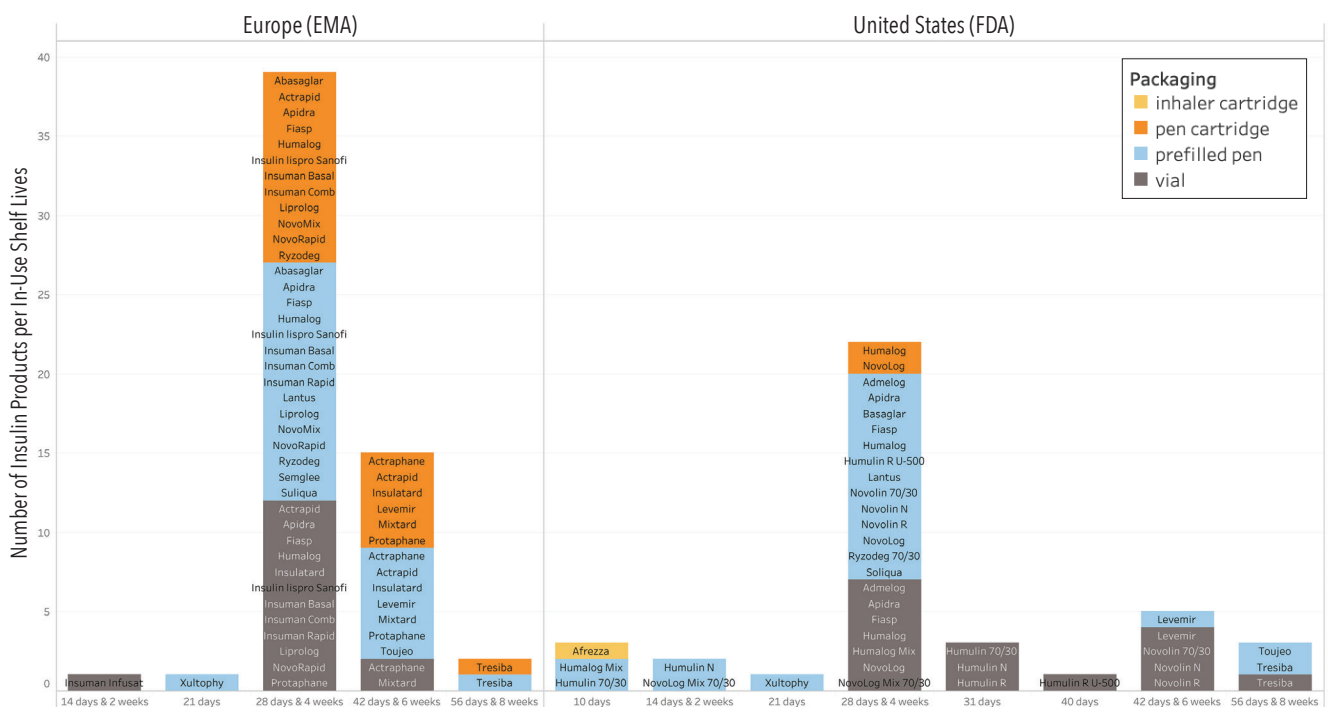
Therefore, the European Commission and WHO impose strict regulations and guidelines for the storage and transport of insulin (3). These apply to manufacturers, distributors, doctors and pharmacists. All parties are obliged to ensure transport and storage at 2-8°C, with temperature monitoring and qualified refrigerators and shipping systems.



Distribution of insulin from manufacturer to the PWDs (transport and storage between 2-8°C is maintained and monitored throughout the distribution chain of insulin, but there is little quality management at PWDs' homes.

Minor deviations from the temperature range are accounted for in the thermal stability budget and are likely harmless. Nevertheless, when they happen, these must be reported to pharmaceutical manufacturers so that they can assess if the products are still safe. Major temperature excursions can happen. This has the potential to affect the medications' effectiveness considerably and can have serious clinical implications. In this situation, when quality is compromised, then entire shipments and batches must be discarded.

The Food and Drug Administration (FDA) also recommend that after manufacture the insulin should ideally be stored in the refrigerator within a range of 2°C and 8°C for long-term storage until expiry date. Once taken out of the refrigerator, when opened or carried as a spare, it can be stored within 2°C and 25°C or 30°C, but should then be used within 3, 4, 6, 8 weeks, depending on the product.



B. Official guidelines on how to store insulin

The official instructions from pharmaceutical manufacturers can be found on medication packages and on the leaflets accompanying every medication. All cold chain products are required to be stored between 2-8°C to guarantee their effectiveness until their expiry date. There is an explicit warning about “not freezing” the medications and clear instructions to never use insulin that has been exposed to freezing temperatures.

Package leaflets of all insulin types and formulations state that insulin needs to be kept at 2-8°C when unopened, to keep best quality until expiry date.

However, there are no practical tips on how to properly store medications in household refrigerators. Furthermore, today there are no harmonized education materials for HCPs and PWDs on a European level on insulin storage beyond the official label.

C. Differences between professional cold chain and conditions at PWDs' homes

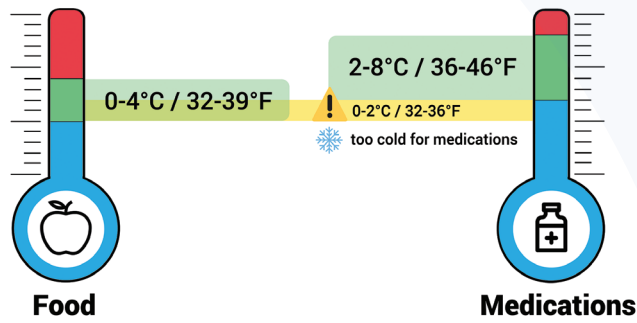
When medications are handed over to PWDs by pharmacists, so is the responsibility to store and transport them in a way that guarantees their quality. However, the average person does not have the same experience, knowledge or training that HCPs do, nor do they use medical grade equipment for storage. There is also no monitoring of storage conditions.

Certified diabetes educators, endocrinologists, nurses and pharmacists all educate PWDs with the same information as on the leaflets, with little to no extra resources. The table below shows the contrast between professional practices and standards after dispensing to PWDs.

	Professional Cold Chain	PWD
Awareness	High awareness due to training, strict guidelines and quality controls	Low awareness due to lack of harmonized education
Guidelines	Good Distribution Practice (GDP) Guidelines by the European Commission and WHO (4,5)	Package leaflet
Risk assessment	Clear protocols to follow including contacting the manufacturer	Discarding medication when in doubt
Refrigeration equipment	Medical-grade refrigerators Regularly serviced and checked	Household refrigerators Low maintenance
Temperature Monitoring	Required	Not required

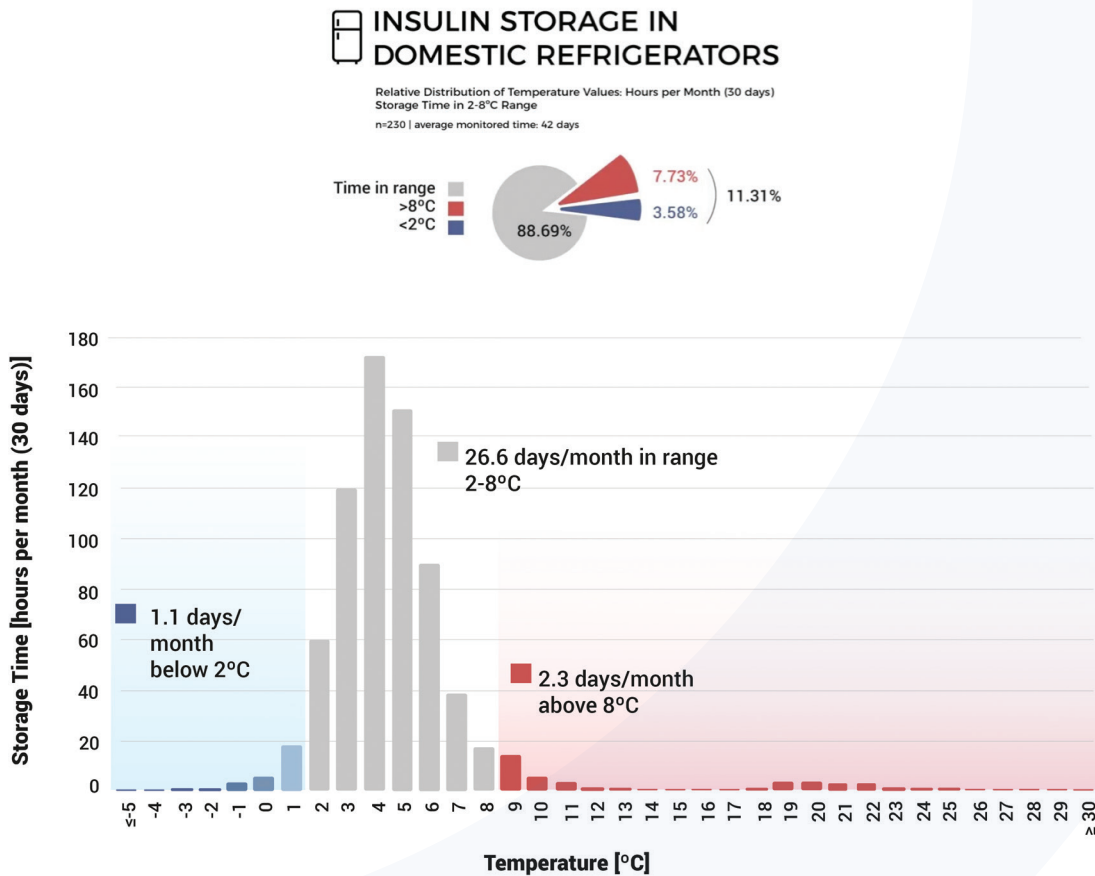
D. Risk of freezing insulin in household refrigerators

Household refrigerators are primarily designed for storing food and optimized for food safety (0-4°C [32-41°F]) with temperatures a few degrees below range for medication (2-8°C [36-46°F]). Temperatures have shown to often drop below freezing point. Unlike pharmaceutical refrigerators that have ventilators for air circulation, the air inside household refrigerators is not circulated, which leads to a temperature gradient and the creation of warm and cold zones within the same refrigerator. Many modern refrigerators can adjust their target temperature. However this regulation is not precise and relies on one measurement only. Compressor cycles introduce fluctuations of high amplitudes. Even if the average temperature is within 2-8°C [36-46°F], there may be great deviations outside of this range (8-10).



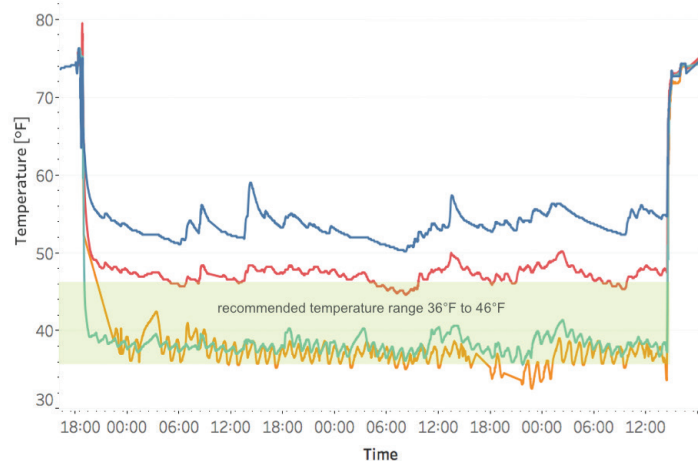
While storage conditions during the professional cold chain are well researched, little is known about how PWDs store their insulin at home.

In a first study investigating storage conditions of insulin after dispensing, the temperature in 230 refrigerators of PWDs in the USA and in Europe were monitored over the course of several months (4).



Surprisingly, insulin was stored outside the recommended 2-8°C range very often. In one of four refrigerators, insulin temperature fell below freezing point. On average, insulin was kept at temperatures that are too cold for one day per month.

This is in line with previous studies that have shown that temperature inside household refrigerators fluctuates over time and that different compartments in the same fridge can differ greatly.



Temperature progression in four different compartments of a household refrigerator over two days (thermostat setting: 8°C)

Frozen insulin does not have full potency which results in suboptimal glycemic control. This is especially the case for young PWDs who are more sensitive to variability in insulin potency and for insulin pump users. There are documented cases of hospital admissions with diabetic ketoacidosis (DKA) caused by using insulin that had been frozen accidentally (8). Better storage by PWDs at home can help to avoid such episodes.

E - Recommendations from IDF Europe

1) People with diabetes (PWDs)

General recommendations on how to store insulin (vials and cartridges) (6,7)

- Read carefully the insulin's package leaflet since it might include specific information for that specific product.
- Vials and cartridges of insulin not currently being used should be stored in the refrigerator (2-8 °C) until their expiry date.

Do not use insulin

- If the expiry date on the vial or cartridge or prefilled pen has been reached.
- If the clear soluble insulin has turned cloudy.
- If the insulin is discoloured.
- If the insulin has been frozen or exposed to high temperatures.
- If the insulin contains lumps or flakes or sticks to the glass.

When storing insulin in the refrigerator at home, there is a risk of exposing it to freezing temperatures which can make it less effective.

Be aware:

- Temperature fluctuates over time in a refrigerator. The thermostat might have to be adjusted periodically.
- Temperatures differ a lot between compartments in the same refrigerator.
- Hotel mini-fridges and dorm-style refrigerators tend to freeze more often than bigger household refrigerators.

A few simple measures can effectively reduce the risk of freezing:

- Using an airtight container to store medications inside household refrigerators to reduce temperature fluctuations.
- Keeping a thermometer to measure (and ideally log) temperature directly next to the medications.
- When using cool bags with ice or ice packs to transport insulin, making sure pens and vials are not in direct contact with the ice packs.

2) Healthcare professionals (HCPs) (6,7,11,12)

Education and Information:

- When prescribing insulin, doctors should ensure that PWDs are aware of the importance of right storage conditions.
- When delivering insulin, pharmacists should provide information to PWDs on the importance of correct storage conditions.
- HCPs should help PWDs in overcoming potential stress resulting from dealing with this risk, and support them with practical advice on how to mitigate it.
- HCPs should inform PWDs of good practices beyond the official label. This includes not only protection from heat when transporting insulin, but also protection from freezing in refrigerators at home.

Clinical practice:

- Take into account that storage temperatures can be a factor in blood glucose management.
- When patients report they believe that their insulin is not working well, a potential cause could be exposure to hot or cold temperatures.

3) IDF Europe Member Associations

- National Associations should support the dissemination of this information document throughout their country.
- National Associations should support the training of all relevant HCPs, including nurses, pharmacists, and educators.
- National Associations should support diabetes education including information about storage of insulin among PWD.
- National Associations should contribute to a coordinated approach among national health services, HCPs (doctors, nurses, pharmacists, educators) and PWDs to ensure safe insulin storage at all times and guarantee effective insulin action for optimal diabetes treatment.

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