

**ELPRO**



CASE STUDY

Secure  
Preservation,  
Storage,  
and Transport  
at down to  $-80^{\circ}\text{C}$

**we prove it.**

**SWISS QUALITY**



## Production authorization for blood products, stem cells, and CAR-T cells: Greifswald University Hospital relies on ELPRO for equipment and process qualification.

In this case study, you will learn how Greifswald University Hospital used a GMP-compliant, sustainable temperature monitoring solution:

- > to create a uniform hardware and software solution for two manufacturing sites;
- > to allow for qualification of a new freezing machine for CAR-T cell therapy; and
- > to ensure future compliance through straightforward re-qualifications of all devices during the biennial audits by the authorities.

### Project partners

- > Greifswald University Medicine, with two pharmaceutical production sites for medicinal products
- > Stem Cell Production Cooperation Center producing stem cell preparations from peripheral blood and bone marrow
- > Transfusion Medicine Institute producing blood products from donor blood
- > CAR-T Cell Application Center, certified since 2022
- > A total of 21 clinics/policlinics, 19 institutes, 1,000 beds, 4,400 employees, 180,000 patients per year (36,000 inpatients)
- > For more information see [www.medicin.uni-greifswald.de](http://www.medicin.uni-greifswald.de)



Cover page image: Nitrogen storage (stem cells)  
Top: Blood bank entrance

“The process for procuring new equipment is extremely laborious and time-consuming. This is why we were interested in a long-lasting solution.”

KONSTANZE AURICH, PHARMACIST SPECIALIZING  
IN DRUG INFORMATION, GREIFSWALD UNIVERSITY MEDICINE



### General conditions

Greifswald University Medicine comprises two pharmaceutical manufacturing facilities for medicinal products, blood products, and stem cell preparations as well as a CAR-T Cell Application Center that has been certified since 2022.

### Qualified equipment, validated processes

The blood products have to be frozen at  $-30\text{ }^{\circ}\text{C}$ , and stem cells need to be cryopreserved at  $-80\text{ }^{\circ}\text{C}$ . This means that the equipment and processes related to the preservation, storage, and transport of the products must be qualified and safely validated.

### Requirements for production authorization and CAR-T cell therapy

In order to extend the existing production authorization for medicinal products and active substances in accordance with §13 of the German Medicines Act (AMG), Greifswald University Medicine must regularly demonstrate re-qualification of the equipment used at the sites in two-year intervals, as part of an audit by the authorities.

As a certified CAR-T Cell Application Center, the hospital must also provide evidence of qualified automated machines for controlled freezing of the cells.

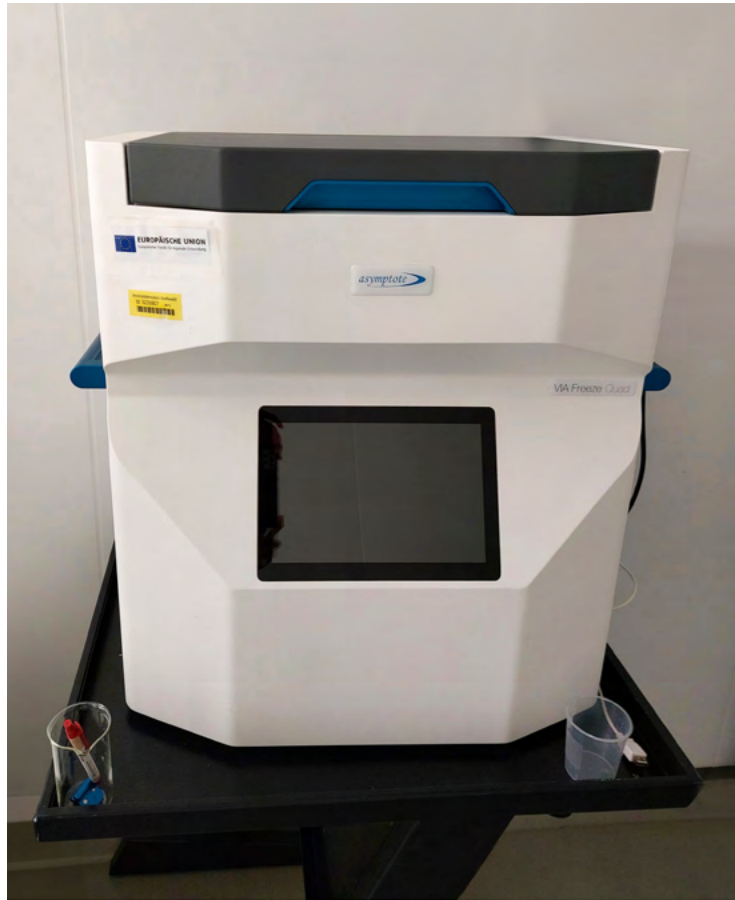
### Challenges

In 2022, the two pharmaceutical production facilities of Greifswald University Medicine – the Stem Cell Production Cooperation Center and the Transfusion Medicine Institute – did not have a uniform temperature monitoring system in place. They relied on different software solutions and data loggers, some of which were becoming outdated.

### Special bags for plasma and cell therapy, new automatic freezer for CAR-T cells

The Transfusion Medicine Institute needed data loggers with external sensors that could be placed in the bags to monitor the freezing process of the blood products. Previously, equipment from the Stem Cell Center had been borrowed for this purpose. For qualification of the plasma and cell therapy freezers, special bags with very small openings had to be used. These bags could not accommodate the existing external probes.

In addition, a new freezing machine had to be purchased and qualified for the controlled freezing of CAR-T cells.



**Targets**

Greifswald University Medicine sought a unified monitoring solution for both areas. This solution needed to ensure the reliable issuance of production authorization through simple device re-qualification during biennial authority audits. Additionally, it had to support the qualification of a new automatic freezing machine for CAR-T cells.

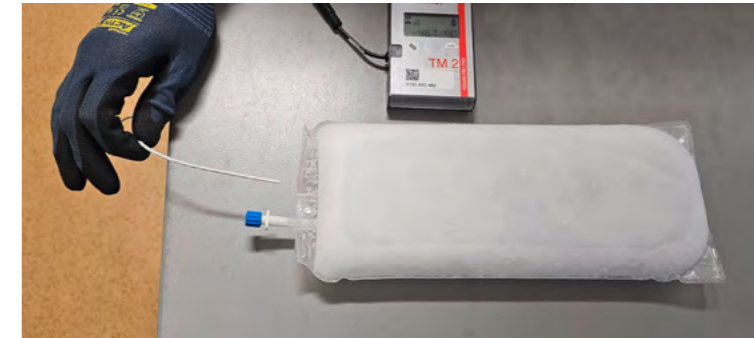
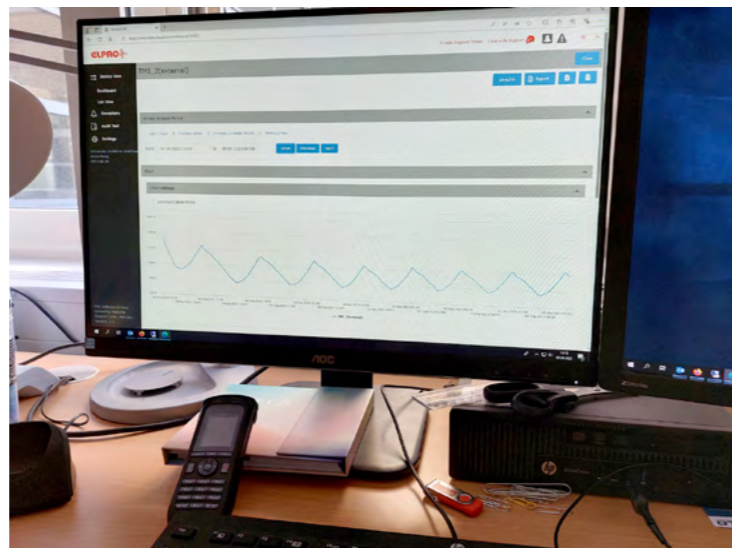
**Requirements**

For acquisition of a uniform solution, Greifswald University Medicine defined the following hardware and software requirements:

- > Data loggers must be capable of recording temperatures down to  $-80^{\circ}\text{C}$ .
- > Data loggers must be fitted with external sensors that can be inserted into special bags with a very narrow opening.
- > Multiple users must be able to gain easy access to the software solution.
- > The solution must be long lasting, sustainable and comprised of multi-use devices.



Top: Freezing machine for stem cells  
 Bottom: Blood plasma during the freezing process  
 Right: Workstation with elproCLOUD screen



Top: Frozen blood plasma after the freezing process  
 Left: Blood plasma before the freezing process

**Fit for purpose**

In the course of an extensive search, Greifswald University Medicine contacted ELPRO, as it was already using some older ELPRO data loggers. After intensive discussions, ELPRO proposed the application of the latest data logger generation in combination with a real-time cloud solution for both centers.

The wireless ECOLOG-PRO xG real-time data loggers are FDA 21 CFR Part 11 compliant and calibrated. This IT-independent solution is easy to install, utilizes public infrastructure for data transmission, and the data logger batteries are replaceable. In addition, the data loggers can be equipped with external sensors that fit the special bags. The elproCLOUD real-time software solution, developed according to GAMP® 5, is also compliant with FDA 21 CFR Part 11 and can be configured and used independently by the client. It is also accessible to a large number of users.

**Approach**

Throughout the project, the ELPRO sales representative provided close support and was always available for any queries. In the consulting and planning phase and during the installation of the solution, he took time to personally guide individuals based on their specific prior knowledge and needs.

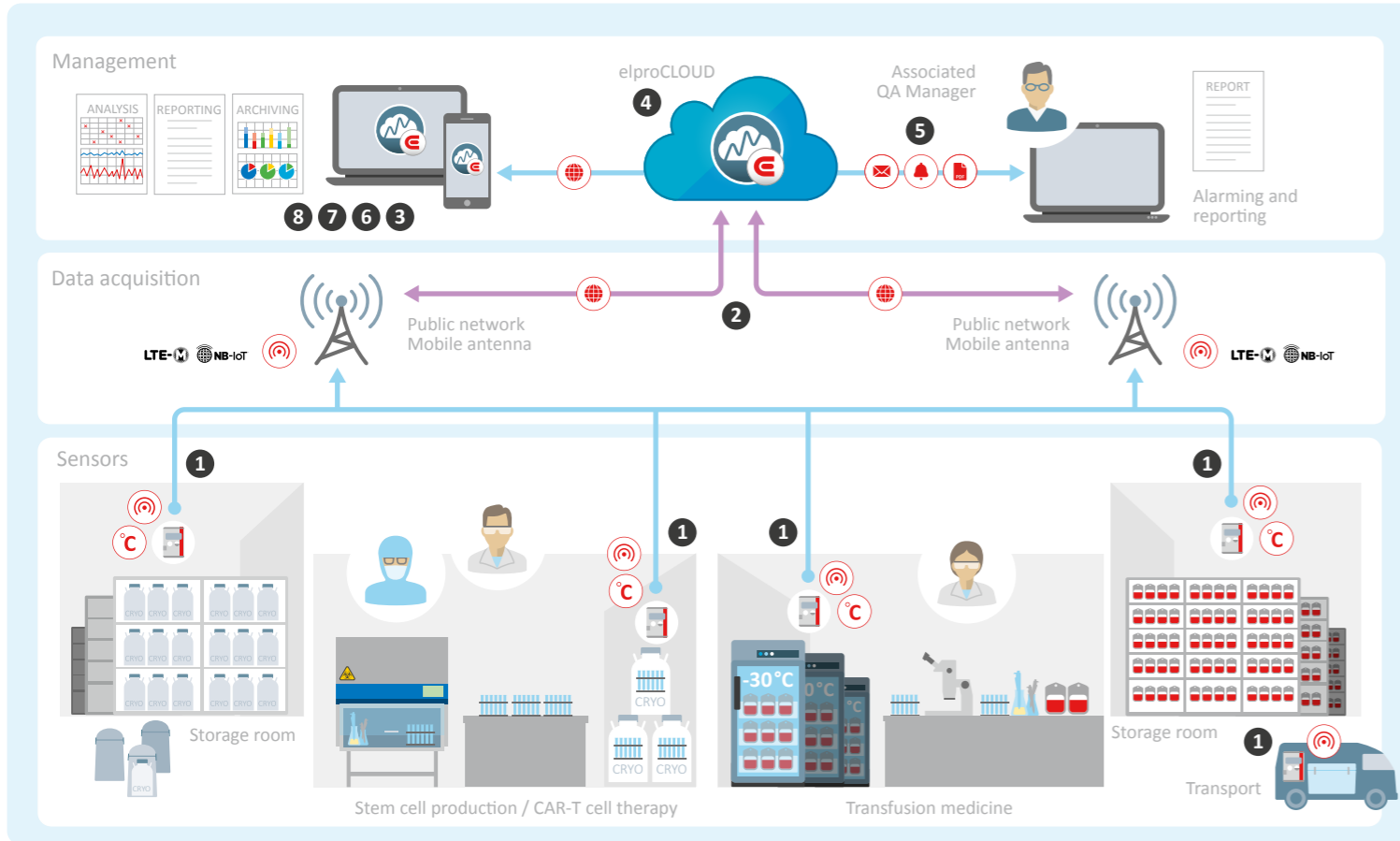
“Henry Wolf from ELPRO is the only one who, through a lot of effort, has managed to find a probe that fits precisely into the very narrow opening of the bags that we have to use for qualifying the plasma and cell therapy freezers.”

KONSTANZE AURICH

**Solution**

The elproCLOUD software solution and the ECOLOG-PRO xG real-time data loggers give Greifswald University Medicine an expandable, flexible and sustainable entry-level solution for

GMP-compliant real-time monitoring of their equipment and rooms as well as during transport.



- 1 Battery-powered ECOLOG-PRO 1TGe data loggers with internal and external sensors record temperature data during the freezing process, during storage of blood products and during stem cell preparations. They also protect assets during transport to and from the CAR-T Cell Application Center.
- 2 The data loggers use IoT technology to transmit the temperature data to elproCLOUD in real time via the public infrastructure (NB-IoT / LTE-M).
- 3 elproCLOUD can be accessed throughout the world and around the clock via web browser.
- 4 elproCLOUD monitors and archives the temperature data securely and compliantly.
- 5 Any deviations are immediately reported by e-mail or SMS via defined alarm conditions (Issue Profiles).

- 6 The dashboard provides a clear overview of all sensors incorporated in the system.
- 7 All user actions (e.g. changes and deletions) are traceably controlled and recorded for quality assurance purposes using an audit trail.
- 8 Different users with different access rights can be created via the user management.

“Henry Wolf took the time to train and educate all colleagues on the new system with a lot of patience and perseverance, always aligned with the knowledge level of the individual.”

KONSTANZE AURICH

“The ability to monitor two temperature ranges with the internal and external sensor is especially handy in some situations, such as during transport of stem cells.”

KONSTANZE AURICH



**Outcome**

Konstanze Aurich leads the project at Greifswald University Medicine and is satisfied with the results that have been achieved.

**Successfully amended production authorization for CAR-T cell therapy**

For the new freezing device required for CAR-T cell therapy, the existing production authorization had to be amended to suit the new process. Due to the new data loggers, the qualification required for this purpose was successful. Upon the commissioning of the device, the Greifswald University Medicine can now offer a new therapy in the course of which drugs worth 350,000 euros per preparation are produced.

**Real-time monitoring during transport**

Although real-time monitoring was not one of the Greifswald University Medicine’s explicit requirements, it is now being applied during the transport of stem cells from external areas. This allows both the internal bag temperature and the ambient temperature to be monitored. Consequently, the University Hospital gains real-time information about the temperature profiles inside the transport vehicle and tracks whether the air conditioning system can maintain the appropriate ambient temperature even on very hot days.

**Additional reliable source besides central room monitoring**

This applies to the two -30 °C rooms as well. In addition to the obvious central monitoring of the premises, another reliable source can now be used to monitor the ambient temperature in real time.

**CAR-T cell therapy**

Cancer immunotherapy, in which genetically modified T-cells, so-called CAR-T cells, with synthetic antigen-specific receptors (Chimeric Antigen Receptor) are used. For this purpose, blood is sampled from the afflicted persons and the fraction of white blood cells that is suitable for combating the tumor cells is obtained by filtration. The T-cells are then reprogrammed in external laboratories so that they form receptors that recognize the surfaces of the tumor cells. This allows them to combat these cells significantly better. The modified cells are first proliferated and then re-infused into the patient. The use of modified T-cells (CAR-T cells) is an approved treatment for individual forms of leukemia, lymph node cancer, and multiple myeloma.



## Outlook

Konstanze Aurich can easily see the ELPRO solution being applied in other areas of Greifswald University Medicine as well. For example, an automatic refrigerator for the wards is in the planning phase. Erythrocyte concentrates will be stored there at +4 °C. This means that they no longer have to be distributed around the hospital by pneumatic tube or courier whenever needed. For safe storage, data loggers will be used to monitor the temperature inside a dummy bag and in the refrigerator with internal and external sensors.

“ELPRO’s solution offers us a comprehensive approach for temperature monitoring across all processes where regulatory compliance is crucial.”

KONSTANZE AURICH

## About ELPRO-BUCHS AG

Founded in 1986, ELPRO is a globally acting Swiss provider of innovative monitoring solutions specifically designed for the highly regulated pharmaceutical, life science and healthcare industries. As a leader in these fields, ELPRO is a “full service” organization offering state-of-the-art data loggers, cloud SaaS software platforms including data analytics, and a team of validation engineers to support the system integration into their customers’ business processes. ELPRO is part of the Bosch Group. More information at [www.elpro.com](http://www.elpro.com)



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