

Technical specifications of the PROTON P-15 NEO equipment

PROTON equipment is manufactured by **Ryoho Freeze Systems Co. (Japan)** and distributed in Europe by PROTON Europe SL. Below are some indicative specifications (biomedical model **PF-15 NEO** , “ *High-grade model*”) . *for medical field* ”):



Figure 1: **PROTON Freezer PF-15 NEO equipment** (biomedical model with a nominal capacity of 15 kg/h)

Technical Data Sheet – PROTON PF-15 NEO Magnetic Freezer

This freezer from Ryoho Freeze Systems (Japan) combines a sanitary stainless steel design with electromagnetic coils integrated into the cooling chamber.

The illustrated model, of small industrial size, is designed to facilitate its integration into GMP environments and allows large batches of cell samples to be frozen uniformly.

It is based on the model PF-15C for food freezing but the PF-15 NEO version incorporates a specific electromagnetic system (static magnetic field + RF) not present in the standard model.

The **technical characteristics of the PF-15 NEO** are:

- **Freezing capacity:**

~15 kg/hour of biological material per cycle (enough to process around *150 1 mL vials* per run, depending on the heat load).

This high capacity ensures scalability for cell banks or clinical batch production.

- **Operating temperature range:**

Typical operating range: -30 °C to -35 °C in standard mode.

Cooling is achieved through a cold **forced air system** with precise *PID control*, ensuring stable and homogeneous temperature ramps.

Precise thermal control using a digital PID system with homogeneous stability in the chamber.

- **Electromagnetic fields:**

It includes:

- A **uniform static magnetic field** generated by permanent magnets (or equivalent electromagnet).

This field aligns the water molecules during cooling.

- A **radio frequency (RF)** electric field generated by emitting plates

The RF field is applied simultaneously to the magnetic field to induce multiple nucleation.

Both fields are adjustable to low/medium/high levels according to predefined protocols, or exact parameters for research.

- **Control and programming:**

It has an integrated digital panel and/or external software to program custom **cooling profiles** (with ramps, plateaus, rates in °C/min).

It also allows you to control the intensity of the EM fields during each segment of the program. It has internal memory to store multiple validated programs and automatically records temperature-time data for each cycle (with the option to export reports for GMP compliance).

An electromagnetic field parameter recorder is available as an option.

- **Physical dimensions:**

Approximately **1.5 m (width) × 0.8 m (depth) × 1.8 m (height)** in the PF-15 NEO 15 kg/h model. (In Japanese specifications equivalent: 1200 mm × 870 mm × 1700 mm.)

Weight ~450 kg including the magnetic and cooling system.

The exterior is pharmaceutical-grade stainless steel, with smooth surfaces and rounded corners for easy cleaning.

- **Internal camera and trays:**

Usable dimensions of the chamber ~ **600 mm × 400 mm × 350 mm**, with capacity for **5** stacked special metal trays (of ~600 × 400 mm each).

These trays allow vials, bags, or other containers to be layered, ensuring uniform airflow around each sample (Maximum height per unit: 350 mm)

The chamber has a double-sealed door with high-performance insulation to maintain the temperature and prevent moisture from entering.

- **Cooling systems:**

Use an industrial-grade refrigeration compressor with environmentally friendly refrigerant (e.g., R-448A). Cooling is fast and controlled; typical time to go from ambient temperature to -40 °C is <30 min without load.

The system is designed to prevent excessive vibrations or sudden temperature changes.

- **Electrical requirements and consumption:**

- AC200V power supply , **three-phase** , 50/60 Hz
- Requires **nominal current:** 16.2A (50Hz) / 16.15A (60Hz)
- **Recommended breaker:** 20th
- **Electrical consumption:** 3.4 kW (50Hz) / 3.9 kW (60Hz)

Note: The equipment does not require water connections or drains; only adequate room ventilation to dissipate ~5 kW of waste heat.

- **Laboratory/GMP integration:**

The equipment has **CE certification** for electrical safety and electromagnetic compatibility.

It is designed for use in controlled environments: all materials in contact with samples (e.g. racks, trays) are **sterilizable** (autoclavable or disinfectable) to comply with clean room standards.

It can be installed within a Class D to B laboratory (particle emissions are minimal, as it does not use liquid N₂) . **IQ/OQ/PQ (installation, operation, and performance qualification)** services are provided to facilitate its validation in a GMP process.

- **Safety and compatibility:**

The design ensures that magnetic/RF fields are contained primarily within the camera.

Designed to comply with electromagnetic compatibility regulations (e.g. monitors, incubators) in the same room.

Safety interlock doors prevent accidental openings during a cycle.

It includes visual/audible and historical alarms for temperature deviations or failures, with the possibility of remote monitoring.

- **Maintenance:**

annual preventative maintenance : inspection of the compressor and refrigeration circuit, and verification of the calibration of the temperature and electromagnetic field strength sensors. The permanent magnets do not lose significant power over time, so they do not require routine replacement. Software and firmware updates can be performed on-site or remotely by authorized technicians. The estimated lifespan of the equipment exceeds 10 years of continuous use, thanks to its lack of extreme cryogenics, its robust design (many conventional ultra-low temperature freezers fail around 10 years), and the fact that 100% of its components are manufactured in Japan (Mitsubishi brand).

- **Regulatory status:**

The PF-15 NEO is currently marketed as **laboratory equipment** (not a medical device), with CE marking under the Machinery Directive. The manufacturer is pursuing additional certifications in accordance with local regulations to facilitate its clinical use (e.g., in Europe it could eventually be classified as a Class I device for cell processing). (See *Regulatory Framework* section below.)

- The equipment **does not come into direct contact** with the patient nor does it constitute an **implantable medical device** , but rather process equipment within the manufacturing chain.

PROTON NEO as a technological infrastructure for the cell therapy industry

The industrialization of iPS-derived cell therapies implies a structural change in the manufacturing chain.

Cryopreservation ceases to be an auxiliary laboratory phase and becomes a **critical process infrastructure** within the GMP system.

In this context, PROTON NEO should be understood not as a conventional freezer, but as a **technological platform for structural control of freezing**, with direct implications for quality, reproducibility, and scalability.

1 - Structural control of crystallization

In conventional freezing systems, ice nucleation occurs heterogeneously and partially randomly.

This generates:

- Crystals of variable size
- Local thermal gradients
- Irregular osmotic tensions
- Membrane and cytoskeleton damage

PROTON NEO introduces a differentiating element:

- uniform static magnetic field
- Electromagnetic modulation during cooling

The result is not simply "freezing faster", but **conditioning the formation of crystals**.

From a physical point of view:

- The formation of multiple crystallization nuclei is favored.
- The probability of macrocrystal growth is reduced.
- The intracellular and extracellular ice structure is homogenized.

In a cellular environment (iPS cells, dopaminergic progenitors, MSCs, etc.), this directly impacts:

- Plasma membrane integrity
- Conservation of phenotypic markers
- Post-thaw mitochondrial activity
- Functional recovery

Therefore, the system acts on a **structural variable of the process**, not only on the temperature.

2- Electromagnetic modulation as a process parameter

In GMP processes, every critical step must be:

- Controlled
- Programmable
- Reproducible
- Documentable

PROTON NEO allows:

- Programming of defined thermal profiles
- Electromagnetic field intensity control
- Digital recording of cycle parameters
- Exact repetition of validated conditions

This makes electromagnetic modulation a **controllable process parameter (Process Parameter)**.

From a regulatory perspective:

- It can be defined as CPP (Critical Process) Parameter) if the validation proves it.
- It can be incorporated into the process validation dossier.
- It allows batch-to-batch traceability.

This point is key to its positioning in industrial manufacturing.

3- Batch reproducibility

The transition from clinical trial to commercialization requires:

- Inter-batch homogeneity
- Consistency of post-thaw viability
- Phenotype stability
- Predictability of functional recovery

Freezing is one of the phases that introduces the greatest variability if it is not structurally controlled. PROTON NEO provides:

- Uniformity of forced airflow
- Volume-controlled chamber
- Homogeneous distribution of electromagnetic field
- Load capacity defined by standardized trays

This allows:

- Validation of reproducible thermal curves
- Reduction of deviations between batches
- Establishment of post-thawing acceptance criteria

In a master cell bank (MCB) or working cell bank (WCB), the reproducibility of freezing is crucial for the long-term stability of the product.

4- Applicability in CDMO (Contract Development and Manufacturing Organizations)

CDMOs dedicated to cell therapies require :

- Scalable systems
- Transferable protocols
- IQ/OQ/PQ Validation
- Integration into classified rooms
- Documentation compliant with regulatory audits

PROTON NEO has features compatible with this environment:

- Sanitary stainless steel construction
- Absence of liquid cryogenics (reduces risks and structural requirements)
- Programmable digital control
- Standard industrial electricity consumption
- Easy integration into GMP layout

Besides:

The nominal capacity (~15 kg/h) allows processing relevant volumes for:

- Clinical production
- Initial commercial batches
- Expansion of cell phone banks

This positions the system as an intermediate platform between research laboratory and initial industrial production.

5- Integration into master cell banks (MCB / WCB)

In the manufacture of cell therapies, the master cell bank constitutes the origin of all subsequent production.

Critical requirements:

- Genetic stability
- Phenotypic conservation
- Complete traceability
- Minimal freezing-induced variability

PROTON NEO can be integrated into:

- MCB Generation
- WCB Creation
- Controlled re-expansion
- Preparation of clinical batches

By controlling crystallization and reducing cellular structural damage, the system potentially contributes to:

- Maintaining cellular identity
- Reduce post-thaw variability
- Minimize functional losses

This has direct implications for:

- Robustness of the process
- Product safety
- Therapeutic consistency

6- Paradigm shift: from auxiliary equipment to critical infrastructure

Regulatory approval of iPS therapies in Japan marks the beginning of an industrial phase in regenerative medicine.

In this phase:

- Cryopreservation is not a secondary technical step.
- It is a structural component of the manufacturing system.

PROTON NEO is positioned as:

- Functional freezing platform
- Structural ice control system
- Process reproducibility tool
- Technological infrastructure that can be integrated into GMP

Taken together, these specifications highlight that the PROTON PF-15 NEO is a **highly specialized piece of equipment** that offers precise control of the freezing process at biomedical production scale, while maintaining compatibility with GMP environments and operational safety.

Its incorporation into cell therapy laboratories allows for the standardization and scaling up of functional cryopreservation with minimal additional validation effort, since the manufacturer provides performance documentation and specific technical support.

7- Industrial relevance of PROTON PF-15 NEO in iPS cell therapies

1- Transition to commercial phase

The recent approval in Japan of iPS-derived products for Parkinson's disease (AMCHEPRY® – Sumitomo Pharma) marks the beginning of the first global commercialization of allogeneic iPS cell therapies.

2- Critical quality variable

In the context of industrial manufacturing of cell therapies, cryopreservation ceases to be an experimental procedure and becomes a critical quality variable (Critical Process) . Parameter , CPP).

3- Technical positioning

PROTON technology has been used in scientific studies linked to the development of iPS-derived dopaminergic neurospheres relevant to Parkinson's clinical programs, demonstrating maintenance of dopaminergic markers and post-thaw functionality.

Acquisition Model with Buyback Option

The **PF-15 NEO** is supplied exclusively under a **direct purchase model** ; there are no free transfers or demo units.

In order to facilitate evaluation in a real GMP environment, the contract includes a **time-limited buyback option** .

Structure:

- The customer acquires ownership of the equipment.
- You can evaluate it in your own facilities under real-world conditions.
- If you decide not to continue, PROTON will buy back the equipment within the agreed timeframe.

Main conditions:

- Minimum period: 30 days
- Maximum return period: 180 days (6 months)
- Usage cost: 0.40% of the purchase price per day

In practice, this system works as a **structured and limited rental model** , with a contractual buyback guarantee.

This scheme guarantees:

- Real institutional commitment
- Objective technical evaluation
- Reduction of financial risk
- Technological protection of the system