

Ficoll-Paque™ PREMIUM density gradient media

CELL PREPARATION

Ficoll-Paque™ PREMIUM products are a range of sterile, ready-to-use density gradient media* for the preparation of mononuclear cells. All Ficoll-Paque™ PREMIUM products have low endotoxin levels (< 0.12 EU/mL) and are manufactured under a Quality Management System certified to ISO 13485. Ficoll-Paque™ PREMIUM products are available in densities of 1.073, 1.077, and 1.084 g/mL for the preparation of different density preparations of mononuclear cells from peripheral blood, bone marrow, umbilical cord blood, and placental tissue. Mononuclear cell isolation can be automated and functionally closed by using Sepax™ technology (1, 2).

*For *in vitro* use only.

Features

- Manufactured within a quality management system certified to ISO 13485
- Suitable for *in vitro* applications
- Sterile, ready-to-use reagent
- Low levels of endotoxin (< 0.12 EU/mL) secured and tested

Classical Ficoll-Paque™ PREMIUM with a density of 1.077 g/mL was developed from Ficoll-Paque™ PLUS, which is based on Ficoll™ PM400 (polysucrose) and sodium diatrizoate and has a more than 40 yr track record for large- or small-scale purification of mononuclear cells from human peripheral blood. All Ficoll-Paque™ PREMIUM products differ from Ficoll-Paque™ PLUS in that they are manufactured under a Quality Management System certified to ISO 13485. These require stringency in validation and documentation of manufacturing procedures.

Applications

Ficoll-Paque™ PREMIUM

Ficoll-Paque™ PREMIUM has a density of 1.077 g/mL and is optimized for the isolation of mononuclear cells from human peripheral blood by using a simple and rapid centrifugation technique developed by Bøyum *et al.* (3). The medium can also



Fig 1. Ficoll-Paque™ PREMIUM products are available in densities of 1.073,

be used for the isolation of human mononuclear cells from other sources, including bone marrow and umbilical cord blood. Separation of normal human peripheral blood by the recommended protocol typically yields a mononuclear cell preparation with:

- 95% ± 5% mononuclear cells present in the separated fraction
- > 90% viability of the separated cells
- 60% ± 20% recovery of the mononuclear cells present in the original blood sample
- 3% ± 2% granulocytes
- 5% ± 2% red blood cells

Ficoll-Paque™ PREMIUM 1.084

Ficoll-Paque™ PREMIUM 1.084 can be used for isolating higher-density human mononuclear cells, and for separating blood cells from mice or rats.

Ficoll-Paque™ PREMIUM 1.073

Ficoll-Paque PREMIUM 1.073 can be used when isolating lower-density human mononuclear cells, for example mesenchymal stromal cells (4) or monocytes. The higher-density lymphocytes and granulocytes will sediment through Ficoll-Paque PREMIUM 1.073 to the bottom of the tube, thereby enriching the lower-density cells at the interface.

Cytotoxicity tested

Ficoll-Paque™ PREMIUM (density 1.077) and Ficoll-Paque™ PREMIUM 1.084 were tested for *in vitro* cytotoxicity in cultured mammalian cells. Four separate tests were performed in accordance with the U.S. Pharmacopeia, Method <87> and ISO 10993-5 guidelines (5, 6). Ficoll-Paque™ PREMIUM was mixed with complete cell culture medium (HAM F12 medium with 10% fetal bovine serum and 50 µg/mL gentamycin) at concentrations of 25% v/v and 10% v/v. Cell culture medium (for untreated controls), an extract of polypropylene at 6 cm²/mL (negative control), and an extract of polyvinyl chloride at 0.3 cm²/mL (positive control) were also prepared. Triplicate cultures of L929 cells were treated for 48 h at each test point. The cultures were then stained with Neutral Red stain and examined for cytotoxicity on a scale from 0 to 4 according to USP <87>.

The control cultures exhibited the expected responses, demonstrating the correct functioning and sensitivity of the test system. For all four test batches, the mixtures containing 10% and 25% Ficoll-Paque™ PREMIUM showed no detectable cytotoxicity (reactively grade 0). Thus, Ficoll-Paque™ PREMIUM passed the requirements of the USP <87>, because the reactivity grade was ≤ 2.

Specifications

Density	Ficoll-Paque™ PREMIUM, 1.077 ± 0.001 g/mL
	Ficoll-Paque™ PREMIUM 1.084, 1.084 ± 0.001 g/mL
	Ficoll-Paque™ PREMIUM 1.073, 1.073 ± 0.001 g/mL
Stability	Stable for 3 yr if stored between 4°C and 30°C and protected from direct light

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CY13869-04Mar23-DF

Endotoxins	Contains < 0.12 EU/mL
Sterility	Autoclave steam sterilization with sterility assurance level (SAL) of 10 ⁻⁶

References

1. Richman, S. *et al.* Factors affecting the turnaround time for manufacturing, testing, and release of cellular therapy products prepared at multiple sites in support of multicenter cardiovascular regenerative medicine protocols – a Cardiovascular Cell Therapy Research Network (CCTRN) study. *Transfusion* **52**, 2225–2233 (2012).
2. Kaur, I. *et al.* Comparison of two methodologies for the enrichment of mononuclear cells from thawed cord blood products: The automated Sepax system versus the manual Ficoll method. *Cytotherapy* **19**, 433–439 (2017).
3. Bøyum, A. Isolation of mononuclear cells and granulocytes from human blood. Isolation of mononuclear cells by one centrifugation, and of granulocytes by combining centrifugation and sedimentation at 1 g. *Scand. J. Clin. Lab. Invest.* **21**, 77–89 (1968).
4. Brooke, G. *et al.* Manufacturing of human placenta-derived mesenchymal stem cells for clinical trials. *British J. Haematology* **144**, 571–579 (2008).
5. United States Pharmacopeia. *Biological reactivity tests, in vitro*, chapter <87>.
6. International Standards Organization. ISO 10993-5:2009. *Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity*.

Ordering information

Product	Pack size	Product code
Ficoll-Paque™ PREMIUM	6 × 100 mL	17544202
Ficoll-Paque™ PREMIUM	6 × 500 mL	17544203
Ficoll-Paque™ PREMIUM 1.084	6 × 100 mL	17544602
Ficoll-Paque™ PREMIUM 1.073	6 × 100 mL	17544652

Related products

Ficoll-Paque™ PLUS	6 × 100 mL	17144002
Ficoll-Paque™ PLUS	6 × 500 mL	17144003
Ficoll™ PM400	100 g	17030010
Ficoll™ PM400	500 g	17030050
Ficoll™ PM400	5 kg	17030005
Ficoll™ PM400	40 kg	17030008
Percoll™ PLUS	250 mL	17544502
Percoll™ PLUS	1 L	17544501
Percoll™	250 mL	17089102
Percoll™	1 L	17089101
Percoll™	6 × 1 L	17089109

