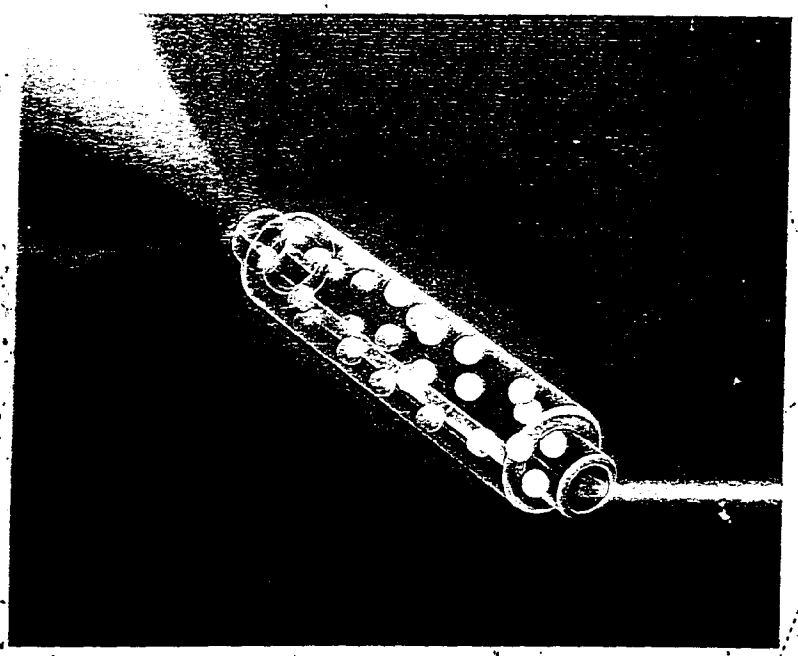
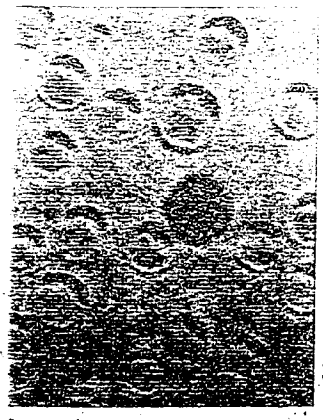


ISOLEX™* 300

Magnetic Cell Separator

Yielding *the* Purity...

...Of Immunomagnetic Selection...

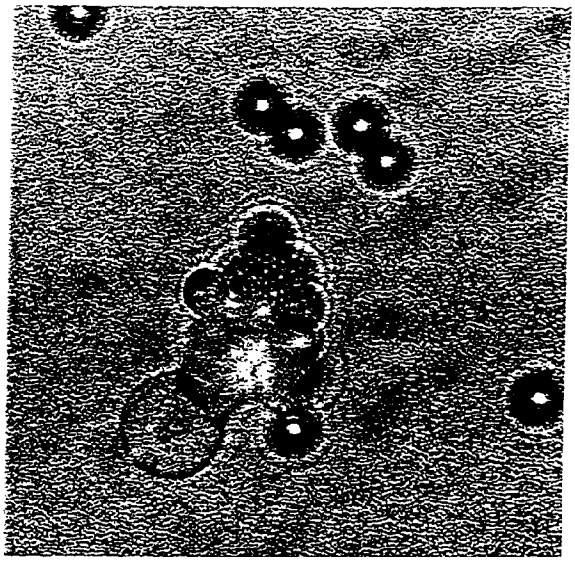


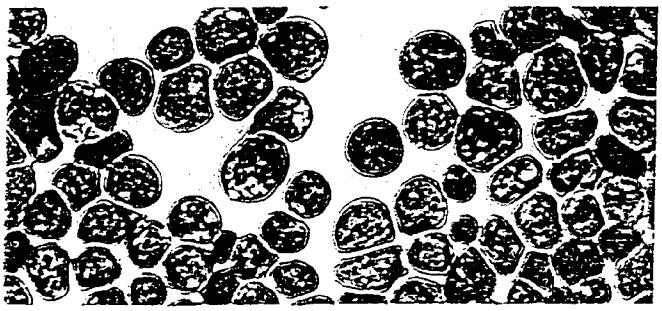
Specific Identification.

The process begins with the 9C5 antibody, a highly specific, high-affinity murine anti-human CD34 antibody, manufactured under GMP quality standards by Baxter. Within minutes, the 9C5 antibody coats and identifies the target CD34+ cells, leaving other subpopulations unmarked.

Specific Capture.

The marked stem cells are captured by rosetting them with magnetic beads coated with a sheep anti-murine (SAM) antibody. The SAM antibody recognizes only the murine 9C5 antibody labeling the target cells, resulting in highly specific capture of CD34+ cells. In addition very efficient capture of CD34+ cells is achieved by using small 4.5 μm beads. The large total surface area that results (2-3m² per run) means an extremely large number of binding sites for capture. The rosetted CD34+ cells are then physically separated from the unrosetted cell population by means of the precisely-engineered Isolex™* magnet.





Specific Release.

After the non-target cells are drained away, a pharmaceutical grade enzyme, Chymo-Cell-T™ (Chymopapain), specifically releases the captured CD34+ cells from the beads, allowing the CD34+ cells to be recovered with a high degree of efficiency. Their surfaces are free of residual primary antibody, which might otherwise cause immunogenic reactions or sterically hinder further antibody-mediated processing.

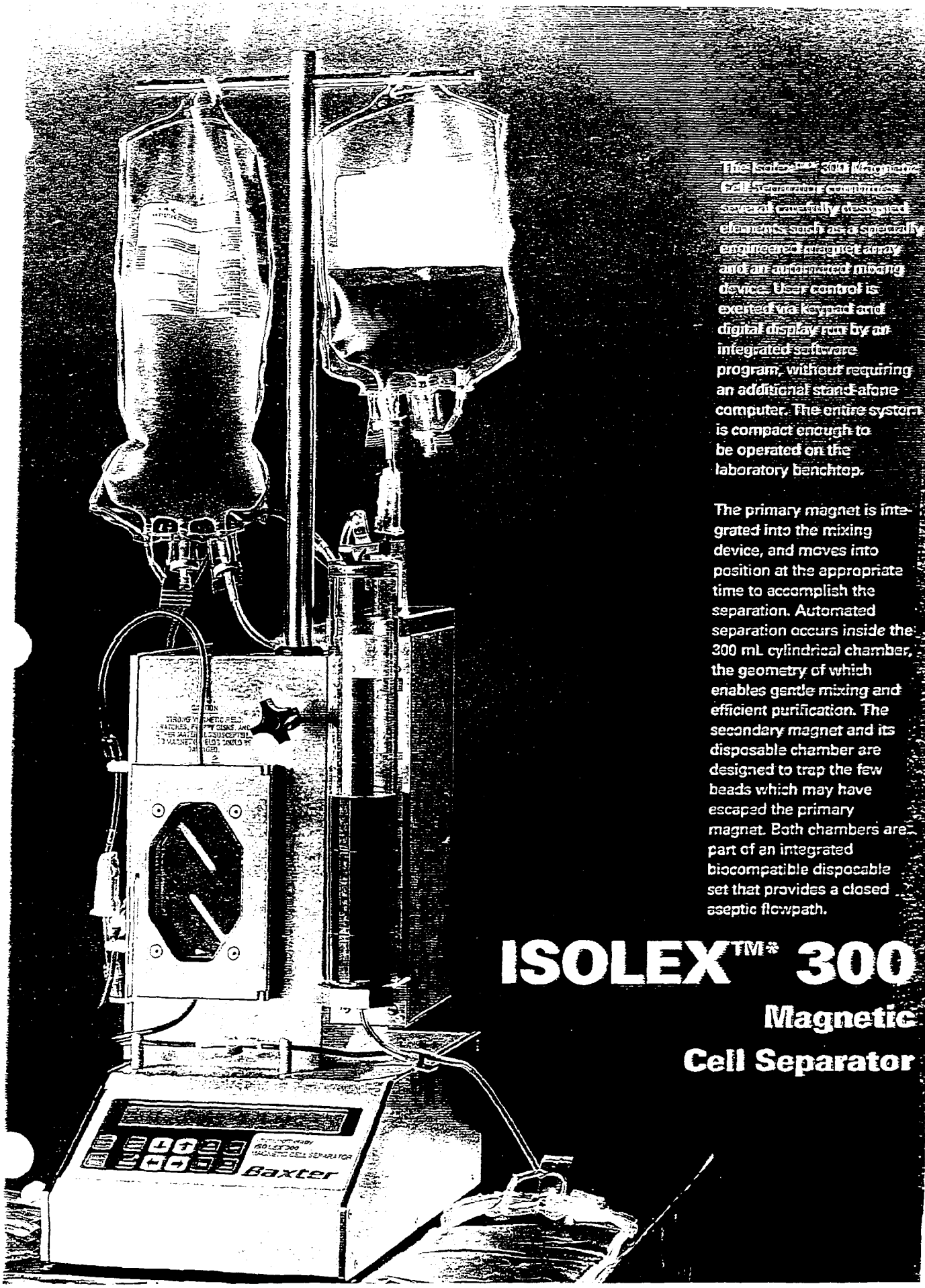
PBSC Pre Selection: 1.2% CD34+

Selected Cells: 95.0% CD34+

High Purification.

By specific identification, capture and release, the Isolex™* system ensures both high yield and purity. This high level of CD34+ cell purity is illustrated by the FACS analysis to the left.

Consistent with this high level of purity, colony culture assays also show 50-200 fold enrichment of CFU-GM, BFUe and CFU-GEMM after Isolex™* selection.



The Isolex™ 300 Magnetic Cell Separator comprises several carefully designed elements such as a specially engineered magnet array and an automated mixing device. User control is exerted via keypad and digital display run by an integrated software program, without requiring an additional stand-alone computer. The entire system is compact enough to be operated on the laboratory benchtop.

The primary magnet is integrated into the mixing device, and moves into position at the appropriate time to accomplish the separation. Automated separation occurs inside the 300 mL cylindrical chamber, the geometry of which enables gentle mixing and efficient purification. The secondary magnet and its disposable chamber are designed to trap the few beads which may have escaped the primary magnet. Both chambers are part of an integrated biocompatible disposable set that provides a closed aseptic flowpath.

ISOLEX™* 300

Magnetic Cell Separator

Background of Safety

Before initiating clinical trials, the Isolex™* 300 system and its component parts passed extensive preclinical safety testing.

Preclinical Tests[10]	Results
Mouse Acute Systemic Injection (Beads)	No Adverse Effects
Rabbit Intracutaneous Injection (Beads)	No Tissue Reaction
Colony Formation After Exaggerated Exposure to Magnetic Field, Magnetic Beads, CD34 Antibody, Chymopapain	No Inhibition of Trilineage Colony Formation
Effect of Chymopapain on CD34 Antigen	9C5 Epitope Re-expression > 90% After 24 Hours; 8G12 Epitope Unaffected by Chymopapain

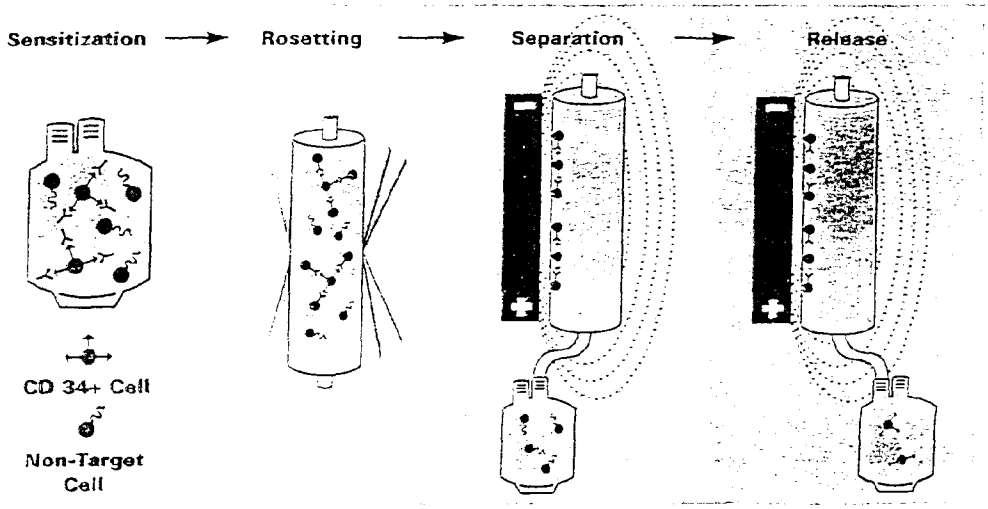
Documented GMP Quality

In accordance with GMP standards, a large battery of tests support the quality of the manufacturing process and the final products:

	Key Process and Release Tests
Dynabeads® CD34 Positive Isolation 50 Separate Tests	*Sterility* *Endotoxin* *Functionality* *Identity* *Particles* *Stability*
Isolex™* Anti-CD34 Antibody 120 Separate Tests	*Sterility* *Endotoxin* *Functionality* *Identity* *Stability* *Purity*

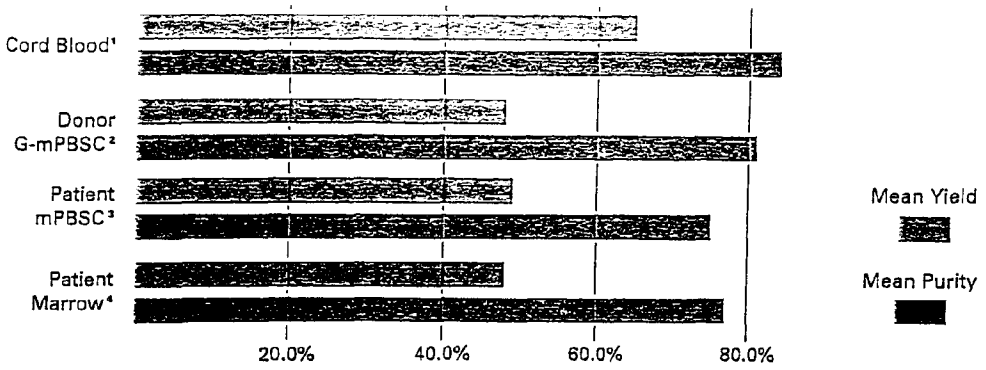
*NOTE: Virus removal and inactivation are achieved by hollow-fiber filtration/column chromatography and Solvent/Detergent treatment, respectively.

Isolex Process



...For Effective:

Stem Cell Purification



Isolex™* 300 gives high purity and yield independantly of the stem cell source. High performance is maintained even at lower starting CD34 percentages.

Tumor Cell Depletion

STEM CELL SOURCE	ORIGIN	TARGET CELLS	LOG DEPLETION
G-mPBPC[2]	Donor	B Cells (CD19)	3,0
G-mPBPC[5]	Donor	Lymphoma cell lines	5.3
BM[6]	Patient	Solid Tumors	2.5

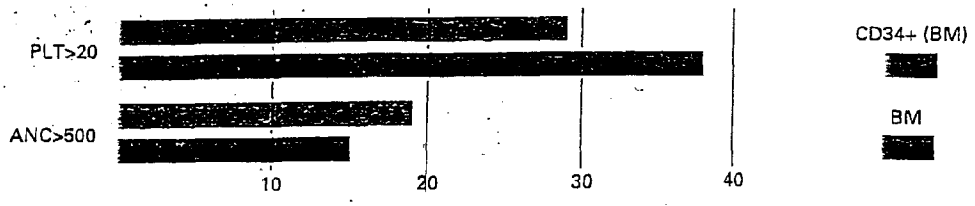
In various studies, the Isolex™* Magnetic Cell Separator has provided substantial depletion of tumor cells and other non-target cells.

T-Cell Reduction

STEM CELL SOURCE	ORIGIN	TARGET CELLS	LOG DEPLETION
G-mPBPC[2]	Donor	CD5	3.0
G-mPBPC[2]	Donor	CD3	3.3
G-mPBPC[7]	Donor	CD3	4.0
BM[8]	Patient	CD3	2.5

T-Cell numbers are significantly reduced after positive selection with Isolex™* system.

Hematopoietic Reconstitution



Initial clinical studies show no significant differences in engraftment between Isolex™*-selected and unselected marrow[9].

ddress and Order Information

Code	Description
R9722	Isolex™* 300 Magnetic Cell Separator
R9720	Isolex™* 300 Disposable Set
R9500	Isolex™* 300 Stem Cell Reagent Kit

For inquiries or placing an order please contact your local Baxter Customer Service listed below:

Austria
Baxter Ges. mbh
Richard-Strauss-Str. 33
1232 Wien
Tel (+43) 1 - 61 04 80
Fax (+43) 1 - 61 55 36 3

Belgium
Baxter S.A.
Rue Colonel Bourg 105B
1140 Brussels
Tel (+32) 2 - 70 21 88 6
Fax (+32) 2 - 73 63 68 4

Denmark
Baxter A/S
Gydevang 43
3450 Allerod
Tel (+45) 48 - 14 01 44
Fax (+45) 48 - 14 02 44

Finland
Baxter Oy
P.O. Box 46
01621 Vantaa
Tel (+358) 0 - 50 73 54 73
Fax (+358) 0 - 87 81 03 8

France
Baxter S.A.
Avenue Louis-Pasteur
Boite Postal 56
78311 Maurepas Cedex
Tel (+33) 1 - 34 61 52 43
Fax (+33) 1 - 34 61 50 25

Germany
Baxter Deutschland GmbH
Edisonstrasse 3-4
85716 Unterschleißheim
Tel (+49) 89 - 31 70 12 72
Fax (+49) 89 - 31 70 15 56

Ireland
Baxter Healthcare Ltd.
Unit 7, Deansgrange Industrial Estate
Blackrock
Co. Dublin
Tel (+353) 12 - 89 27 11
Fax (+353) 12 - 89 27 04

Italy
Baxter S.p.A.
Viale Tiziano N. 25
00196 Rome
Tel (+39) 6 - 32 49 12 43
Fax (+39) 6 - 32 21 64 3

Netherlands
Baxter B.V.
Kobaltweg 50
3542 CE Utrecht
Tel (+31) 30 - 48 89 11
Fax (+31) 30 - 41 17 55

Norway
Baxter AS
Gjerdrumsvei 10 B
0486 Oslo 4
Tel (+47) 22 - 18 41 01
Fax (+47) 22 - 18 41 09

Spain
Baxter S.A.
s/Solsones, No. 2 bajo, local 7
Edificio Muntadas
Parque de Negocios
"MAS BLAU"
El Prat de Llobregat
08820 Barcelona
Tel (+34) 3 - 47 87 16 2
Fax (+34) 3 - 47 87 10 9

Sweden
Baxter Medical AB
Isafjordsgatan 30B
16494 Kista
Tel (+46) 8 - 632 64 00
Fax (+46) 8 - 752 01 12

Switzerland
Baxter A.G.
Industriestr. 31
8305 Dietlikon
Tel (+41) 1 - 83 33 36 0
Fax (+41) 1 - 83 30 42 0

United Kingdom
Baxter Healthcare Ltd.
Wallingford Road
Compton, Newbury
Berkshire, RG16 0QW
Tel (+44) 635 - 20 63 24
Fax (+44) 635 - 20 61 26

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1 **Tseng-Law J et al,** *Exp Hematol* 22:20 (1994) and Data on File, Baxter Healthcare Corp.
2 **Lane TA et al,** *Blood* 85(1):275 (1995)
3 **Marolleau JP et al,** *Blood* 84(10):370 (1994) and Data on File, Baxter Healthcare Corp.
4 **Traycoff CM et al,** *Exp Hematol* 22:554 (1994)
5 **Paulus U et al,** *Exp Hematol* 22:15. (1994)
6 **C Civin,** Personal Communication, (1994) and data on File, Baxter Healthcare Corp. (data obtained using MY-10 anti-CD34 antibody)
7 **Dreger P et al,** *Exp Hematol* 23:L147 (1995)
8 **Broun ER,** Personal Communication, (1994) and data on File, Baxter Healthcare Corp.
9 **Broun ER et al,** *Exp Hematol* 22:362 (1994)
10 Data on File, Baxter Healthcare Corp.

Note: All data has been obtained using the Isolex™ 50 and Isolex™ 300 Magnetic Cell Separation systems

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