ACTIVATED
CELL THERAPY

December 21, 1995

To Whom It May Concern:

The following material is being sent to you in response to your request for a 510(k) Summary for ACT's device for preparation of somatic cells.

Product Name

ACT Buoyant Density Solution

Device Classification

Class 1

General Description and Use of Device

Activated Cell Therapy's device is an inert, high resolution density separation medium used for *in vitro* preparation of somatic cells such as mononuclear leukocytes. It may be used with whole blood, apheresis products and other suitable biological cellular preparations. The device consists of a silanated colloidal silica [illegible] It is sterile and nonpyrogenic. The device separates cells by physical interactions based upon the cell's buoyant density. Cell separation does not depend upon biological or chemical interaction with the cell. Cells prepared with ACT's device are suitable for research, diagnostic and therapeutic applications.

ACT's Buoyant Density Solution is formulated for preparation of specific somatic cells such as mononuclear cells that express the [illegible] CD34 antigen (hematopoietic progenitor cells), [illegible]. Table 1 presents the names of those formulations.

TABLE 1. Specific Formulations of ACT's Device

Mononuclear Cell Type	Formulation Name
[illegible]	[illegible]
[illegible]	[illegible]
[illegible]	[illegible]
CD34	
Peripheral Blood	ACT CD34 Buoyant Density Solution (PBPC)
[illegible]	[illegible]
[illegible]	[illegible]

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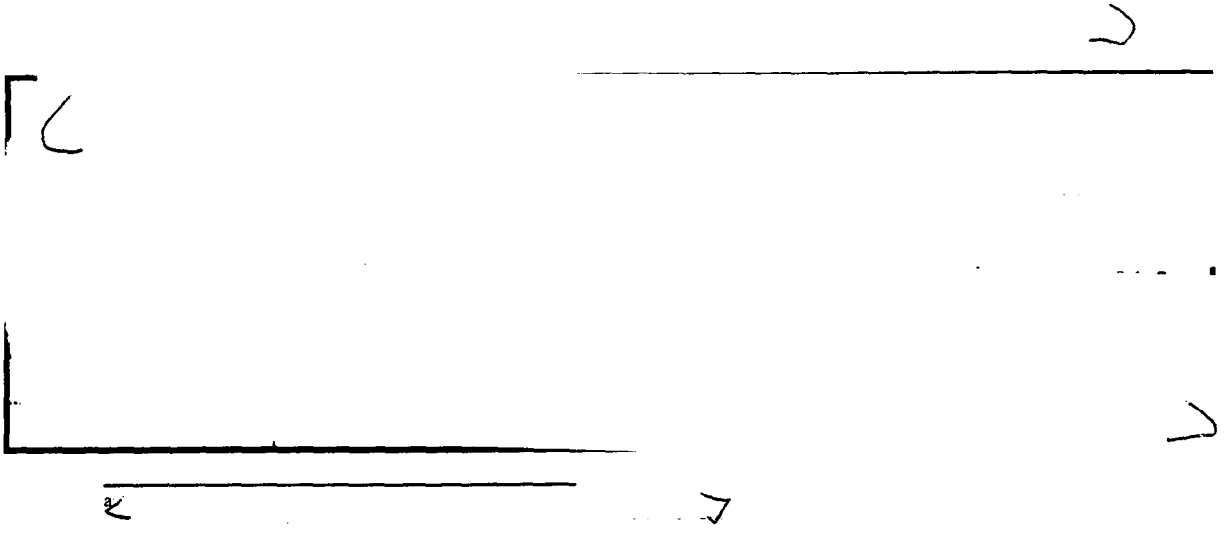
Predicate Devices

This summary will refer to two predicate devices: Ficoll and Percoll. "Ficoll" refers to several commercially available preparations which consist of polysucrose (Ficoll 400) plus either sodium diatrizoate or sodium metrizoate.

ACT's device and the predicate devices Ficoll and Percoll are solutions with precisely known densities which separate cells in a mixture based upon each cell's intrinsic buoyancy. Density separation of cells is achieved by first layering the mixture of cells over the density solution in a centrifuge tube after which the tube is centrifuged. Each cell will sediment until it enters a density solution where an equilibrium is established in which the cell's buoyancy precisely counter balances the centrifugal force. Centrifugation is continued until all cells in the mixture have reached this equilibrium. Cells with different densities are then recovered by removing sequentially different layers of the density solution.

device



Recovery of Mononuclear Cells that Express the CD34 Antigen

CD34 cells are typically prepared from bone marrow obtained by direct aspiration or from peripheral blood progenitor cells (PBPC) obtained by apheresis after mobilization with chemotherapy and/or the colony stimulating factors G-CSF or GM-CSF. Table 3 shows recovery of CD34 cells and Colony Forming Units from PBPC prepared with either ACT's Buoyant Density Medium or Percoll. Recovery of CD34 cells was slightly higher for ACT's device than for Percoll. In a separate set of experiments, recovery of CD34 cells with ACT's Buoyant Density Medium was also slightly higher than recovery with Ficoll (83.4 ± 4.0 vs 81.6 ± 6.9, mean ± SEM, n=9). These tests demonstrate that ACT's device is substantially equivalent to the predicate devices for recovery of CD34 cells.

TABLE 3. Recovery of CD34 Cells and CFU with ACT's Device or Percoll

	ACT Device (n=20)	Percoll (n=44)
CD34 Cells	91.7 ± 2.3[a]	87.6 ± 2.1%
CFU	92.2 ± 2.0	91.1 ± 1.6%

[a]Mean ± SEM; all data are % recovery

Safety Considerations

The safety of ACT's device was tested in four ways: 1) trypan blue dye exclusion; 2) functional capacity of CD34 cells to form colonies; 3) *in vitro* hemolysis tests; and, 4) *in vivo* toxicity in animals. Greater than 98% of cells recovered with ACT's device are viable as shown by trypan blue dye exclusion. Preparation with ACT's device did not affect the viability and clonogenic potential of CD34 cells (CFUs) (Table 3). The device did not cause hemolysis or flocculation when mixed with human or rabbit blood nor did it produce an antigenic response when tested in guinea pigs. The LD_{50} in rats following a single intravenous injection of density medium was greater than 5 mL/kg. ACT's device was not pyrogenic after intravenous administration to rabbits.

Summary

The data presented above demonstrate that ACT's device is substantially equivalent to the predicate devices, Ficoll and Percoll, for preparation of somatic cells and that ACT's device is safe for its stated use.

Sincerely,

Frank H. Valone

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