Table 3. Other Miscellaneous Equipment Needed in the Cell Processing Laboratory

Dedicated Equipment		
Cooler/transport container	Micropipettes	Balance (scale)
Dry shipper	Tubing stripper	Barcode scanner
Liquid nitrogen (LN_2) tanks	Tubing sealer	Personal computer
Thermometer (reference)	Plasma extractor	
Shared Equipment		
Apheresis machine for red cell reduction/ buffy-coat enrichment	Microbiology lab (aerobic, anaerobic, and fungal culture)	

Projected Operational Budget and Revenue

The projected operational budget should include spending for all manufacturing and maintenance costs, including salaries, maintenance of equipment and software, facility occupancy costs, and product storage cost (LN_2). Manufacturing costs will include those for supplies, reagents, testing, and storage required for product manufacturing and may be as high as 50% or more than the entire facility spending. To estimate the cost of manufacturing, one should have a good understanding of all the supplies and reagents that will be required for the manufacture of each product, the prices, and how many of each item will be used for a single manufacturing procedure. The cost of product testing should also be added to the calculation of manufacturing costs. Once data on

these factors are available, the estimated annual manufacturing volume can be used to calculate estimated annual spending.

The projected revenue can be calculated as well and can be used to offset expenses. Processing facilities that can charge for manufacturing either directly or by patient medical billing should consider the cost of supplies and reagents, product testing, labor, storage, and shipping, as applicable. Other revenue can be generated from billing for clinical trials or other contracted services.

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The functions of the cellular therapy processing laboratory will be dependent on the scope of the HSCT and/or cellular immunotherapy program that it supports. These could include processes involved in the provision of autologous, allogeneic, or cord blood grafts, as well as IEC therapy products. For most products that are collected, additional processing may be required before the final product is released for infusion; however, for the majority of HSCT products, only minimal manipulation of the product is required, as covered in this section.

As defined by the US *Code of Federal Regulations* [21 CFR 1271.3(f)(1)] for HCT/Ps, "minimal manipulation" is processing that does not alter the original relevant characteristics of the structural tissue relating to the tissue's utility for reconstruction, repair, or replacement.[11,12] As mentioned in a previous section, such HCT/Ps are referred to as "361 HCT/Ps" (see also later discussion on regulatory aspects).

Processing provided by a CTL involved in the minimal manipulation of 361 HCT/Ps and marrow products, as well as processes involved in the preparation for infusion of cord blood or IEC therapy products, is listed in Table 4. The table includes some more specialized procedures that may be performed in non-GMP processing laboratories [CD34+ cell or T-cell (CD3+) selection, etc].

CTL processes are supported by common regulated operations that are involved in ensuring the provision of a safe, well-

Table 4. Processes Performed in the Cellular Therapy Processing Laboratory

More Common	Less Common
Cryopreservation	CD34+ cell enrichment
Storage	T-cell depletion
Thawing	
Washing	
Red cell depletion/buffy-coat enrichment	

characterized, and effective cellular therapy product. These may include transportation to and from the CTL (with receipt, shipping, and release procedures), product tracking, appropriate labeling, QC, laboratory testing, and environmental monitoring.

Equipment

The equipment required for a CTL involved in processing 361 HCT/Ps is minimal and discussed in more detail in the previous section on business plans. Certain equipment may be shared with another laboratory if located within reasonable proximity, especially if the equipment is expensive and for low-volume use. Every piece of equipment (including backup) must undergo qualification and validation before it is used.

Temperature and humidity of the laboratory and storage space should be controlled and monitored to maintain proper storage conditions and ensure optimal performance of sensitive electronic equipment. Critical equipment such as product storage and supply storage refrigerators and freezers must have a reliable power supply and should be in a secure location accessible only to authorized personnel. All critical refrigerators and freezers should have full-time temperature monitoring with working alarms.