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#### A WEB BASED FORUM FOR EDUCATION & COMMUNICATION IN A CHALLENGING WORKPLACE ENVIRONMENT

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**Background:** The Dana Farber Cancer Institute's Cell Manipulation Core Facility (CMCF) is approved to provide clinical stem cell transplant services to all Harvard affiliated hospitals. Providing in-service education to clinical team members is particularly complex given the everyday challenges of communicating technical details, allocating time for busy staff, and providing access to restricted GMP lab space. In addition to educating the clinical team, it is paramount to disseminate information as well as train internal department members within the CMCF.

**Methods:** In order to meet these challenges, we have developed a website which provides in-service training specifically centered on video and pictorial methods of communication. The website features a facility tour, as well as an overview of product types, all major processing steps, and standards for release. Additionally, links to the site are present on CMCF cell processing standard operating procedures.

**Results:** Prior to the implementation of the in-service training website, 8 staff members in the stem cell transplant laboratory had current working knowledge of cell processing procedures. Post implementation, all 40 internal departmental staff members, as well as the entire bone marrow transplant program, have access to the most up to date cell processing techniques and standards.

**Conclusion:** The in-service training website proved efficacious as an efficient method to expand the knowledge base of new technologists, non-technical staff members within the CMCF, and external bone marrow transplant team members. By utilizing this simplified strategy, we have bridged the gap that exists in our current training and education process.

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#### ENSURING SUPPLY CHAIN OF CELL THERAPY PRODUCTS DURING COMMERCIALIZATION: EASY RECONSTITUTION AT THE BEDSIDE

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Promethera HepaStem is the company's therapy product to treat serious metabolic liver disorders. An European phase I/II clinical trial is ongoing to treat Crigler-Najjar and Urea Cycle Disorders in a pediatric setting. As of today, 20 patients have been treated with HepaStem. Currently, Promethera is preparing its next clinical phases in US and Europe. The challenge is to provide a drug product easy-to-reconstitute at clinical sites. In order to guarantee a flexible, highly qualitative, and economically sustainable supply chain during commercialization, Promethera has developed a ready-to-use off-the-shelf product for direct reconstitution at the hospitals. The product preparation is simply carried out like conventional reconstitution of freeze-dried sterile medicinal products (e.g. vaccine). The challenge was to find an appropriate final container (i) compliant to liquid nitrogen storage, (ii) allowing automated in-line filling and (iii) reconstitution without changing the product quality (safety/identity/purity/potency). The Aseptic Technologies closed vials perfectly fit within this concept. This approach does not only simplify the preparation procedure and operation time, it also reduced the storage footprint and improved the product's quality in terms of viability, yield, content uniformity and batch-to-batch consistency. Shelf-life, the key-bottleneck of most cell therapeutic products, is substantially less critical. The idea for the upcoming clinical phases is to provide an all-in-one kit, including the cryopreserved cell therapeutic product HepaStem and all material needed for reconstitution (syringe/adaptor/disinfectant/prefilled vial with reconstitution media). In conclusion, Promethera has developed a ready-to-use product, allowing worldwide availability and easy reconstitution at the bedside. This technology guarantees a sustainable supply chain during commercialization and offers opportunities in the field of cell-based products with limited shelf-life.

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#### RED CELL DEPLETION OF BONE MARROW USING THE THERMOGENESIS AUTOEXPRESS SYSTEM

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The ThermoGenesis AutoXpress (AXP) system is an automated closed device commonly used to harvest the buffy coat from cord blood. We validated its use with the bone marrow since it was available in our laboratory, which includes also the Padova Cord Blood Bank. 16 bone marrow samples were obtained from a second buffy coat collection during the processing of ABO incompatible products with the COBE 2991. Each sample contained  $3.8 \pm 2 \times 10^9$  nucleated cells (range  $0.8-8.9 \times 10^9$ ) and  $47 \pm 13$  ml of red cells. The BM samples were concentrated to  $127 \pm 21$  ml, HES was added at 20% to facilitate the concentration and separation of the fractions: plasma, buffy coat and red cells. After the 2 steps centrifugation, at 1400g for 20 minutes and at 80 g for 10 minutes, the buffy coat was concentrated into a 20 ml volume in the freezing bag of the disposable set. The recovery of total nucleated cells and of CD34+ cells was  $90 \pm 8.7\%$  and  $103 \pm 9.7\%$  respectively. Cell viability (7AAD) pre and post AXP centrifugation was not significantly different ( $91.3 \pm 4.1\%$  vs  $91.8 \pm 4.2\%$ ). A consistent volume of red cell was measured in the final product:  $5 \pm 0.5$  ml. These results are comparable with those obtained with cord blood by our laboratory. In our hands the AXP system designed for cord blood concentration showed an excellent performance also with bone marrow. AXP system alone or in combination with COBE2991 can represent a reliable system for the depletion of red cells especially in paediatric ABO incompatible transplants.

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#### BONE MARROW PROCESSING OF ABO INCOMPATIBLE PRODUCTS BY THE COMBINED USE OF THE COBE 2991 AND THE THERMOGENESIS AUTOXPRESS SYSTEM

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We developed a new processing approach based on the combined use of COBE 2991 and the ThermoGenesis AXP system for depletion of red blood cells in ABO incompatible bone marrow transplantation. Here we present the results of 16 procedures. Bone marrow buffy coat were collected in two consecutive steps using the COBE 2991 cell processor, and transferred in two bags labelled buffy coat 1 and buffy coat 2. The mean volume of buffy coat 1 was  $90 \pm 31$  ml and it contained most of the total nucleated cells (TNC) and a relatively low volume of red cells ( $14 \pm 9$  ml). The mean volume of buffy coat 2 was  $127 \pm 21$  ml and it contained less TNC ( $3.8 \pm 2 \times 10^9$ ) and a higher volume of red cells ( $47 \pm 13$  ml). Buffy coat 2 underwent a further concentration using the AXP system after the addition of HES at 20%. The combined use of COBE 2991 and AXP system resulted in 91% reduction of red blood cells (range 83 to 98%). The mean recovery of TNC was  $88 \pm 13\%$ . The initial mean volume of the bone marrow aspirates was  $695 \pm 322$  ml and the final mean volume was  $109 \pm 38$  ml. The TNC and CD34+ cells infused were  $3.6 \times 10^8 \pm 7$ /kg and  $3.4 \pm 2 \times 10^6$ /kg respectively. The mean volume of red cell infused was  $0.48 \pm 0.17$  ml/kg. Engraftment occurred in all the patients and no adverse reactions have been observed. This is a convenient and reliable method for processing ABO incompatible products with a reduced risk of contamination since processing is performed in closed systems.

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#### GMP LABORATORY FOR ACADEMIC CELLULAR THERAPY; TISSUE ENGINEERING AND GENE THERAPY DEVELOPMENTS AND CLINICAL TRIALS SUPPLY AT MAIMONIDES UNIVERSITY-ARGENTINA

GA Moviglia

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To accomplish the legal national and international requirements for the elaboration of elements for advanced therapies, the Maimonides University of Buenos Aires, Argentina built a GMP laboratory of 400 square meters divided in three different areas distinguished one from other through their level of Biosafety: Level 2 (BIO 2) dedicated to quality control and quality assurance test as well as animal studies. Level 3 (BIO3) dedicated to the process of non contaminated human cells to be used in cell therapy and / or tissue engineering, cell freezing and banking and Tissue Culture Media