ISHAGE Telegraft ©

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# Bienvenue à Québec

ISHAGE 2001 will be held in Québec City, capital city of the Province of Québec, Canada and cradle of French civilization in North America. The City of Québec has been designated a world heritage site by UNESCO. Its fortifications, narrow winding streets and changing elevations make it one of the most picturesque and European cities in North America. The city has a rich history and its museums and architecture are certainly worth exploring.

## History of Québec City

Following Jacques Cartier's explorations of the St.Lawrence River in 1534, Samuel de Champlain landed on the banks of the river in 1608 at a place the Indians called Kébec. A trading post was founded on the Place Royale, within the oldest part of what is now Québec City. This fortified city, originally a center for the fur trade, is now a vibrant seaport and cultural center. The Chateau Frontenac Hotel, the impressive building featured on the cover of the Annual Meeting brochure and location of the ISHAGE 2001 Gala Banquet, dominates the skyline and overlooks the river below. The views from the hotel and the boardwalk of the adjacent Terrasse Dufferin are impressive. Nearby are the Plains of Abraham, the site of a historic battle that changed the history of North America. Before the battle, control of the land that is now Canada was divided between England and France. On September 13, 1759 the British armies led by Major General James Wolfe attacked the French troops led by Louis Joseph de Montcalm. The French were defeated, both generals lost their lives, and the stage was set for New France to became a British colony. Four years later, New France was ceded to the King of England in the Treaty of Paris. English forces later resisted siege by Americans fighting the Revolutionary War in 1775-1776. Québec City, as part of Lower Canada, joined the Confederation of Canadian Provinces in 1867.

## Annual Meeting

The meeting sessions will be held at the Québec City Convention Center, centrally located close to the old city and across the street from the Parliament Buildings. The Organizing Committee has put together an impressive program. FAHCT Training Workshops and a Flow Cytometry Workshop will be held on Thursday June 14th. The meeting symposia will begin on Friday June 15th and conclude the afternoon of Sunday June 17th. The sessions will cover the full range of cell therapy related topics, including hematopoietic progenitor cell transplantation, adoptive immunotherapy, gene therapy and non-hematopoietic/ mesenchymal stem cells. An increased number of Technical Breakfasts, of particular interest to laboratory technical staff, have been added this year. Your feedback on these and the other sessions are critical to the success of future Annual Meetings. Please don't forget to fill out the evaluation forms.

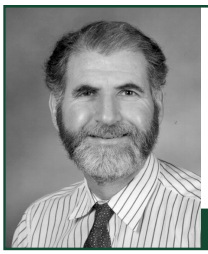
## ISHAGE Committee Meetings

The annual meeting is also an opportunity for the many ISHAGE committees to meet in person. If you belong to a committee, please inquire at the registration desk if and when your committee(s) will be meeting.

I look forward to seeing you all at the Welcoming Reception Thursday evening and the days that follow.

*Iain Webb*

## What's Inside



# From the President's Desk

Robert Negrin, MD

Much has been happening behind the scenes of our Society. Most importantly, we look forward to greeting you all in Quebec City. We have put together what I hope you agree is an outstanding group of plenary speakers, technical breakfast presentations and workshops, as well as ample time for the presentation of original abstracts. The meeting is shaping up well with good corporate support and almost 400 delegates who are already planning to attend. I would like to thank all of our corporate sponsors and exhibitors for their generous support. We look forward to seeing all of you in Quebec City which should be a wonderful setting in which to greet our friends from around the world.

I am pleased to announce that John Barrett has agreed to join Nancy Collins as a co-editor of Cytotherapy. John brings a wealth of experience and expertise, as well as a critical eye which will hopefully continue to develop Cytotherapy as a leading voice in the field of cellular therapy. I wish to thank our outgoing co-editor, Adrian Gee, whose guidance and effort has been critical to the foundation and success of the society. I continue to encourage you to send original studies to Cytotherapy.

In addition to the Quebec City meeting, there are several other meetings which have taken place through the support and guidance of ISHAGE. These included the mechenchymal stem cell meeting in New Orleans, Louisiana, which was a major success. This meeting, organized by Ed Horwitz and his colleagues, has been critical to furthering the development of this interesting cellular population and developing the scientific basis for future therapeutic concepts. In addition, the Somatic Cell Therapy Meeting organized by Steve Noga and his colleagues also proved to be an important voice in the field of experimental cellular therapeutics.

With the upcoming plan for additional regulation, we encourage you to send your comments either directly to the FDA or to the Legal and Regulatory Committee chaired by Donna Przepiorka. It remains unclear how these regulations will affect us but clearly during this period of transition, it is important that we make our thoughts heard. Additional information concerning these regulations can be found in this issue, as well as previous issues of the Telegraft. Now, more than ever, it is important that we come together as scientific societies to help guide this field. Clearly our voice is an important one in collaboration with ASBMT and FAHCT.

Please vote on new officers for the society. This mailing will be on your desk soon. Every vote counts and results of this election will be announced at the meeting in Quebec City. No chads please.

I look forward to seeing you all in Quebec City for what will be a wonderful event. If you have not already done so, please check out the website which provides information about the meeting, housing, schedule of events, as well as registration materials.

As always, please send any suggestions and/or comments directly to ISHAGE Head Office c/o Lee Buckler or directly to myself. We are always interested in hearing your comments and further developing our society.

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# From the Editor's Desk

Iain Webb, MD

# A New Editor

My two-year term as Editor of the Telegraft ends this June. This issue of the Telegraft is the eighth issue and last issue produced since I became Editor in June. In June I will begin a three-year term as Treasurer of ISHAGE. Scott Burger, Director of the Cell Therapy Clinical Laboratory at the University of Minnesota and member of the Telegraft Editorial Board for the past two years will begin his two-year term as Editor this June. I am confident that he will further improve the quality of this publication.

The past two years have been quite eventful for the society and its members, giving me and the other members of the editorial board much to report on in this newsletter. There have been significant scientific as well as changes in the regulatory framework.

On the scientific side, there have been a number of new developments in the understanding and use of immunotherapy, nonablative transplantation, non-hematopoietic and mesenchymal stem cells, etc., many of which will be discussed in Quebec City.

Here in the United States, we are still observing fallout from the gene therapy clinical trial related death that occurred at the University of Pennsylvania in the fall of 1999. Many academic centers involved in early phase trials of gene therapy have been dealing with the consequences. The review of all gene therapy related IND applications subsequently became more stringent and the number of applications has fallen dramatically. In addition, the regulatory framework for non-gene therapy related cellular approaches has also become more defined, particularly in the United States where, as outlined in previous issues of the Telegraft, one final and two proposed rules have been released by FDA in the past few months.

There have also been a lot of changes for ISHAGE. Among the most significant is that the litigation between Mary Ann Liebert and ISHAGE has been resolved and we can again shift our energies to the growth and success of the society and its journal, Cytotherapy.

Our laboratories also face significant practical challenges as well. In the Boston area as well as in many other areas, it is becoming increasingly difficult to attract and retain qualified staff members. This is that no small part related to of the boom in biotechnology and pharmaceuticals, but also represents the growth of biomedical sciences as a whole.

I am excited to begin my term as treasurer of ISHAGE. Bob Preti has done an excellent job the last six years and, despite some difficult challenges, has left the society on a sound financial footing. I hope to keep it there.

Please join me in thanking Anita Jong and Lee Buckler as well as the members of the Telegraft Editorial Board for their excellent work the last two years. Their efforts to produce a well formatted newsletter with quality content cannot be underestimated.

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# NHLBI and NCI BMT Clinical Trials Network

On January 4, 2001, NHLBI and NCI issued an RFA (request for applications) for clinical centers and a data center to participate in a blood and marrow transplant clinical trials network. The objective of this program is to establish a network that will accelerate research in hematopoietic stem cell transplantation by comparing novel therapies to existing ones for children and adults undergoing blood or marrow transplantation. Therapeutic trials may involve investigational drugs, drugs already approved but not currently used, and drugs currently used. Randomized trials are encouraged; non-randomized trials will be supported in exceptional cases only.

## Need for a BMT Clinical Research Network

There is an urgent need to evaluate promising new therapeutic approaches to hematopoietic stem cell transplantation and to disseminate the findings to health care professionals, patients and the public. Each year, thousands of patients undergo hematopoietic stem cell transplants in the United States, yet few of these patients are offered the option to enroll in a research protocol to study and improve the outcome of this life-saving but toxic and expensive procedure. There are several reasons why a blood and marrow transplant clinical research network would accelerate clinical research and evaluate new approaches to transplantation. The heterogeneity of hematopoietic stem cell transplant patients makes it difficult to accumulate a large number of comparable patients in one center. Multi-center trials will reduce the number of patients needed at each clinical center and allow accrual to be completed more rapidly. Further, a common treatment protocol will reduce variables that contribute to patient outcome and allow valid comparisons between treatments. Finally, the Network approach will increase the number of comparative trials that are conducted by providing a framework for rapid initiation of important studies, a focus on randomized studies, and efficient use of pooled clinical expertise and data management resources.

The Blood and Marrow Transplant Clinical Research Network (Network) will be a cooperative network of sixteen Core Clinical Centers, one Data Coordinating Center, the National Heart, Lung, and Blood Institute (NHLBI) and the National Cancer Institute (NCI). Core Clinical Centers will be responsible for proposing protocols that could be adopted by the Network, guiding protocol development, enrolling patients, analyzing results, and disseminating research findings.

## Data Coordingating Center

A centralized Data Coordinating Center will support the activities of the Network. These include developing protocols, devising novel comparative study designs, providing sample size calculations and statistical advice, developing data forms, performing data analyses, coordinating the activities of the Steering Committee, Protocol Review Committee, and Data and Safety Monitoring Board, and overall study coordination and quality assurance. In addition, in order to hasten accrual in Phase III protocols, the Coordinating Center with NHLBI and NCI and the Steering Committee will have the responsibility to identify qualified and interested investigators at non-Core centers who wish to enroll patients on these protocols. Arrangements for data collection and reimbursement of trial-related data collection costs at non-Core centers will be the responsibility of the Data Coordinating Center.

The Data Coordinating Center will also be responsible for obtaining biologic reagents, organizing correlative laboratory studies, arranging for storage of patient samples, and procuring other resources as required by the clinical protocols.

## Steering Committee

A Steering Committee will be the main governing body of the Network and, at a minimum, will be composed of the principal investigators of the Core Clinical Centers and the Data Coordinating Center and the NHLBI and NCI Project Scientists. The Steering Committee Chairperson, who will be someone other than an NHLBI or NCI staff member and may be someone other than a principal investigator, will be selected by NHLBI and NCI. All major scientific decisions will be determined by majority vote of the Steering Committee.

The Steering Committee will have primary responsibility for the general organization of the Network, finalizing common clinical protocols, facilitating the conduct and monitoring of the studies, and reporting study results. Topics for the protocols will be proposed and prioritized by the Steering Committee with input from the wider transplant community. For each protocol, one investigator (or small group) will take the lead responsibility for drafting the protocol along with the Data Coordinating Center, although the Steering Committee will provide input and will be responsible for assuring development of a common protocol to be implemented by other Clinical Centers.

## Establishing Subcommittees

Subcommittees of the Steering Committee will be established as necessary; for example, it is envisioned that a Publications and Presentations Committee will prioritize,

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facilitate and supervise preparation and review of manuscripts prior to submission for publication. Subcommittees to oversee reporting of graft versus host disease and establishment of an infectious diseases registry are also envisioned. Data collection will be monitored in a manner consistent with NHLBI Guidelines for Data Quality Assurance in Clinical Trials and Observational Studies.

## Protocol Review Committee

An independent Protocol Review Committee will provide peer review for each protocol. An independent Data and Safety Monitoring Board (DSMB) will monitor patient safety and review performance of each study approximately semi-annually. As a part of its monitoring responsibility, the DSMB will submit recommendations to NHLBI and NCI regarding the continuation of each study and prepare a report for principal investigators to provide to their institutional review boards (IRBs).

It is anticipated that each protocol will be implemented in at least two of the Core Clinical Centers. Clinical protocols must be approved by local IRBs and the Protocol Review Committee before initiation. The exact number of protocols supported in the five year program will depend on the nature and extent of the investigations proposed by the Steering Committee. The full text of the RFA can be found at http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-01-004.html.

The project period for the Blood and Marrow Transplant Clinical Research Network will be five years. If after three years, a review of the Network shows that it is meeting the objective of conducting effective clinical trials, there may be an announcement of a competitive renewal for an additional five years.

The network will be supported through the cooperative agreement (U01) administrative and funding mechanism. Under the cooperative agreement, the NIH assists, supports, and/or stimulates, and is substantially involved with recipients in conducting a study by facilitating performance of the effort in a "partner" role. An estimated sixteen awards for Core Clinical Centers and one award for a Data Coordinating Center will be made under this RFA. A maximum of $40 million (total costs) over a five-year period will be awarded.

Applications were received on March 19 and will be reviewed in June. Awards are anticipated by September 30, 2001.

*LeeAnn Jensen*

## Upcoming Meetings

7th International ISHAGE Annual Meeting. June 14-17, 2001. Quebec City, Quebec, Canada. Contact: ISHAGE Head Office, 777 West Broadway, Suite 401, Vancouver, BC, Canada, V5Z 4J7. Tel: 604-874-4366; Fax: 604-874-4378. E-mail: ishage@malachite-mgmt.com; Website: www.ishage.org

ISHAGE/AABB Teleconference Series. February-August 2001. Contact: Sandra Rosen-Bronson, PhD, Preclinical Science Bldg, Room LE8H, Georgetown University Hospital, 3900 Reservoir Road NW, Washington, DC, 20007. Tel: 202-784-2909; Fax: 202-687-1244. E-mail: bronson@gunet.georgetown.edu

- May 30, 2001: State of the Art in HPCs - An Overview.
- July 11, 2001: Immune Effector Cell Therapies: Tumor Vaccines and Donor Lymphocyte Infusions.
- September 5, 2001: Stem Cell Plasticity; Mesenchymal, Embryonic and Stem Cells Teleconference Series: Current Topics in Histocompatibility and Transplantation for Technologists 2001.

Cell Culture and Separations for Cell and Gene Therapies. October 1-4, 2001. Omni Hotel at the CNN Center, Atlanta, Georgia. Plant Tour: Thursday afternoon, October 4, 2001. CEUs: 2.8. Cost: Member ASME or ISHAGE $1,895; Non-Member $1,995. Enrollment Limited to: 35. Website: www.asme.org/pro_dev/ce2/bio.html

ISHAGE cGMP 2001 Workshop. December 6, 2001 (the day before ASH). Rosen Center Hotel, Orlando, Florida. Contact: ISHAGE Head Office, 777 West Broadway, Suite 401, Vancouver, BC, Canada, V5Z 4J7. Tel: 604-874-4366; Fax: 604-874-4378. E-mail: headoffice@ishage.org; Website: www.ishage.org

## 2001 Corporate Members

ISHAGE wishes to thank its 2001 Corporate Members for their support. They are:

**Amgen Inc.**
**Cell Science Therapeutics Inc.**
**Chimeric Therapies Inc.**
**MVE-Chart Industries Inc.**
**Nexell Therapeutics Inc.**
**Protide Pharmaceuticals**
**SEBRA Inc.**

ISHAGE Corporate Memberships for 2001 are now being sold. For further information on the benefits of membership see the ISHAGE website (www.ishage.org) or contact the ISHAGE Head Office by phone at 604.874.4366 or e-mail at headoffice@ishage.org.

# Graft Engineering to Define T Cell Doses in Allogeneic Transplants

**A Symposium Sponsored by Nexell Therapeutics Inc. in association with the International Bone Marrow Transplantation Meeting, Keystone, Colorado, USA. February 18th, 2001.**

The meeting was opened by Dr. J. Kemshead, Nexell Therapeutics, Irvine, California, USA, who briefly reviewed data on the performance of the Isolex 300i running the latest version of software (2.5). This dataset was compiled from customers using the Isolex, with all runs submitted to Nexell being included in the analysis (n=332). The median purity and yield of CD34 cells obtained from apheresis products was in excess of 95% and 64% respectively, for both autologous and normal donor products. No significant difference in the yield of CD34 cells was observed when comparing CD34 selection alone with procedures undertaken employing the +/- technology that is licensed for sale in a number of countries outside of the United States. The median level of T cell depletion achieved by CD 34 selection was 4.2 logs. The use of the +/- procedure enhanced this to 4.9 logs. A variety of different anti-T cell antibodies were used in the selections involving the +/- procedure; these including MoAbs to the CD4 and CD8, and CD2 antigens. Dr. Kemshead explained how these levels of T cell depletion fitted into the clinical need to remove T cells from different types of allogeneic grafts so as to reduce GvHD, minimize the possibility of graft failure, and potentially maintain a graft v tumor effect.

This point was elaborated upon in an elegant presentation by Dr. E. Waller, Emory University, Atlanta, Georgia, USA, who reported data on thirteen patients (median age31) who received T cell depleted PBSC grafts (+/- technology) from HLA haplo-identical family donors. Eleven of the group had either relapsed or refractory leukaemia/ lymphoma and two were transplanted with poor risk AML in first remission. The preparative regimen used was a variation upon that developed by Prof. M. Martelli, Perugia University, Italy; this involving fractionated TBI, Thiotepa, Fludarabine and anti-Thymocyte Globulin (ATG) (horse ATG n=3; rabbit ATG n=10). The median number of CD34 cells given to patients was 8.1 x $10^6$ /Kg body weight with a median T cell dose of 1.9 x $10^4$ cells / Kg. In eleven evaluable patients engraftment was rapid, with the time to an absolute neutrophil count of 500 achieved in a median of 11 days (range 9-11). Full donor chimerism was achieved in both the lymphocytic and granulocytic compartments. One patient developed grade 1 GvHD and one Grade 2 GvHD. No chronic GvHD was observed. Survival of patients at 100 days was 30%, with four patients remaining alive; three of these are in remission at 460, 310 and 220 days post transplant. Dr. Waller stressed the importance of these pioneering haplo-identical transplants undertaken in patients with a very poor prognosis. The study demonstrates the feasibility of the approach and shows that a combination of *in vitro* and *in vivo* T cell depletion is an effective GvHD prophylaxis without additional post transplant immunosuppression. However, delayed immune reconstitution remains a major clinical problem for patients receiving this type of transplant.

Dr. M. Horwitz, NIH, Bethesda, Maryland, USA, also used the +/- Isolex technology to remove T cells from PBSC grafts given to patients with chronic granulomatous disease (CGD). This is an inherited disorder, with patients presenting with a defect in neutrophil oxidase leading to recurrent life threatening pyrogenic infections. Patients received HLA matched allografts following a non-myeloablative conditioning therapy consisting of low intensity cyclophosphamide, fludarabine and ATG. Cyclosporine was also given for the first 100 days. Patients received a median of 7.9 x $10^6$ CD34 cells with a standard dose of T cell dose of 1 x $10^5$ cells / kg (T cells being added back to the CD 34 selected product). Donor lymphocyte infusions (DLI) were given on day 30 (2 x $10^6$ CD3 cells / kg) and day 60 (1 x $10^7$ CD3 cells / kg) if patients showed less than 60% T cell chimerism. Toxicities associated with the transplant were significant but clinically manageable. In addition, four patients developed acute GvHD following DLI, one responding to thalidomide and the others to oral steroid therapy. With a median follow up of one year eight of the patients have oxidase normal neutrophils at a level that is considered curative for the disease.

Dr. M. Lowdell, Royal Free Hospital, London, UK, presented pre-clinical studies involving the manipulation of allografts to deplete selectively the T cell subsets responsible for GvHD whilst retaining lymphocytes capable of eliciting a Graft verses leukemia (GvL) and an anti-viral effect. Mononuclear cells from HLA matched donors were

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co-cultured with irradiated recipient cells that had been pre-stimulated with cytokines in a modified mixed lymphocyte culture. The alloreactive donor lymphocytes were removed following incubation of cells with an anti-CD69 MoAb and anti-mouse Ig coated Dynabeads using Isolex technology. In an animal model established to study GvHD Dr. Lowdell showed that animals receiving non-manipulated donor grafts ($10^7$) cells suffered fatal GvHD within 10 days of administering the graft. In contrast, animals given a similar number of cells depleted of the alloreactive component survived beyond 70 days without any evidence of GvHD at post mortem. Recently, the group has also shown that human alloreactive T cells can be removed from grafts using the same methodology. These grafts retained anti-CMV reactivity as determined by tetramer staining and Elispot analysis. Dr. Lowdell is striving to begin a Phase I study applying this strategy with a view to developing safer allogeneic transplants with lower transplant related mortality.

During the 90 minute session the audience, of approximately 400 delegates, enjoyed a hearty breakfast as well as the stimulating questions that followed each presentation.

*John Kemshead*



# San Diego Stem Cell Meeting

The 9th Annual International Symposium on Recent Advances in Hematopoietic Stem Cell Transplantation was held at the Catamaran Resort Hotel in San Diego on March 29-31. Over 150 participants attended the two day event. Presentations on basic research focused mainly on the plasticity of the stem cells, mesenchymal stem cells, as well as division control and motility of the cells. Besides the much needed updates on the clinical progress in autologous and allogeneic transplantation in different diseases, special attention was given to the use of autologous stem cells in auto-immune disease, and non-myeloablative conditioning with allogeneic stem cells. As many clinical cell processing laboratories are involved in producing immune-competent cells (such as dendritic cells and T cells) for clinical trials, two sessions were allotted to address the potential applications of peptide and cellular vaccines. Topics of immune potentiators were also discussed. Early clinical results were encouraging. It appears that the scope of cell processing laboratories is expanding beyond the traditional bone marrow, PBPC and cord blood to include dendritic cells and T cells, with and without activation. All participants enjoyed the mild weather of San Diego, although only Friday afternoon was sunny. Plans for the next and 10th annual symposium are already under discussion. Anyone with ideas and suggestions are welcome to contact UCSD CME office (http://cme.ucsd.edu), Ping Law (plaw@ucsd.edu) or Edward Ball (tball@ucsd.edu).

*Ping Law, PhD*

# Mesenchymal and Nonhematopoietic Stem Cells Meeting: Report on the March 22-24, 2001 Meeting in New Orleans, LA

This meeting was sponsored by ISHAGE, St. Jude Children's Research Hospital and Tulane University Health Science Center. Drs. Edwin Horwitz, Armand Keating, Malcolm Brenner, Darwin Prockop and Brian Butcher comprised the organizing committee. This was one of the first meetings to concentrate specifically on the science related to nonhematopoietic stem cells - and was certainly ISHAGE's first venture into this meeting format.

*Workshop Panel*

The meeting began with a reception that was immediately followed by a keynote address by Dr. John Gearhart of the Johns Hopkins University. He discussed his ground-breaking research on the characterization and transplantation of human embryonic germ cell derivatives. Dr. Gearhart went into great detail on the varied cell and tissue types that can be derived from these primitive cells and also covered some of the ethical and political issues now confronting researchers involved in this field.

On Friday, the sessions concentrated on the characterization of mesenchymal stem cells (MSC) and marrow stromal cells. In contrast with Dr. Gearhart's lecture, Dr. Catherine Vefaillie, at the University of Minnesota, discussed the "plasticity" of multipotent stem cells derived from adult tissue. It was clear that there is now more than one pathway for deriving a vast array of cell types and tissues from a variety of original sources. There were several lectures on human MSC (one of the derivatives of nonhematopoietic stem cells). These cells can be differentiated into several cell types which showed promise in wound healing, tissue regeneration, the delivery of gene products to specific sites and for engrafting sub optimal numbers of Hematopoietic stem cells. There were also discussions on the *ex vivo* cytokine expansion of bone marrow derived stem cells. The clinical trials sessions mainly discussed current trials involving marrow derived stromal cells and genetically modified, *ex vivo* expanded MSC. These trials, although promising, are in the early stages of development and await Phase III trial development.

*Conference Co-chairs: Edwin Horowitz and Armand Keating*

*Darwin Prockop and Massimo Dominici*

There were two workshops. The first centered on the side effects of systemic infusion of MSC. Malcolm Brenner chaired Workshop I. Essentially, most of the infusional side effects were related to increased volume, possible allergic sequellae and cytokine-mediated responses and were easily controlled with standard prophylaxis used for hematopoietic stem cell infusion. Dr. Keating chaired Workshop II that discussed the characterization of MSC. The majority of the presentation centered on flow cytometric characterization of specific cell types and current attempts at standardization of the clinical materials.

Other cell and tissue types were targeted for Saturday's morning sessions. A fascinating talk was delivered by Evan Snyder of Children's Hospital of Boston on neural stem cells. A rat animal model clearly demonstrated that these cells have the ability to travel throughout the CNS and aid in the repair of damaged motor neurons. Interestingly, preliminary data indicated that the infused neural stem cells seemed to nurture already existent neural cells resulting in regeneration rather than replacing their function. A second session discussed the differentiation and function of skeletal muscle stem cells. The meeting ended with a discussion of current problems in clinical applications of these cell types. It was clear that many difficulties lay ahead in translating these research techniques to full-scale clinical trials with wide utility. However, the potential for cellular therapy using these cell types is very exciting and will no doubt lead to treatment breakthroughs in the not-to-distant future.

*Steve Noga*

# Somatic Cell Therapy Conference Held on Captiva Island, FL

The 1st Annual Somatic Cell Therapy ($SCR_x$) meeting took place at South Seas Plantation, May 4-6, 2001. This was a little more than a month after researchers convened for the Mesenchymal and Nonhematopoietic Stem cell meeting in New Orleans. This meeting was sponsored by The Johns Hopkins University, ISHAGE and AABB. The organizing committee consisted of Steve Noga (chairman), Janice Davis-Sproul (workshop chairman), Scott Burger, Andrew Pecora, Scott Rowley and Leana Harvath. The goal of the meeting was to bring together experts in clinical trials, $SCR_x$, regulatory issues, ethics and the law to discuss the many hurdles that await the establishment of clinical $SCR_x$ programs. This tranquil, out of the way location was chosen to allow participants to network in an informal manner throughout the symposium. Nearly 100 registrants and faculty attended the conference.

*Joyce Frey Vasconcells and Janice Davis-Sproul*

As with the New Orleans meeting, Dr. John Gearhart from Johns Hopkins University delivered the opening presentation. Dr. Gearhart covered several of the problems facing investigators who are trying to move embryonic stem cell derivatives into the clinic. Dr. Catherine Vefaillie from the University of Minesota continued the theme in her discussion of the moltipotentiality of adult stem cells. Drs. Christopher Stevens and Zorina Pitkin discussed the current clinical trials taking place at Circe Biomedical involving porcine liver support systems for patients requiring liver transplantation. Their initial trials show successful prolongation of life while awaiting transplant. Zorina Pitkin covered the many requirements and issues surrounding the use of xenogeneic cell based therapies, in general and specifically pertaining to their porcine systems.

Workshops composed the afternoon sessions for both Friday and Saturday. Registrants had their choice of sessions on Tissue Engineering, Cell Expansion and Core technologies on Friday and Facility Issues, Standards/Legal issues or Gene Therapy regulatory issues on Saturday. The workshops, which were each presented twice, had great attendance and strong audience participation. A casual Friday evening reception by poolside provided another opportunity for faculty and registrants to socialize and network.

Dr. Camillo Ricordi, University of Miami, started off Saturday's session with a discussion of pancreatic islet cell processing and current clinical trials. Multi-center trials have now begun due to the encouraging data from initial studies showing durable implantation of pancreatic islets and regulation of insulin levels. Hurdles include the current need for more than one pancreas per patient and more diabetics in need of therapy than the current supply of organs can support. There were a series of lectures on regulation, legal issues and ethics. Scott Burger gave an excellent review of good clinical practice guidelines, which was also echoed, in part, during Joyce Frey Vasconcells' presentation on the FDA's issues with cell and gene therapy. Current ethical issues and IRB requirements for $SCR_x$ were discussed by Dr. Melody Lin from the Office of Human Research Protection. Saturday morning concluded with a lecture from Jeffrey Johnson, Esq, Vinson & Elkins, on the current status of litigation in the $SCR_x$ field and what $SCR_x$ facilities and individuals can do to prevent being involved in litigation.

Sunday morning began with a lecture by Dr. Scott Rowley, Hackensack Medical Center,on good tissue practice (GTP). Scott contrasted the FDA guideline document for somatic cell therapies with the current standards used by FAHCT for hematopoietic stem cell processing. It should be noted that similar comparisons were discussed with current AABB standards during a workshop by AABB spokesperson, Brenda Alder. The remainder of the symposium was devoted to future directions in cell and tissue-based engineering. Dr. David Avigan, Beth Israel, Deaconess Medical Center,lectured on dendritic cell therapies and vacinnes and Dr. Cynthia Dunbar, NIH,NHLBI, discussed the trials and tribulations of American Gene Therapy. The very promising initial pre-clinical studies were covered as well as the later clinical trials. Dr. Dunbar noted the disappointing lack of translation of gene therapy to the clinic and stated the concerns of the NIH that little has been delivered in terms of therapy despite significant expenditures in government-sponsored research. Still, she noted that new vectors may

*John Gearhart*

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show greater promise for future clinical trials. Dr. Mary Malarkey, FDA gave an in depth report on current requirements and guidelines for cellular processing facilities. This generated considerable discussion among participants. Emphasis was placed on the many sources that can be accessed *via* the FDA or its website in designing both facilities and clinical trials in $SCR_x$. Dr. Burger followed with a discussion on the translational development of novel therapies. Scott emphasized the enormous impact on resources (both financial and human) that cell therapy trials have on a cell processing facility and institution. Academic centers are not prepared to incur this kind of drain with the realization often taking place after becoming committed to a particular therapy or protocol. It became clear that few academic or even pharmaceutical entities have a committed way of actually bringing cellular therapies from bench to bedside.

In the final lecture, Dr. Stephen Noga asked the audience to look ahead and envision $SCR_x$ in the future. Given the new guidelines being developed for good clinical practice and regulations for good tissue practice, it may be impossible for both academia and biotech/pharma to develop extensive $SCR_x$ trials on their own. Unprecedented cooperation, both within the institution, among basic researchers, clinical processing and among clinical trial physicians and in collaboration with biotech/pharma may be mandatory at the earliest stages of trial development for future studies to be successful. Dr. Noga suggested that BMT units may become the obvious choice to perform cellular therapies due to their regulatory structure, especially if the trend towards outpatient transplant continue to reduce their utilization. Also, he suggested that currently accredited hematopoietic stem cell processing facilities can be adapted to handle many of the $SCR_x$ procedures outside of the more specialized protocols (gene therapy, etc.) Given the high potential for benefit in this field and the expected controversies and many as yet-to-be-defined issues awaiting $SCR_x$ specialists, the organizers agreed to consider an annual meeting format for this topic.

*Steve Noga*

# Tech Talk... Assessing PBPC Graft Quality

In this edition of Tech Talk we respond to a few questions that occasionally arise regarding the assessment of PBPC graft quality. While some of these issues are common to several types of cellular products, we will focus on PBPC as this is the most commonly used source of autologous hematopoietic grafts in the U.S. and because the characteristics of these mononuclear cell fractions present unique challenges to lab analyses.

While CD34 quantification has become the primary method for graft assessment, most centers still quantitate dose of nucleated cells or MNC, as well as CFU-GM. Determining CFU-GM dose by progenitor assay is less commonly performed today than in recent years, due in part to the 14-day delay in obtaining results, the challenge of controlling assay variability, but perhaps most importantly reflecting improvements in CD34 measurement.

Several options exist for nucleated cell and mononuclear cell counting methodology. Impedance-based automated hematology analyzers often are used for this application. These instruments have been designed to identify and enumerate peripheral blood cells, however. The atypical mononuclear cell populations present in mobilized peripheral blood may not be accurately counted or, more precisely, not accurately categorized by these devices. These problems are more often seen with cell counters intended for use in physician office laboratories. For reasons of size, maintenance, and cost, however, these are precisely the instruments most likely to be purchased for a cell engineering laboratory. While the Coulter STKS, for example, may not have the limitations of a smaller cell counter, the STKS cell counter is usually located in the hospital hematology laboratory, rather than the cell engineering laboratory.

Some centers use particle counters to enumerate cells. While not generally capable of discriminating cell subpopulations, particle counters may be less likely to produce spurious results due to interfering substances, such as fat, present in some cellular products.

Recent advances in cell enumeration technology have led to additional alternatives. Some cell counters, for example, are intended to differentiate hematopoietic progenitor cells. Some of these newer devices use refractive index and other methodology to give more accurate results for these products. As transplant centers gain experience with these instruments it will be interesting to examine the growing body of performance qualification and correlation data, particularly in regard to predicting optimal collection date. Given the challenges laboratories face when attempting to add new equipment, however, these novel instruments may not reach widespread use for some time.

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A manual cell count, performed using a hemacytometer, is always an alternative. Correlation between the manual and automated count varies between centers, however, likely due to use of different types of automated cell counters, as well as proficiency in manual counting. There are two contrasting theories regarding the accuracy of manual cell counts. One position contends that since humans are only counting a few hundred cells and multiplying by large dilutions, the manual method cannot be as reliable as an automated method which counts many more cells. The opposing view is that manual counts are less vulnerable to interfering substances, and are therefore more accurate.

Different centers have varying policies for when manual cell counts and differentials are to be performed. In general, manual counts seem to be more commonly performed for bone marrow products than for PBPC. An informal survey reveals some disappointingly circular reasoning at work. Centers performing manual differentials generally describe poor correlation with automated differentials, a finding often used to justify the practice of manual counting. The centers that have found favorable correlation between manual and automated methods understandably use the less time-consuming, automated method routinely.

Once the cell count is obtained most centers will quantify the mononuclear cell dose for the PBPC product. Again, it seems there is no standard here. Some perform manual differentials on slides, some accept the automated differentials, and still others assume that the apheresis machines and their operators are so efficient that the nucleated cell and mononuclear cell dose are not significantly different and use the two interchangeably. There is, however, some variability in purity among manufacturers and operators of apheresis instruments and this should be considered. We recommend that, before assuming that nucleated cell dose is equivalent to mononuclear cell dose, one should validate that this is, in fact, the case.

However the differential is obtained, several conventions can be used for calculating the percent mononuclear cells. Some laboratories simply add the percent monocytes and percent lymphocytes, while others add together lymphocytes, monocytes, and blast-like cells. One can also enjoy a long-lasting argument over whether or not to include myelocytes-mononuclear cells, but destined to become granulocytes.

Evidently there is no uniform practice regarding manual or automated cell counts and differentials. The ramifications of this can be substantial, as many centers determine graft $CD34^+$ cell content as the product of the percent $CD34^+$ cells and the nucleated or mononuclear cell concentration. This uncertainty vanishes, however, when single-platform methods are used to enumerate $CD34^+$ cells, with internal controls to permit accurate measurement of $CD34^+$ cell concentration. Under these circumstances, is it relevant at all to attempt to measure mononuclear cells?

Perhaps the wisest approach of all is embodied in the FAHCT guidelines, which do not specifically address methodology, but rather require the laboratory director to establish tests to assess product quality. The key aspect is that each facility decides what path to take, records this path in the SOP, and follow it. Certainly as technology improves, we can then revisit these practices and consider revising them based on data.

*Scott Burger and Kathy Loper*

# GOOD MANUFACTURING PRACTICES WORKSHOP 2000 DELEGATE MATERIALS

## The ISHAGE GMP 2000 Workshop Materials are now for sale in binder and cd-rom format from the ISHAGE Website or Head Office (while limited supplies last)

These materials are designed to expose you to the knowledge of a diverse group of authors with experience in industry and hospital-based cell engineering laboratories. ISHAGE and the GMP Organizing Committee hope that these materials will prove a useful for you in gaining information about GMP principles and how they can be applied in your laboratory.*

The materials, sold either in binder or CD-ROM format, include the following topics:

**A. OVERVIEW**
- GMP Overview

**B. FACILITY**
1. Facility Design and Environmental Monitoring
2. GMP and Cell Therapy: Facility Design and Monitoring
3. Environmental Monitoring in the Cell Processing Laboratory
4. Design and operation of a current good manufacturing practices cell-engineering laboratory

**C. EQUIPMENT & SOFTWARE**
1. Equipment and Software Validation and Monitoring
2. Examples of Facility & Equipment Policies

**D. PROCESS**
1. Process Validation & Control
2. Process Control: Examples of Policies and Procedures
3. Process Policy and Procedure Examples

**E. PERSONNEL**
1. Personnel Training, Competency and Proficiency Testing
2. Additional Examples of Personnel Documentation

**F. QUALITY CONTROL**
1. Quality Control and Release Testing
2. Product Release Assays
3. Quality Control Policy Examples

**G. GMP IMPLEMENTATION**
1. Implementation of cGMP in a Hospital-Based Cell Processing Laboratory
2. GMP Implementation: Examples & SOPs
3. Centralized Laboratory Cell Processing in a cGMP Environment
4. Implementation of ccGMP in a Gene Therapy Laboratory

**H. FAHCT**
1. FAHCT: Standards, Inspection & Accreditation
2. FAHCT Accreditation: Common Deficiencies During O-site Inspections

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*The sample procedures provided are designed to provide examples of good manufacturing practices for facilities and individuals performing hematopoietic cell transplantation and therapy or providing support services for such procedures. These samples are not intended to include all of the procedures and practices that a facility or individual should implement if the standard of practice in the community or federal or state laws or regulations establish additional requirements. Each facility and individual should analyze their practices and procedures to determine whether additional standards or procedures apply. ISHAGE and its sponsors disclaim any responsibility for setting maximum standards and expressly do not represent or warrant that compliance with the sample standard operating procedures included herein are an exclusive means of complying with the standard of care in the industry or community.

## FAHCT Workshops at ISHAGE 2001

***Preparing Your Facility for FAHCT Inspection***

Facilities who have applied for FAHCT accreditation and are in the process of preparing for their on-site inspection are encouraged to attend the FAHCT Workshop on June 14, 2001 in Quebec City, Canada. The workshop is designed to explain the FAHCT accreditation requirements, answer questions, clarify the intent of the checklist questions, and assist applicants and potential applicants in organizing and preparing their program for a FAHCT on-site inspection. The fee for this course is $500 prior to June 1, 2001 and $550 after June 1, 2001.

***Inspector Continuing Education***

A new FAHCT Inspector Continuing Education course will be offered at the annual ISHAGE meeting in Quebec City, Canada on June 14, 2001. The workshop is designed to update current FAHCT inspectors on inspection requirements, provide feedback regarding the inspection/accreditation process and to stimulate discussion about effective and ineffective inspection practices and techniques. Representatives from the FAHCT Board of Directors, including the FAHCT Accreditation Chairman, and members of the FAHCT Accreditation Office will be in attendance at this workshop to answer questions and contribute to inspector discussions. All active FAHCT Inspectors will be required to attend a continuing education course at either the annual ISHAGE meeting or ASBMT meeting.

Participants interested in attending either course should contact the FAHCT Office at (402) 595-1111 to register.

## Accreditation Renewals

The first transplant programs to earn FAHCT-accreditation are approaching their renewal dates for certification. FAHCT-accreditation is valid for three years. Programs required to renew their accreditation will receive a renewal registration form, an inspection checklist and a list of required documentation prior to their expiration date.

## Accredited Facilities

Seven additional BMT centers have gained FAHCT accreditation since the last issue of the *Telegraft*. FAHCT has now accredited 69 centers. There are 125 other centers in various stages of application, inspection or accreditation pending.

The latest facilities to gain voluntary accreditation, along with their Program Directors are listed in the categories below:

*Autologous peripheral blood progenitor cell transplantation, including collection and laboratory processing:*

- Evanston Northwestern Healthcare, Evanston, IL; Program Director: Lynn Kaminer, MD

## Just the FAHCTs

*Allogeneic & autologous marrow, peripheral blood progenitor cell transplantation, including collection and laboratory processing:*

- Emory University, Bone Marrow and Stem Cell Transplant Center, Atlanta, GA; Program Director: Edmund K. Waller, MD, PhD
- LDS Hospital, Salt Lake City, UT; Program Director: Finn Petersen, MD
- Penn State Milton s. Hershey Medical Center and Penn State University College of Medicine, Hershey, PA; Program Director: Witold B. Rybka, MD
- Medical College of Virginia Hospitals/Virginia Commonwealth University, Richmond, VA; Program Director: John McCarty, MD
- University of Colorado Health Science Center, Denver, CO; Program Director: Roy Jones, MD, PhD

*Allogeneic & autologous peripheral blood progenitor cell collection, PBPC and bone marrow laboratory processing and storage:*

- ItxM Clinical Services, Pittsburgh, PA; Program Director: Joseph E. Kiss, MD

For a complete list of accredited facilities, please visit the FAHCT website.

*Linda Miller*

Foundation for the Accreditation of Hematopoietic Cell Therapy

FAHCT Accreditation Office: (402) 595-1111
**www.fahct.org**

| | |
|---|---|
| Facilities Registered | 188 |
| Facilities Inspected | 123 |
| Accredited | 62 |
| Inspected/Pending Accreditation | 61 |
| Inspections in Process | 18 |
| Facilities Completing Checklists | 47 |
| Inspectors Trained | 306 |

# Second JACIE Training Course in Barcelona in Collaboration with FAHCT

The Joint Accreditation Committee of ISHAGE Europe and EBMT (JACIE) held its second inspectors training course in Barcelona on March 1st and 2nd. More than 30 professionals representing most countries in Europe attended the meeting. In addition to the teaching course professionally given by FAHCT representatives, Dr. Adrian Gee and Dr. Fred Le Maistre. FAHCT also performed training inspection of the clinical program and stem cell collection units of the "Hospital de la Santa Creu i Sant Pau" as well as to the cell processing unit of "The Cryobiology and Cell Therapy Department of the Cancer Research Institute of Barcelona". We are grateful to our Spanish colleagues who made a great job preparing the inspection. This practical training inspection made also Europeans believe that accreditation acceptance is achievable following the training protocols made by FAHCT.

During the last day of the meeting a general discussion concluded with that many transplant centers around Europe are interesting in joining JACIE and start the accreditation.

*(l-r): Gunnar Kvalheim, Alois Gratwohl, Alvaro Urbano-Ispizua, Adrian Gee, Fred LeMaistre*

Importantly, the Spanish health authorities is the first country that has adopted JACIE standards as an reference for excellence accreditation of transplant teams. Hopefully this will lead to that other countries consider to do the same.

Altogether, the second JACIE training course has been a crucial step ahead in the implementation of the Accreditation Program for Hemopoietic Progenitor Transplants in Europe.

*Gunnar Kvalheim*

# 2001 AABB/ISHAGE Audiconference Series

ISHAGE and the American Association of Blood Banks (AABB) will again cosponsor a series of three audioconferences on cell processing topics this spring and summer. Responding to feedback received concerning last year's series, Scott Burger, JoAnna Reems and I have put together the following program:

| | | |
|---|---|---|
| May 30, 2001 | - | Director/Moderator: Iain Webb, MD, Dana Farber Cancer Institute, Boston, MA, USA<br>Topic: State of the Art in Hematopoietic Progenitor Cells |
| July 11, 2001 | - | Director/Moderator: Scott Burger, MD, University of Minnesota, Minneapolis, MN, USA<br>Topic: Immunotherapy; Dendritic Cell Vaccines and DLI (Lymphocytes) |
| September 5, 2001 | - | Director/Moderator: JoAnna Reems, PhD, Puget Sound Blood Center, Seattle, WA, USA<br>Topic: Stem Cell Plasticity; Mesenchymal, Embryonic and Stem Cells |

The level of content of these audioconferences is meant to be a compromise between the content of the audioconferences presented the first two years. The first audioconference should have a broader appeal than the subsequent ones, which will cover topics in greater detail.

The audioconference format is one that has been successfully used by the AABB for several years. It allows groups of attendees to hear recognized experts present current material, without the expense of travel to annual meetings. Facilities across the world are able to register to be sites for the program. The speakers and moderators present and discuss material from their home locations, while the slides or other audiovisual materials are shown simultaneously at each of the registered sites. You may register using the registration form enclosed or available from the "meetings" section on the ISHAGE website (press "refresh" on your browser if you do not see it) or by contacting the ISHAGE Head Office.

*Iain Webb*

# FAQ on the FDA Final Rule on Establishment Registration and Listing

## (Federal Register, Volume 66, No.13, pp.5447-69, January 19, 2001)

The new FDA rule on registration and listing engendered a number of questions. With assistance from Martie Wells at the FDA, we have prepared a series of FAQ to help cell processing labs understand application of the rule to their own establishments.

HCT/P refers to "human cells, tissues, and cellular and tissue-based products".

1. **Where can I find a complete copy of the final rule?**
   Access the Federal Register via the GPO web site (www.access.gpo.gov/su_docs/aces/aces140.html ) or use the link on the ISHAGE Legal and Regulatory web page (www.ishage.org/committees/Committees/LRAcommittee.htm). Instructions to obtain the forms to submit are also at those sites.

2. **When do we have to register?**
   For hematopoietic HCT/P establishments, the registration rule is effective January 21, 2003.

3. **If we chose to register early, will we be inspected before 2003?**
   No. Hematopoietic HCT/P manufacturers may register voluntarily now, but they will not be inspected until the rule becomes effective in 2003.

4. **Do establishments outside the US who collect, process and distribute hematopoietic HCT/P to US transplant programs need to register?**
   Yes. Any foreign establishment sending to the US hematopoietic HCT/P regulated under this rule will need to register and list in 2003 just as the US operations are required to do.

5. **If we manufacture only one product that has to be listed, and the rest of our products fulfill the criteria for exemption, will that make inspections easier for us to handle?**
   No. You will still have to assure that you are in compliance with all of the applicable requirements. You have until 2003 to get all aspects of the operation ready for Good Tissue Practice (GTP).

6. **I understand that minimally manipulated marrow from a closely related allogeneic donor is not regulated under this rule. What does minimally manipulated mean?**
   The FDA has defined minimally manipulated as "processing that does not alter the relevant biological characteristics of cells or tissues". Examples are given in Table 1 *according to the current interpretation of the rule*. However, this may change.

   Note: Minimally manipulated bone marrow (autologous, family-related and unrelated) for homologous use and not combined with a drug or device (except for a sterilizing, preserving or storage agent, if the agent does not raise new clinical safety concerns with respect to the bone marrow) is not considered an hematopoietic HCT/P by the FDA.

Table 1. Examples of Minimally Manipulated and Manipulated HCT/Ps

| Minimally Manipulated | Manipulated |
|---|---|
| Plasma depletion by expression<br>Cryopreservation<br>Buffy coat preparation by cell processor<br>Platelet removal by centrifugation<br>Mononuclear cell preparation by cell processor<br>Mononuclear cell preparation by density gradient<br>Red blood cell depletion by starch<br>Selective depletion of B, T or tumor cells by antibody + complement<br>Selective depletion of B, T or tumor cells by magnetic separation using antibody-coated beads<br>Positive selection of $CD34^+$ cells<br>Positive selection of B or T lymphocytes or subsets | Chemical purging<br>Ex vivo expansion<br>Elutriation<br>Complex negative selection procedures<br>Genetic Manipulations |

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7. **I understand that labs processing and releasing peripheral blood stem cells and cord blood cells will need to register. Is that true even if the components are for autologous or closely-related recipients?**
   All peripheral blood and cord blood stem cell establishments must register. Table 2 summarizes which hematopoietic HCT/Ps commonly processed by ISHAGE members labs must be listed. Closely-related is defined as first or second degree blood relatives under this rule.

8. **If the product fulfills the criteria for listing, but manufacture is on an IND or IDE, does it need to be listed? If this is the only product made at the establishment, does the establishment need to register?**
   The background section on the rule interprets regulation to cover hematopoietic HCT/Ps made on an IND or IDE, but this issue is still under discussion, and further information will be available at a later date.

Table 2. Commonly Processed Products That Must Be Listed

| HCT/P | For Autologous Use | | For Closely-Related Use | | For Distantly-Related or Unrelated Use | |
|---|---|---|---|---|---|---|
| | No or Minimal | Manipulated | No or Minimal | Manipulated | No or Minimal | Manipulated |
| Marrow | No | Yes | No | Yes | No | Yes |
| Mobilized PBSC | Yes | Yes | Yes | Yes | Yes | Yes |
| Cord Blood | Yes | Yes | Yes | Yes | Yes | Yes |
| Donor Lymphs | Yes | Yes | Yes | Yes | Yes | Yes |
| Cytotoxic Lymph | - | Yes | - | Yes | - | Yes |
| Dendritic Cells | - | Yes | - | Yes | - | Yes |
| Mesenchymal | - | Yes | - | Yes | - | Yes |
| Marrow RBC | Yes[1] | - | Yes[1] | - | Yes[1] | - |
| PBSC Plts | Yes[1] | - | Yes[1] | - | Yes[1] | - |

[1]Regulated as a blood product

9. **If the product fulfills the criteria for exemption from listing, but manufacture is on an IND, does it need to be listed?**
   Whether exempt products made on an IND or IDE need to be listed is still under discussion, and further information will be available at a later date.

10. **We produce minimally manipulated peripheral blood mononuclear cells by apheresis from nonmobilized donors for immunotherapeutic use (donor lymphocyte infusions or DLI). Do these need to be registered?**
    Yes. DLI is considered an hematopoietic HCT/P.

11. **What about mesenchymal cells?**
    Mesenchymal cells will need to be listed, and they will fall under the 2003 effective date. The same will be true for other stem cells, such as SP cells, for which applied technology may be developed between now and the 2003 effective date.

12. **Our lab removes platelets from PBSC by centrifugation and returns them to the PBSC donor. We also remove RBCs from marrow using a cell processor, and return the RBCs to the marrow donor. Will these be regulated as hematopoietic HCT/P?**
    No. Platelets from PBSC and RBCs from marrow are regulated as blood products. If they go back to the donor from whom they were collected, they are considered autologous blood products.

More information can be found at the FDA FAQ site (www.fda.gov/cber/tissue/docs.htm). As updates on interpretation become available, they will be published in the Telegraft and posted on the ISHAGE web site. The LRA workshop at the annual meeting in Quebec will cover this issue in greater detail, and members are encouraged to bring more questions to that workshop.

*Donna Przepiorka*

**Third Bi-Annual Conference on**

# Applications of Flow Cytometry in Blood and Marrow Stem Cell Transplantation

**Thursday, June 14, 2001**
**Québec City Convention Centre**
**Canada**

**Program Chair: Lawrence Lamb, Jr., PhD**

### High Speed Cell Sorting of Specific Graft Populations for Immunotherapy and Graft Engineering

**Lawrence Lamb, Jr., PhD**
South Carolina Cancer Center

**Mr. Peter Lopez**
The Aaron Diamond AIDS Research Center

**Michele-Keane Moore, PhD**
Division of Cellular and Gene Therapy
OTRR/CBER/FDA

**Adrian Gee, MIBiol, PhD and April Durett, MSc**
Center for Cell & Gene Therapy
Baylor College of Medicine

**Frits van Rhee, MD, PhD**
University of Arkansas

### Quantitative Flow Cytometry in the Assessment of Immune Function Following Stem Cell Transplantation and Immunotherapy

**Gerald E. Marti, MD, PhD**
Division of Cellular and Gene Therapy
OTRR/CBER/FDA

**Lawrence Lamb, Jr., PhD**
South Carolina Cancer Center

**Smita Ghanekar**
BD Pharmingen