

## What does the Lab Contribute to an IND/IDE Study?

Report from the ISHAGE 2001 Legal and Regulatory Affairs Workshop

The field of hematopoietic stem cell transplantation has matured greatly over the past two decades, and there are presently numerous indications for which allogeneic or autologous transplantation has become the standard of care. Nonetheless, in an effort to continue to improve outcomes and expand indications, many patients are still treated on protocols testing investigational drugs, novel biologics, or new devices for cell processing.

With the adoption of Good Tissue Practice (GTP), operation of the cell processing laboratory has largely been standardized. It is important to know, however, what to do when conduct of an IND or IDE study differs from the routine practices of the cell processing laboratory, and what the laboratory must provide even at the stage of preparation of the IND. The purpose of the workshop was to provide expert opinion from authorities in the field regarding specific scenarios of IND and IDE studies.

**SCENARIO 1: Your clinical colleagues have signed up to participate in a multicenter study of a new growth factor administered after autologous marrow transplantation to reduce the period of neutropenia. The IND is held by the sponsor/manufacturer. The treatment plan in the protocol indicates that the patients will received a TNC dose of  $1-2 \times 10^8/\text{kg}$ . What are the responsibilities of the cell processing lab?**

All elements of GTP should be followed. In addition, the lab should review the IRB-approved protocol and keep the protocol in a place easily accessible by the laboratory staff. The protocol should be reviewed to identify differences from current practice. In the scenario provided, the TNC dose range for marrow may be different from what is currently used in the lab, and a process must be put into place to ensure that products issued are consistent with the protocol-specified cell dose. This might include a protocol-specific worksheet.

There should be a mechanism to identify the protocol on the cell processing orders, so that the technologist is able to use the correct worksheet and crosscheck the component against the protocol prior to release. An algorithm should be designed to deal with deviations from protocol-specified parameters. The plan should include notifying the Principal Investigator, since any treatment deviation must be reported to the sponsor and FDA.

Finally, the product should be released with an component form for the medical record, so that the monitors auditing the charts can confirm that the correct cell dose was administered.

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**SCENARIO 2: Your clinical colleagues have signed up to participate in a multicenter study of a new disposable device for CD34-selection of autologous peripheral blood stem cells. The IDE is held by the sponsor/manufacturer. The research nurse drops off in the lab a case of the devices, a copy of the procedure from the manufacturer, and a set of case report forms which consist essentially of detailed worksheets. What are the responsibilities of the cell processing lab?**

First and foremost, secure the devices. Inspect the shipment, review the manufacturer's instructions for proper storage conditions, store in a locked place under the appropriate conditions, and set up a tracking mechanism for the inventory that includes the protocol number, device identification numbers and expiration date. At some institutions, investigational devices are kept in the investigational drug pharmacy to avoid the need for the cell processing lab to duplicate the secured storage area and detailed tracking system. At the time of expiration, outdated devices should be returned to the manufacturer and a new shipment ordered. Outdated investigational devices should not be destroyed or discarded without written instructions from the manufacturer.

Next, prepare the lab for the procedure. All the responsibilities listed in Scenario 1 apply here. In addition, although the manufacturer supplied a procedure, an SOP should be written specifically for the protocol. The SOP should include vendors that might be needed for special reagents dictated by the manufacturer, and the expected results of the procedure as indicated by the manufacturer. The SOP should then be validated using nonclinical material (discarded or extra collections obtained with IRB approval or a "mocked-up" component using alternate sources). A summary of the validation studies should be maintained. Personnel should be trained using nonclinical material. Ideally, the initial training should be done by the sponsor; the technologists should not have to "figure it out" themselves.

The worksheet should be validated as well. If the manufacturer's worksheet does not include all the usual elements dictated by the laboratory's SOP for worksheets, then an addendum page may be needed, or a new worksheet devised. Since the case report form needs to be completed no matter what, transcriptional errors are avoided if only an addendum is used rather than preparing a whole new worksheet.

Finally, the protocol should also be reviewed to determine if reference samples need to be stored or sent to a central laboratory, or if specific assays need to be validated across centers in the multicenter setting. In the scenario described above, enumeration of CD34 cells might need to be

standardized for all institutions participating in the study. In addition, some sponsors provide patient-care funds for protocol-specific charges. Since most clinical cell processing facilities operate from fixed budgets driven by clinical procedures only, the Lab Director should submit a budget to the Principal Investigator to include in the contract in order to recoup lab costs for research.

In monitoring engraftment in the lab, you notice that engraftment is much more rapid with the experimental device than with the old device that you were using. There is an abstract deadline coming up for an ISHAGE meeting. Is it okay for you to submit an analysis of engraftment comparing the two devices?

No. Data from such studies are considered confidential, and use of the data is generally dictated by a contract between the Principal Investigator and the Sponsor. It is hazardous to publish or present data from any protocol without first obtaining permission from the Principal Investigator, since premature publication of partial results may adversely affect the ability of the Principal Investigator to publish the final results. In addition, if patient-specific clinical correlates or demographic information are needed, IRB approval would be required for a chart review, if the patients did not provide consent for the medical records to be reviewed by personnel not related to the clinical study.

**SCENARIO 3: You've been reading about a new antigen, CD265, which has been found on T cells that cause GVHD but not on T cells that cause GVL, and you want to develop the procedure to deplete CD265<sup>+</sup> cells from allogeneic marrow. Your clinical colleagues are excited about the possibility. They find a source of CD265 antibody of appropriate grade for clinical use and ask you to provide the preclinical technical data for the IND they will file for the Phase I study. What do you need to provide to them?**

The major concerns are safety, efficacy, purity and potency of the product. This will require information about the reagents used, process controls for the manufacturing procedure, and quality assurance. There should be SOPs for the manufacturing procedure, for the tests used to determine if the products meet the release criteria, and for the QC assays. The manufacturing procedure should be validated on a clinical scale. The QC assays should also be validated, and the assays for the release criteria should at least be qualified. For unapproved reagents, certificates of analysis should be obtained from the supplier, or there should be an SOP to certify such reagents in-house.

For the scenario described above, documents needed for the IND include SOPs for the depletion process, for enumeration of CD265<sup>+</sup> cells, and for titrating each lot of CD265

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antibody. SOPs for other release criteria (viability, TNC and/or progenitor number, sterility, mycoplasma testing, residual antibody content, etc.), the results of any validation studies (with coefficients of variation), and the certificate of analysis for the CD265 antibody may also be requested. Development of new assays and validation of the SOPs may take several months. At many institutions, this work is generally performed in the technology transfer lab or a grant-funded translational research lab rather than in the clinical lab.

**SCENARIO 4: One of the investigators in the department has created a new monoclonal antibody that stimulates T cells to kill leukemia cells selectively. He has done all the preclinical studies to refine the stimulation procedure. He drops off hybridoma supernatant and a copy of the procedure he has used in the research lab. A Phase I protocol has been approved by the IRB, and he is preparing the IND. What does the cell processing lab have to provide, and what do you need to do before the study starts?**

All the information listed for Scenario 3 apply here. However, many labs are not prepared to deal with purification of a monoclonal antibody from hybridoma supernatant. Since preparation for such a study represents a serious time commitment in the cell processing lab, the investigator may need to have the antibody produced by a commercial firm instead. If the cell processing lab is willing to make the master cell bank and produce the antibody under GMP conditions but questions arise about various requirements, the lab director should consider asking the Principal Investigator to schedule a pre-IND meeting with the FDA to obtain guidance.

Prior to initiation of the study, the IRB- and FDA-approved version of the protocol should be reviewed as described in Scenarios 1 and 2, personnel should be trained, and the SOPs and worksheets should be validated.

The Phase I study is completed, and now other institutions want to do studies of their own using this procedure. The investigator does not want to release the antibody. He thinks the lab should do the stimulation for other institutions for a fee, sending the stimulated cells back for administration to the patient. Any additional requirements for a central lab supplying product to multiple outside institutions doing their own IND studies?

The central lab may chose to submit a master file to the FDA with the manufacturing information. Any one cross-filing on the master file or otherwise obtaining product from the central lab should be notified of any substantial changes in the manufacturing process that might affect clinical outcome. It is helpful to highlight the changes in the circular of information provided with each component. Shipping methods should be validated.

The central lab should also have an agreement with each investigator regarding reporting adverse events that might be related to the product and any serious adverse events; reporting to the central lab is in addition to the investigator's communication directly with the FDA. The quality management plan in the central lab should include a mechanism to review the adverse events, take corrective actions if needed, and communicate to all institutions using these products any adverse event information that might be germane to patient outcome.

IND and IDE studies can be a substantial challenge for the cell processing lab. Protocols that involve reagents prepared in-house can be especially expensive; start-up for a study such as described in Scenario 4 was estimated to be as much as \$250,000. If external funding is not available, most laboratories would not have the resources to participate in such studies, in which case it would be appropriate to decline participation.

*John McMannis, Stephen Noga, Robert Preti and Donna Przepiorka*



## Upcoming Meetings

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](http://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](mailto:headoffice@ishage.org); Website: [www.ishage.org](http://www.ishage.org)

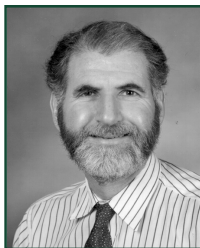
10th Annual International Symposium on Recent Advances in Stem Cell Transplantation. April 25-27, 2002. Heidelberg, Germany. Contact: Maureen Helsinki. Tel: 858-534-1301. E-mail: [mhelsinki@ucsd.edu](mailto:mhelsinki@ucsd.edu)

2nd Annual Somatic Cell Therapy Symposium. May 3-5, 2002. Sanibel Island, Florida. Chair: Dr. Stephen Noga. Contact: Colette Shoukas. Tel: 410-955-6046. E-mail: [cshoukas@jhmi.edu](mailto:cshoukas@jhmi.edu)

Biological Therapies in the New Millenium, 2002 Annual Meeting. May 25-28, 2002. Barcelona, Spain. Contact: Moya Berli, ISHAGE-Europe. Fax: +47 22 52 43 20; E-mail: [moya@ishage.org](mailto:moya@ishage.org); or through the ISHAGE Head Office: Tel: 604-874-4366; Fax: 604-874-4378. E-mail: [headoffice@ishage.org](mailto:headoffice@ishage.org). Further information on the program, registration, abstracts, accomodation, etc. will be coming soon!

ISHAGE 2003 Annual Meeting. May 29-June 1, 2002. Phoenix, Arizona. For more information contact the 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](mailto:headoffice@ishage.org); Website: [www.ishage.org](http://www.ishage.org)

2nd Annual Conference on Mesenchymal & Nonhematopoietic Stem Cells: Recent Progress and Current Controversies. September 26-28, 2002. New Orleans, Louisiana. Chair: Dr. Edwin Horwitz. Contact: Jean Winter. Tel: 901-495-2349. E-mail: [jean.winter@stjude.org](mailto:jean.winter@stjude.org)



## From the President's Desk

Robert Negrin, MD

The annual meeting in Quebec City was a huge success. Thanks to all of you who attended this wonderful event. I received many positive comments and helpful suggestions. Two over-riding themes for new innovations and improvement were apparent to me while listening to the various presentations and speaking to the meeting participants. First is our continued efforts to expand our society into new arenas. It is clear that the concept of cellular therapy continues to grow in unusual ways with the use of hematopoietic cell therapy, as well as dendritic cell therapy, T cell and other immune-based therapies, as well as the broadening array of potential stem cell therapies. Clearly our society remains at the forefront of these different disciplines. We need to understand not only the underlying biology but also the

technical and regulatory requirements of manipulating these cellular populations for therapeutic purposes.

The second major issue was our on-going responsibility and need for education, particularly for the medical technologists who form one of the pillars of our society. In particular, the need to make sure that the basic underlying biology, as well as the technical procedures that are used to isolate and evaluate various populations of cells are clearly articulated and explored. Along those lines, I have asked Terry Thomas in the education sub-committee, as well as Carlos Lee and Donna Rill of the technologists committee to take a leading role in developing educational materials and plans for enhancing the educational experience for technologists at the annual meeting, as

well as other satellite meetings. These plans are being developed and any suggestions that you may have, please direct them to these individuals or myself.

We are proud to announce that we received official confirmation that ISHAGE has been approved by the California Department of Health Services and Laboratory Field Services as an accrediting agency for continued education for California Clinical Laboratory Scientists. Clearly this is only the beginning and serves as a major milestone for the role of our Society in providing continuing education for laboratory technologists in other areas around the globe.

Due to the expanding role of the society, it is apparent that we continue to move beyond just hematopoietic cell therapeutics and therefore a name change would better reflect our society's goals and directions. Therefore we are actively pursuing this goal which has a number of ramifications and hope to announce the official change in the society's name at the upcoming annual meeting in Barcelona. I look forward to seeing all of you there.

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**EDITOR:** Scott Burger, MD  
Merix Bioscience, Durham, NC, USA  
Fax: 919-287-6301; E-mail: sburger@merixbio.com

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### ISHAGE Head Office:

777 West Broadway, Suite 401, Vancouver, BC, Canada V5Z 4J7  
Phone: (604) 874-4366 Fax: (604) 874-4378 Email: headoffice@ishage.org

**Website:** [www.ishage.org](http://www.ishage.org)





# From the Editor's Desk

**Scott Burger, MD**

This year's ISHAGE meeting as always was a heady mixture of exciting developments, new ideas, and a wonderfully collaborative atmosphere. This issue of Telegraft includes a summary of the meeting's highlights - though surely you participated in the meeting yourself.

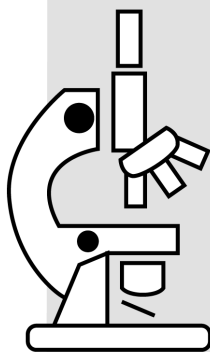
I had the special satisfaction of attending ISHAGE 2001 with some new colleagues from MERIX Bioscience as well as those from my former laboratory,

the University of Minnesota Cell Therapy Clinical Laboratory. Their incisive questions and enthusiasm were a reminder, if ever I needed one, of how vital it is for laboratory staff to participate in ISHAGE. The role of the laboratory technologist is central to our society's unique focus on developmental, clinical laboratory, and regulatory aspects of cell therapies. Let's make sure the laboratory staff can continue both to benefit from and strengthen ISHAGE.

Some changes accompany this issue of Telegraft. We are glad to announce that two outstanding cell therapy laboratory managers will write the Telegraft Tech Talk column. Kathy Loper, of Johns Hopkins University, has graciously agreed to continue to co-author the column, joined now by Diane Kadidlo, of the Cell Therapy Clinical Laboratory at University of Minnesota/Fairview University Medical Center. They will need your participation; don't be shy about sending your cell therapy laboratory questions, problems, and ideas to loperka@jhmi.edu (Kathy Loper) and cellther@tc.umn.edu (Diane Kadidlo).

We have a new regular ISHAGE committee column, focusing on the activities of one or two committees with each issue. We hope these columns will showcase the not-always visible work of ISHAGE committee members, and may spur you to participate in a committee yourself. (Notice to each committee chairperson - if you haven't already been asked to write one of these, it's only a matter of time.) This issue we hear from the Graft Evaluation and the Membership Services committees. Thank you also to the Legal and Regulatory Affairs committee for a report on their ISHAGE 2001 workshop on IND/IDE Studies. You will find updates about FAHCT and Cytotherapy as well, ISHAGE news - all this and more in this very issue.

## Mark your calendar!



### The 14<sup>th</sup> Annual **BIOPROCESS TECHNOLOGY SEMINARS**

Omni Hotel at CNN Center • Atlanta, Georgia  
October 1-5, 2001

- Bioreactor Process Technology
- Bioprocess Separations Technology
- Bioprocess Equipment Design
- CIP Technology
- Bioprocess Purification Scale-Up
- Bioprocess Fermentation & Cell Culture Design & Scale-Up
- Bioprocess Targeted Validation
- Cell Culture & Separations for Cell & Gene Therapies **ISHAGE**

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### Plant tour!

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### 2001 Corporate Members

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

- Amgen Inc.**
- Cell Science Therapeutics Inc.**
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- MVE-Chart Industries Inc.**
- Nexell Therapeutics Inc.**
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- StemSoft Software Inc.**

ISHAGE Corporate Memberships for 2002 are now being sold. For further information on the benefits of membership see the ISHAGE website ([www.ishage.org](http://www.ishage.org)) or contact the ISHAGE Head Office by phone at 604.874.4366 or E-mail at [headoffice@ishage.org](mailto:headoffice@ishage.org).

# The ISHAGE Graft Evaluation Committee

This committee previously operated under another name, i.e. the Stem Cell Enumeration committee, a sub-committee of Andrew Pecora's "Graft Engineering Committee". The main 'raison d'être' of the Stem Cell Enumeration Committee was to develop Clinical Guidelines for the Enumeration by flow cytometry of CD34<sup>+</sup> cells in fresh Peripheral Blood and Apheresis products. The Graft Engineering Committee mandated that the new 'Guidelines' be based upon flow methodology recently published in *Experimental Hematology* (22: 1003, 1994). The Guidelines, when eventually published in 1996 (*J Hematotherapy* 5: 213), became known, essentially by default, as the 'ISHAGE Guidelines'. One important development has been the incorporation of counting beads and viability dyes that convert this method into a single platform assay for the determination of the 'absolute viable CD34<sup>+</sup> cell count' (*Cytometry* 34: 61, 1998). These methods are in widespread use and have influenced clinical practise worldwide.

One can rightfully say that the members of the committee were actively involved in their committee work and did not hesitate to widen the forum for their differences of opinion, involving the scientific community through public discussions (e.g. ISHAGE conference in Bordeaux), published letters and scientific publications. But as history teaches, countries and continents need struggle, and sometimes war, to evolve into solid democratic States, and so did we and we came out stronger for it.

We also recognize that graft evaluation has many more sides. This is clear from the mission statement of the Graft Evaluation Committee to serve those working in the field of hematopoietic cell processing by being a source of technical information and professional standards and guidelines on progenitor and stem cell detection, enumeration and manipulation. The committee will communicate with ISHAGE members using the ISHAGE website where members can pose their questions and/or comments directly with experts in the field.

The following individuals continue to serve on the Graft Evaluation Committee: Stephen Noga (USA), Rob Sutherland (Canada), Hans Johnsen (Denmark), Eric Braakman (Netherlands), Mike Keeney (Canada), Emer Clarke (Canada) and Rob E. Ploemacher (Chair) (Netherlands). The membership of the committee was further expanded this year and we welcomed John Jackson (USA), Miles Prince (Australia) and Tatsutoshi Nakahata (Japan). Robert S. Negrin (USA), who chaired this committee until 1999, resigned as a member when he took the Presidency of ISHAGE. We are very glad to have widened our geographical representation to include East Asia and Australia.

A number of issues and tasks have recently been addressed by the Graft Evaluation Committee as follows:

## Quality Control of CD34<sup>+</sup> Cell Determinations

The committee continues to recognize that an area of major importance is assessing the reliability and quality control of an individual laboratory in regards CD34 enumeration. This issue requires ongoing attention as well as approaches to assure that a given laboratory is capable of accurately measuring CD34 cell content by the method used at that institution. Although it is beyond the scope of ISHAGE to monitor this process, there should be a focus on recommendations which could be useful for other organizations, for example, FAHCT.

## The Annual Meeting in Quebec, Canada

The members of the Committee (except the members entering in 2001) reviewed **abstracts** for the Annual Meeting in Quebec City. A teleconference was held to discuss and select four abstracts for the Graft Evaluation Oral Abstract Presentation Session. The session during the Quebec Meeting was chaired by Emer Clarke and Mike Keeney. Dr Bregni discussed CK19 and RT-PCR in the detection of epithelial ovarian cancer cells in autografts, while Dr Schuurhuis discussed the detection of early apoptotic cells in post thawed apheresis products using Syto 16 dye. Dr Roy described a photodynamic strategy for purging non-Hodgkin's lymphoma cells using TH9402 and lymphoma cell lines. Dr Jackson finished the session with a description of his labs attempt to produce monoclonal antibodies to the Hoechst low, CD34<sup>+</sup>/<sup>-</sup> "side population" enriched for stem cell activity. The session stimulated lively discussion and rounded off an excellent afternoon.

Two **Workshops** were organised by our committee: (a) Workshop 4A: "*In vitro Analysis of Stem Cells beyond the CD34<sup>+</sup> cells*", moderated by Mickie Bhatia, Steve Noga and Rob Ploemacher; (b) Workshop 4B: "*Practical vs. Refined methods predicting hematopoietic engraftment*", moderated by Steve Noga and Rob Ploemacher.

This year we did not have any formal speakers in the workshops. Instead, the moderators introduced the subject of the workshop and initiated and stimulated discussions with the audience. This was a well-attended two hour session and exceedingly well moderated by Mick Bhatia and Steve Noga. The exchange of ideas that ensued with the audience was extremely stimulating and often good humoured. It is good to

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see and hear how many colleagues appreciate an open discussion on topics that concern us all in the transplantation field.

In Workshop 4a, Mick Bhatia removed most ground beneath our feeble feet by summarising recent reports on the plastic phenotype of engrafting stem cells. Not only can hemopoietic stem cells be heterogeneous for CD34 and CXCR4 expression, they may traverse between the CD34<sup>+</sup> to the CD34<sup>-</sup> status and vice versa dependent on e.g. their proliferative activity. Even more, it has been suggested that the CD34<sup>+</sup>CD38<sup>-</sup> phenotype may flip-flop with the CD34<sup>-</sup>CD38<sup>+</sup> one. The question then arises although we aim to transplant CD34<sup>+</sup> progenitors, while we know that grafts may have different origins (mobilized peripheral blood versus cord blood versus steady state bone marrow, autologous versus allogeneic, different chemotherapy strategies, etc.): is there a chance that we may transplant the wrong stem cells, or only a fraction of what we could have transplanted?

In Workshop 4B, Steve Noga stimulated an entertaining discussion in response to some participants' anecdotal observations of failed hemopoietic engraftment in patients who had apparently received a more-than-adequate infusion of CD34<sup>+</sup> cells. While such cases are thankfully very rare, the discussion focussed on what parameters could possibly have been evaluated pre-transplant to be able to predict such a dramatic event. It is clear that many in the audience knew from experience with semi-solid progenitor cell assays (CFU-C) that these often did not always predict engraftment, or failure thereof. However, it is at least a functional assay which may give additional information to that from simply counting CD34<sup>+</sup> cells. For instance, one may assume that any graft treatment (including freezing, thawing and selection) that severely diminishes the graft CFU-C content will be detrimental to the quality and number of the engrafting stem cells as well. Yet, CFU-C have been demonstrated in animal models to show no correlation with engraftment, while long-term stroma-supported assays do. These latter are difficult to perform on a routine basis, as there are limitations on time, experience and personnel to perform these assays in the clinical setting. The workshops showed that many questions live amongst us, and next year will surely want to continue pursuing answers to them.

Another activity of the Graft Evaluation Committee during the Quebec Meeting 2001 included the organisation of a **Simultaneous Plenary Session**. This session was chaired by Rob Ploemacher. Dr Norman Iscove gave an overview of his methodology for analysis of gene expression in hemopoietic cells and their direct progeny, and presented some impressive data. Dr John DiPersio gave a comprehensive overview on

the effect of cytokines on stem and accessory cell mobilization. Dr Mickie Bhatia showed the audience the complexity of the stem cell phenotype and the attempts to isolate these elusive cells. Finally, Dr. Jan Gratama presented 20 years of clinical data on the immune reconstitution following stem cell transplantation, and the effects of type of graft and cytomegalovirus infection. The presentations were very well received.

The Graft Evaluation Committee also organised two Technical Breakfasts. The first meeting had been successfully held in previous years, i.e. the one on "CD34<sup>+</sup> enumeration and troubleshooting", where Rob Sutherland and Mike Keeney were the experienced moderators. A Technical Breakfast on "*In vitro* assays for hemopoietic progenitors (CFC, CAFc, LTC-IC, etc.)" was moderated by Emer Clarke and Rob Ploemacher and was held for the first time. If the many attending these two meetings enjoyed the discussions as much as the proffered breakfast, these Technical Breakfasts can be called a great success and should be organised again in Barcelona next year.

## Report for Cytotherapy

The Annual Report for publication in Cytotherapy was discussed during the committee meeting in June 2000 in San Diego. It was decided to focus our Report on "Clinical parameters for graft evaluation", and in addition on "The validity of current assays as predictors of engraftment". Finalisation of this report is planned for September 2001.

## Web Page

The following issues were mounted or updated on the committee's Web Page:

- Committee's mission statement.
- List of committee members and their E-mail addresses.
- Frequently Asked Questions (FAQ) section on CD34<sup>+</sup> cell enumeration.
- Sample list of mode files and dot plots
  - ISHAGE single platform with 7-AAD (BD FACScan)
  - ISHAGE single platform with 7-AAD (Coulter XL)
  - CD34<sup>+</sup> Cell Subset Analysis Template (BD FACScan)
  - CD34<sup>+</sup> Cell Subset Analysis Template (Coulter XL)
  - Simultaneous absolute counting of CD34<sup>+</sup> and CD3<sup>+</sup> cells (BD FACScan)
  - Simultaneous absolute CD3 and CD34 on allogeneic donors (Coulter XL)
  - ISHAGE single platform with 7-AAD (BD FACSCalibur)
- Currently discussed is a FAQ section on hemopoietic progenitor assays.

We would appreciate hearing from you about additional topics of general interest that could be posted on the website.

*Rob E. Ploemacher, on behalf of the committee*

# ISHAGE 2001 Meeting Review

Wow! Quebec City was a beautiful historic location for the annual meeting which was held at the conference center June 14-17. There were almost 450 attendees and over 130 exhibitors/sponsors. This was an increase over last year and can be attributed to a great program assembled by the organizers and the excitement in our rapidly evolving field. Most were from North America (55%) and Europe (15%). In total 26 countries or geographic regions were represented including Australia, New Zealand, Africa, Asia, South America and the Middle East. Since 200 of the attendees were non-members, we have a nice target audience as our society strives to increase membership. Our vendor support was up this year as well as there were over 25 sponsors and 35 exhibitors.

## More Technical Topics

The organizers, led by ISHAGE President Robert Negrin stayed true to last year's commitment to provide more technical topics. Thursday brought the FAHCT inspector training as well as an in-depth conference on flow cytometry applications. Each morning eager participants gathered for small group technical breakfasts ranging from cell processing technical issues and *in vitro* assessments to regulatory considerations and outcomes analysis. With 5-6 to choose from each day, there was something for everyone. These were well reviewed by attendees. Since over one third of the conference participants were technologists, these sessions were extremely informative and allowed specialized networking and effective exchanges (in both directions).

## Something for Everyone

Overviews of the latest developments were covered in the plenary sessions. Ranging from transplantation issues to gene therapy to tumor and graft evaluation, there was something for every specialty. These led to the simultaneous sessions which were more in depth cutting edge communications on the field. Immunotherapy, plasticity, and various graft and transplantation issues were thoroughly covered with lively discussions afterwards. The workshops provided the opportunity for more in-depth review and exchange of information. Specific *in vitro* analyses and relevant parameters such as characterization of CD34 or other expanded cells were covered in several sessions. Mesenchymal cells, dendritic cells, and other immunotherapy applications were presented, each with their own set of issues and discussion. Finally, there were clinical issues such as data from mini and haploidentical transplants keeping us true to clinical and traditional transplant issues. Most of the groups touched on

some way on the ever-present regulatory considerations. Participants found it refreshing to share struggles and triumphs as these difficult issues were wrestled with, demonstrating once again, the creativity that permeates our field!

## Abstract Presentations

The abstract presentations reflected the broadening scope of our field and included topics such as targeted cell population studies, pancreatic islet cells, tumor vaccine preparation, and new photodynamic purging technologies. Clinical management and outcomes analysis and all aspects of cord blood (collection to expansion of progenitor cells) rounded off the topics. Each one was fascinating and space does not permit an in-depth review but abstracts may still be reviewed at [www.ishage.org](http://www.ishage.org).

The social highlight of the meeting was an exquisite gala at the Chateau Frontenac which gave a breathtaking view of the city and an incredible dinner complete with music, hand created one-of-a-kind desserts, and dancing.

## Committee Meetings

In addition to the scientific discussions, the society conducted a significant amount of business. Each committee met as well as the Executive Committee. Important topics such as ISHAGE's accreditation for technologist CEUs in several states, increased technical programs (aside from the annual meeting), and our journal publication issues were reviewed. For more details on these and other topics, stay tuned to Tech Talk as each edition will feature a report from two of the committees. Finally, it is always nice to place a face with a name and we all got to meet those hard workers at the ISHAGE office who manned the booths, supplied pens, tape, and other necessities and answered the same questions countless times, always with a smile.

A quick review of the evaluations reveals overall satisfaction with the meeting site and organization/convenience. Specific requests included more printed materials in advance, more small working groups, handouts of simultaneous sessions, and making the organization/format of the workshops more consistent. Overall, the comments were positive and suggestions helpful. The organizing committee will continue to seek improvement and give the suggestions careful consideration as they plan for next year... ISHAGE 2002 in Barcelona!

*Kathy Loper*



## Contributing Authors

### Moya Berli

ISHAGE-Europe Administrator  
Chair, ISHAGE Membership  
Services Committee  
Oslo, Norway

### Susan Carnoutsos, MNZIMLS

Specialist Hematology  
Cantebury Health Laboratories  
Christchurch, New Zealand

### David Ford, MAppSc, FAIMLS

Principal Hospital Scientist  
BMT Lab  
Prince of Wales and Sydney  
Children's Hospital  
Sydney, Australia

### Diane Kadidlo, MT(ASCP), SBB

Technical Supervisor  
Fairview University Medical Center  
MMCT Facility  
St. Paul, MN, USA

### Lawrence S. Lamb, Jr., PhD

Associate Professor of Pediatrics  
Division of Hematology and Oncology  
University of South Carolina  
School of Medicine  
Columbia, SC, USA

### Kathy Loper, MHS, MT(ASCP)

Manager, Graft Engineering Laboratory  
Johns Hopkins University  
Oncology Center  
Baltimore, MD, USA

### John McMannis, PhD

MD Anderson Cancer Center  
BMT Transplantation Department  
Houston, TX, USA

### Linda Miller, MPA

FAHCT Administrative Director  
University of Nebraska Medical Center  
Omaha, NE, USA

### Stephen J. Noga, MD, PhD

(ISHAGE President-Elect)  
Sinai Hospital of Baltimore  
Cancer Institute  
Baltimore, MD, USA

### Rob E. Ploemacher, PhD

Department of Hematology  
Erasmus University  
Rotterdam, The Netherlands

### Robert Preti, PhD

Progenitor Cell Therapy, LLP  
Saddle Brook, NJ, USA

### Donna Przepiorka, MD, PhD

Associate Director,  
Stem Cell Transplant Program  
Medical Director,  
Cell and Molecular Therapy Lab.  
Baylor College of Medicine,  
Center for Cell and Gene Therapy  
Houston, TX, USA

## Telegraft Editorial Board

### Scott R. Burger, MD

(Editor)  
Vice-President of Research and Development  
Merix Bioscience,  
Durham, NC, USA

### Joan Garcia, MD, PhD

(ISHAGE Europe, Regional Secretary)  
Cancer Research Institute, Barcelona, Spain

### Diane Kadidlo, MT(ASCP), SBB

Technical Supervisor  
Fairview University Medical Center  
MMCT Facility  
St. Paul, MN, USA

### Kathy Loper, MHS, MT(ASCP)

Manager, Graft Engineering Laboratory  
Johns Hopkins University Oncology Center  
Baltimore, MD, USA

### Stephen J. Noga, MD, PhD

(ISHAGE President-Elect)  
Sinai Hospital of Baltimore  
Cancer Institute  
Baltimore, MD, USA

### H. Miles Prince,

### MB BS (Hons), MD, MRACMA, FRACP, FRCPA

Head, Haematology Unit  
Director, Blood and Marrow Transplant Service  
Peter MacCallum Cancer Institute, Melbourne, Australia

### Iain J. Webb, MD

(ISHAGE Treasurer)  
Medical Director  
Cell Manipulation Core Facility  
Dana-Farber Cancer Institute, Boston, MA, USA

## ISHAGE Name Change

Its happening! Cellular therapies have grown beyond hematopoietic cell therapeutics and ISHAGE has grown with the field to encompass many of these exciting new therapies and areas of research. Increasingly being recognized as the leading society in the field of cellular therapies and the transition from bench to bedside, ISHAGE has decided to pursue its long-discussed name change to the INTERNATIONAL SOCIETY FOR CELLULAR THERAPY.

Robert Negrin, ISHAGE President is excited to be proceeding with this change saying, "Beginning with the initiatives of Past President, Malcolm Brenner, ISHAGE has been looking at a name change for some time. Feedback sought and obtained from the membership indicates support for such a change. As an Executive

Committee, we believe this name change will reflect the Society's current scope and activities, as well as solidify the Society's growing reputation as the leading Society in the field of cellular engineering and therapies. As such, we expect it will fuel the Society's growth.

We hope you will exercise your voting rights as outlined in the notice enclosed with this issue of the Telegraft. We look forward to a future of exciting growth for the Society regardless of a name-change but do hope you agree with the change we recommend."

You will find enclosed with this issue, a Notice of a Special General Meeting in which all Active members are entitled to attend and cast a vote. In the event you are unable to attend please exercise your proxy in accordance with the enclosed instructions.

# ISHAGE 2001 - An Australian and New Zealand Perspective

Quebec City, the capital city of the Province of Quebec, Canada is the cradle of French civilisation in North America and has been designated a world heritage site by UNESCO due to its special character. To a kiwi travelling all the way from Christchurch, New Zealand it is a daunting experience to be faced with the prospect of all that flying and a language barrier at your final destination. Add in the fact that there was a good chance that your luggage would not make it at the same time that you did (at least five of us), and you have the ingredients for very grumpy delegates! However the choice of Quebec City was an inspired one as shortly after arrival, all worries were pushed aside - the city is beautiful, the people friendly, the weather fantastic and the conference (socially and professionally) certainly well worth the effort! Our luggage eventually arrived!

## The FACHT Training Workshop

The focus of my attendance at the ISHAGE meeting was the FACHT Training Workshop: "Preparing your Facility for FACHT Inspection", which was held prior to the meeting on the June 14. The delegates included nursing and medical personnel as well as administrators and laboratory scientists. As you are all no doubt aware FACHT standards, inspection and accreditation are gaining worldwide acceptance and our Clinical and Laboratory Transplant Team is keen to investigate the possibility of adopting the programme in this part of the world. This process can take a number of years to complete so is not for the faint-hearted - not to mention the fees in American dollars! The objectives of the workshop were to explain and clarify the accreditation requirements while assisting applicants and potential applicants in organising and preparing their programme for FACHT accreditation. From my viewpoint, the aims were to make contact with the FACHT staff, gain knowledge into the process and assess the feasibility of implementation. The large amount of information that I gained from attendance at the workshop has already been put to good use in both clinical and laboratory areas particularly in the area of documentation and accountability. Possibly the greatest benefit however came from meeting scientists who are undertaking inspection and having that network of colleagues who are but an e-mail away!

## Other Meeting Topics

The Meeting itself covered a wide range of cell therapy related topics, including haemopoietic progenitor cell

transplantation, adoptive immunotherapy, gene therapy and non-haemopoietic/mesenchymal stem cells uses and transplantation. Technical breakfasts prior to each day's session focused primarily on issues of particular interest to laboratory based delegates. Topics ranged from viability testing, freezing mixes, overnight storage of HSC and the usefulness of the CFU-GM assay to the optimum conditions required for retroviral gene transduction. The sessions dedicated to the potential use of mesenchymal stem cells in transplantation were particularly stimulating and thought provoking. We have selected four quite different presentations to review.

## Selected Presentations at ISHAGE

**John DiPersio**, from the Washington Uni. St Louis group presented a large data set of cytokine mobilization normal peripheral blood (PB) stem cell donors. They observed if an individual's pre-mobilised CD34 was less than one per  $\mu\text{L}$  in the PB, then mobilization resulted in low CD34 yields. These observations were repeatable with the same individual tested over an extensive time interval. Another observation was that males mobilize to higher levels than females however, with increasing age this advantage disappears as CD34 yields decrease. On the other hand, females CD34 yields increase with age and surpass males around the age of 50 years plus. These findings have implications in deciding on the use of PBSC v/s BM for matched unrelated donors. The NMDP offer to collect of PB stem cells in place of a bone marrow donation has made the decision difficult especially if insufficient CD34 were collected on the first day. If this did occur, the courier costs involved with a second collection practically to an overseas transplant center would be a factor in the decision of which stem cell source to accept. The general information from St Louis may be of help.

**Scott Rowley's** presentation of the work carried out in Seattle comparing cryopreservatives 10% DMSO or a mixture of 5% DMSO and 6% HES, required data from well over 100 subjects in each arm of the study. The group observed a one day faster engraftment of granulocytes with the latter cryopreservative mixture. There was no difference in platelet

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engraftment. This finding however was not carried through in practice in the lab, as the reagent preparation for the cryopreservative mixture was time consuming and implementation over the standard 10% DMSO would result little clinical benefit.

**The Tübingen group from Germany**, using CliniMacs™ for positive stem selection have shown successful engraftment from allo PBSC donors in the sibling mismatch setting. Mega dose CD34 to values usually above  $20 \times 10^6/\text{kg}$  produced sustained engraftment without significant GvHD. The level of CD3 cells did not approach the threshold level where acute GvHD presents a problem. This was made possible with the very high purity of CD34 in the CliniMacs™ selection.

**The New York Cord Blood Bank** presented work on transient warming events (TWE) of cryopreserved cord blood cells. Extensive testing examined the effect of transferring frozen cells out of liquid nitrogen storage for set times and exposures to various temperature points, then re-banking the

cells (single and multiple times), back into liquid nitrogen. The manoeuvre produced an additive effect on cell death with repeated transfers and higher cell death with higher temperature and time exposure. However, major cell death did not occur until the frozen unit was treated to extremes to temperature difference. A unit placed in a  $-40^\circ\text{C}$  bath for four minutes, resulted in a 21% loss in CFU-C, after one cycle of warming. TWE increased to a 50% loss CFU-C after x5 cycles of warming to  $-40^\circ\text{C}$ . In contrast only a <5% of loss CFU-C resulted when the sample cells were warmed to  $-140^\circ\text{C}$  with five repeated cycles. The study has very practical implications. These observations add solace to transplant centers that store cryopreserved stem cells in vapor phase of liquid nitrogen. The small temperature rises that occur to units remaining in a tank when the lid is removed to add or extract units has been a concern.

We certainly recommend attendance to ISHAGE - it is well run and it is nice to have an all inclusive registration fee. I am sure many of us will be looking forward to Barcelona in 2002!

*Susan Carnoutsos (Christchurch, New Zealand)*

*David Ford (Sydney, Australia)*

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# ISHAGE Communication and Membership Committee Update

ISHAGE recently decided to combine the committee duties of the previous Membership Committee and the Communications and Membership Services Committee. Both these committees have historically overlapped in many of their duties and goals with the common goal of enhancing the services offered to the membership.

The new committee members are: **Moya Berli**, ISHAGE-Europe Office, Norway (Chair); **Michele W. Sugrue, MS, MT(ASCP), SBB**, Stem Cell Laboratory, Shands, University of Florida (Co-Chair North America); **Kay Krueel, MT**, MERIX Biosciences (North Carolina); **Gail Lazarro**, Haematopoietic Stem Cell Facility, Red Cross Transfusion Service (Australia); **Kathy A. Loper, MHS, MT(ASCP)**, Manager, Graft Engineering Laboratory, Johns Hopkins Oncology Center (Maryland); **Adriana Seber, MD**, Instituto Oncologia Pediatrica (Brazil); **Panteli Theocharous, MD**, Cell Biology Department, Onyvax (UK).

The committee first met at the 7<sup>th</sup> Annual ISHAGE meeting in Quebec, Canada. The purpose of this meeting was to establish the committee and review the guidelines of the

previous committees. The main goals of the Committee will be to recruit new members worldwide and to improve services for the existing ISHAGE members, as well as to review the activities of the Society's Journal, Newsletter, website, membership directory and membership surveys.

The Head office of ISHAGE will perform the administrative duties which includes keeping track of the database, processing new membership applications, taking care of all the renewals to mention some of the duties. The Communication and Membership Committee will in many respects act in an advisory role to the Head Office, The Executive Committee, and the Editors of the Telegraft and Cytotherapy.

An important issue for the Committee will be to form new guidelines for the membership services. By utilising the website we hope to be able to reach the membership and create an interactive environment where the members can actively take part in forming the Society.

*Moya Berli*

# C y t o t h e r a p y   N e w s

## Dr. John Barrett Named Co-Editor

ISHAGE is pleased to announce that **John Barrett MD, FRCP** of the *National Institutes of Health* will become the new Co-Editor of **Cytotherapy**. ISHAGE is developing Cytotherapy as the home for translational research in cellular therapy, first reports of exciting applications of laboratory research in the clinic, and papers on practical application of cellular therapies. Dr Barrett's outstanding contributions to both the clinical and laboratory sides of cellular therapies typify the type of work for which the journal is increasingly becoming recognized and will strengthen the type of journal we have sought to create.

## New Publishers

On March 1, 2001 the rights to some titles published by ISIS Medical Media (including Cytotherapy) were acquired by **Martin Dunitz Limited**, part of the Taylor & Francis Group. The acquisition included the agreement to publish Cytotherapy. The new publishing company, is listed on the London Stock Exchange and is a leading publisher of over 800 independent and society-owned journals, covering a wide range of academic disciplines. Martin Dunitz Ltd manages a growing list of quality journals and international in scope. They are delighted to be the new publisher of Cytotherapy and look forward to a successful and strong partnership with ISHAGE.

## Production and Publication

We are aware that there have been many difficulties in maintaining a regular schedule of publication prior to the change of publisher. However, we hope you have noticed that with Martin Dunitz we have succeeded in publishing Issues 1-4 of Volume 3 this year on time. Dispatch of reprints, which has also been affected by the events of last year, should now resume for contributors.

## On-Line Publication

Journals within the Taylor & Francis Group are published on-line by **Catchword**, a platform owned by Ingenta. It is Martin Duntiz's intention to integrate Cytotherapy into this system and they have begun the process of testing the typesetter's files to ensure a smooth transition. There are several benefits in using Catchword:

- a. allows seamless access to Medline,
- b. users have access to other resources and databases,
- c. pre-publication facility for accepted papers being introduced,
- d. contents alert by email.

Users who wish to access the journal via **Ingenta** will still be able to do so.

Access to Medline will again be in place shortly. The journal is already indexed by ISI (which publishes the Science Citation Index) and we anticipate will receive an impact factor in the coming year.

## Upcoming Issues

The Cytotherapy Editors plan to bring you more theme issues such as the "Campath" issue, Volume 3, Number 3 put together with the tremendous assistance of Dr Geoffrey Hale who was the issue's Guest Editor. In Volume 4, we are planning a number of theme issues and welcome your suggestions.

In summary, the Society is working with the new publishers to significantly raise the profile of Cytotherapy in the coming year with the researchers and authors in the field, subscribers, institutional libraries, and the corporate community. We thank all of you for your contributions and commitment to the journal in the past two years and look forward to continuing to develop a quality publication that will assist those working in or interested in the field of cellular therapy.

# ISHAGE News

It is time to renew your membership for 2002! You may do so online ([www.ishage.org](http://www.ishage.org)) or respond to the membership renewal notice you will be receiving soon. Please note the Laboratory Membership option for those wishing to sign up together from one lab.

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At the Annual Meeting, the following newly elected and appointed officers were announced: **Iain Webb** (Treasurer); **Klaus Pantel** (ISHAGE-Europe Treasurer); **Scott Burger** (Telegraft Editor); **John Barrett** (Co-Editor, Cytotherapy); **Donna Przepiorka** (Advisory Board Rep. (MD, PhD)); **Joy Cruz** (Advisory Board Representative (Technologist))

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

The third Bi-Annual Conference on Applications of Flow Cytometry in Blood and Marrow Stem Cell Transplantation was held on June 14, 2001 in concert with the ISHAGE 2001 annual meeting in Quebec City, Canada. The meeting was sponsored by BD Biosciences of San Jose, CA; Cytomation, Inc of Ft. Collins, CO; and Chimeric Therapies of Laguna Niguel, CA. Over 100 attendees from North America, Europe, and Asia were present.

The first program examined advances in high speed cell sorting of specific graft populations for immunotherapy and graft engineering. The second program covered the role of quantitative flow cytometry in the assessment of immune function following stem cell transplantation and immunotherapy. A panel discussion with the presenters was held at the end of the meeting. Speakers at the meeting included Drs. Michelle Keane-Moore and Gerald Marti (Bethesda), Peter Lopez (Boston), Adrian Gee (Houston), Frits van Rhee (Little Rock), Lawrence Lamb (Columbia), Ger van der Engh (Seattle) and Smita Ghanekar (San Jose).

Mr. Lopez opened the first program with a comprehensive introduction to high-speed sorting and safety measures currently in development for clinical applications. Dr van der Engh showed the design for a GMP-compliant cell sorting system. Among the issues that generated discussion were the proceedings from the FDA/ISAC workshop on safety issues pertaining to clinical flow cytometry and cell sorting that were held in April of 2001. This review, combined with Dr. Gee's presentation on release criteria and regulatory issues pertaining to sorted graft material, formed the basis for ISHAGE participation in future discussions regarding FDA regulation of sorted human cells for transplantation. A working group was appointed at the April FDA/ISAC meeting and will continue to review potential requirements for cell sorting laboratories and issue recommendations. Following these presentations, Dr. van Rhee presented protocols from his laboratory for the generation of therapeutic numbers of virus-specific cytotoxic T lymphocytes using tetramer-based cell sorting.

The second program opened with an introduction to the science of quantitative flow cytometry, a method designed to enumerate the density of cell surface antigens using standardized fluorescent antibodies and a reference fluorescence system. Dr. Lamb then presented data from his laboratory on the use of quantitative cytometry to determine the level of lymphocyte activation by quantitating the expression of activation-associated antigens. Smita Ghanekar of BD Biosciences then reviewed methods, reagents, and

software for quantitative cytometry and immune function currently available from BD Biosciences and other sources.

Selected manuscripts from this conference will be published in an upcoming issue of *Cytotherapy*. We look forward to your participation in the fourth workshop scheduled for 2003.

*Lawrence S. Lamb, Jr.*

## cGMP 2001

### ISHAGE Current Good Manufacturing Practices Workshop

Rosen Centre Hotel, Orlando, FL

December 6, 2001

The International Society for Hematotherapy and Graft Engineering is again pleased to present its annual one day intermediate/advanced level workshop focusing on the implementation of the principles of cGMP in cell processing laboratories - this year with a regulatory focus. The morning sessions will feature a group of speakers with extensive experience in all facets of cell manipulation. The program also allows delegates to participate in interactive workshops during the afternoon. Delegates will be provided with an excellent resource binder including examples of relevant SOPs and policies. Materials on CD-ROM will be available at a discount to registered attendees.

#### Workshop Program:

- cGMP & GTP Introduction
- Validation Overview
- Facility & Equipment CFR 211 Subparts C & D
- Production & Process Controls CFR 211 Subpart F
- Laboratory Controls CFR 211 Subpart I & CFR 610

**Afternoon Workshops (below) are interactive and will each be presented twice during the afternoon.**

- CFR 211.25: Personnel Qualifications  
Creating a Competency Program
- CFR 211.200: Written Procedures; Deviations  
Preparing a Deviation Tracking System
- CFR 211: cGMP for Finished Pharmaceuticals  
Creating a Development Plan for a Novel Cell Expansion Process

**For further information about the Workshop, or to register for the Workshop, please contact the ISHAGE Head Office:**

777 West Broadway, Suite 401 • Vancouver • BC • V5Z 4J7 • Canada  
Phone: 604-874-4366 • Fax: 604-874-4378 • E-mail: headoffice@ishage.org

Register using the form on-line at [www.ishage.org](http://www.ishage.org)



# Tech Talk... A Precious Resource



Though some articles are more bleak than others, they all shout the same message. Health care professions will continue to experience shortages and our organizations must find ways to recruit, train and retain staff or compromise patient care. There seems to be no middle ground and this is true even for our profession of cell processing, which might be a microcosm of all highly technical and specialized fields. How do we do it? In this edition of Tech Talk, we present some information, possible solutions applicable to our field, and open the door for you to share your experiences. Just like our science, we can build on the lessons of others.

## Human Resources are Important

No one likes to talk about the human resources or administrative part of our jobs as managers. Rather, we prefer to focus on pure science: scintillating new technology with a few regulations thrown in for good measure. However, the reality is that as we face the day to day grind, this aspect is just as important. Moreover, some might argue, even more important since the best ideas in the world won't get accomplished without skilled hands and sharp minds performing the critical functions. According to HR Magazine<sup>1</sup>, "the expansion of the nations labor supply is slowing to a crawl... since 1996 the number of people... for hire has increased at an anemic rate of 1.1% per year." They attribute this to the aging population. Baby boomers are approaching retirement and the younger workers are too few to fill the gap. Additionally, the 20-something employees may possess unconventional notions about productivity, motivation and career.<sup>1</sup> Other references report statistics just as alarming with some quoting up to 20% vacancy rates in certain technology sectors.<sup>2</sup> Regardless, the future looks grim unless we take prompt action to improve our processes on this front.

Nationwide employment projections for clinical laboratory technicians and technologists reported by the Bureau of Labor Statistics<sup>4</sup> between 1998 and 2008 estimate:

1. 93,000 additional clinical laboratory scientists will be needed to fill 53,000 new jobs and to replace the 40,000 clinical laboratory scientists who are expected to retire. Average age of CLS is 45 years.
2. The shortage of CLS is growing 4,000-5,000 per year.
3. In 1999, there were 4990 graduates from new graduates from clinical laboratory scientist and laboratory technician programs.

## Why are We Losing People?

Some of the reasons people leave their field include disenchantment with their leaders or organizational goals or ranking among similar institutions, lack of adequate pay (for the amount of education and responsibility required, lack of recognition, and stress caused by overwork<sup>2</sup> and undesirable work schedules (24 hours, weekends, holidays). The lay media reports the increases in union activity of some of our professional counterparts such as nurses and physicians to add evidence to these issues. Estimates vary but most agree advertising, recruitment and training are expensive endeavors. Many training programs have closed in effort to save money. In Minnesota, for example, ten years ago there were 13 four year clinical laboratory scientist accredited training programs. Today there are only two. Once we have these precious professionals on site, we must make every effort to retain them. This makes sense from a financial perspective as well as from a patient care model. In some of our more specialized facilities, it routinely takes one full year to train staff. This is 12 months that they are less than optimally productive and 12 months that someone else is as well, given the coaching/mentoring that must take place. So, how do we resolve these in our specialized scientific field or prevent it from occurring should we be lucky enough to be spared thus far?

The *scientist* in us wants to study the problem, to learn why. Then we will propose solutions, try them out, summarize the data and draw a conclusion. If necessary, we can modify our strategy. While that seems like a worthwhile approach to curing cancer, the statisticians will tell you that most of our cell processing facilities are too small for such results to have meaning and we aren't willing to wait out the failures to learn what doesn't work. Therefore, we must rely on our creative nature, study some proposed solutions, and sift through them as we look for ways to reward and retain our valuable staff.

## Recruitment

On the recruitment front, we will require fundamental changes. Perhaps we should leave our microscopes and cell counters and step into high schools and college Biology classes and tell our story, share our mission and some of the hands on stuff we get to do... *it is really cool!* Secondly, cell processing facilities will need to become more involved in

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medical technology programs and invite these clinicians into our labs for “show and tell” as well as some real hands on practical applications (mocked up, of course). Finally, we all have a professional responsibility to our societies. When is the last time you shared the benefits of ISHAGE or AABB membership with a neophyte?

### **Training**

Training could be its own Tech Talk column as most of us feel our programs are in a continual state of improvement. We have seen beautiful documentation shared by some centers and the more elaborate they are, the more we wonder where they find the time! Employees should feel valued and appreciated right from the beginning. Training should be as complete and thorough as if they were staying for 10 years. This process starts at the top of an organization and continues all the way down to our labs. Most candidates in orientation prefer a mentor or coach. Ideally, this is someone who is highly skilled as well as desiring of this position. It carries much responsibility and the tech you bribed with a day off or candy bar may not be the best choice in the long run. Regardless of your approach, most of us should apply the continuous improvement model and enhance our training packages every time we hire someone new. This also presents an opportunity for our professional organizations to develop training guidance or technology levels complete with recommended competencies or perhaps a certification exam. In fact, rumor has it some of these conversations are already taking place.

### **Keeping Employees Happy**

When it comes to retention, the literature is full of good ideas, some more applicable to our field than others. Once employees the mentoring/training process, they are ready for new opportunities to enhance their skills. How we keep these valuable individuals engaged in their job is paramount. Many employees have a need to feel valued but they also need to feel respected. Traditionally, the attitude seems to be for the employee to feel as if they are the lucky to have a job. If we continue with this mind set we will lose the few valuable employees we have left. “Employee First” should be the mantra for the employer. Listening to the employee and actually hearing what their needs are is a powerful weapon in the battle to retain employees. What are the goals of the staff? Time off? Attend school? Focusing on a particular job responsibility, such as quality assurance, statistics or teaching? When is the last time your boss asked you what do you want from the job and from management? It is time they did. It is not an easy task, trying to meet staff’s needs, but from personal experience the rewards are well worth it in terms

of employee satisfaction, positive moral and organization loyalty. It will require some creativity for modifying work schedules, restructuring job duties, and workload in our already unpredictable settings, but if we use the same determination as we do for those late night marrows or cord bloods, we should be able to find a way to accommodate.

### **Flexibility**

As professionals we want to be challenged in our job, but also want to have some amount of control and flexibility at work. Flexible hours (within reason) can allow staff to meet personal needs, provides a sense of control and communicates to the individual that management cares about them as an individual not just as a worker. Offering a staff person the opportunity to head a special project empowers them to utilize their ingenuity, provides ownership and makes it known to the individual that they respected as a professional. Projects can range from quality assurance data collection, development of new technologies, and increasing basic skills such as computer and statistical applications. What is key is to match the project to the individual. Projects should be proportional to work experience, talents and interests.

### **Continuing Education**

Continuing education funding is often the first item to be reduced or eliminate in times of budgetary uncertainty, but it really should be one of the last items cut. Ask anyone who has attended a major meeting or regulatory workshop and he/she will most likely tell you it was absolutely invaluable. Additionally, the opportunity to meet others struggling with the same issues, is priceless. Most who attend these seem to agree that the very act of their employer sending them is motivating. Certainly, motivated employees chose to stay in their positions more often than not. All of these cost money and in the face of shrinking profits, organizations are forced to make tough choices. Hopefully, once the benefits (retention, satisfaction, etc) are clarified, administrators will be on-board. For those of us at academic or private hospital centers, this is our chance to capture the support of our adoring medical staff whom we tirelessly support. Perhaps the next time a patient runs late or there is a product problem and the doctor says, “Thanks. I really appreciate this,” one might pounce on the opportunity to ask for a meeting to discuss some of these issues and how he/she can support the lab. Now, that would be a real thanks! Regardless, keeping valuable employees is paramount. For the latter, Both our labs and the organizations we support will benefit from the application of these new skills. Specific training in our field is more important than ever.

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## **Creativity a Key**

Organizations should be creative, allowing financial support or reimbursement, time off or other mechanisms such as continuing and distance education as the new cyber-students call it. Early reports show these to be quite successful.<sup>3</sup> Even basic cell processing labs can utilize these skills or seek other groups such as data managers and researchers who might need such assistance. Giving them the acknowledgement of performance and publicly acclaiming their critical role are good ways to start. Some ideas include special recognition weeks (such as National Medical Laboratory Week or starting your own cell processing week).

## **Salary**

Salary is another issue that arises when we address retention and most of us feel we are underpaid, under-appreciated and under-respected. Additionally, scientists in our field seem to be divided into two groups: traditional scientists and medical technologists. Both groups bring tremendous assets to the table. Both received on the job training on cell based therapies. With this pool, we struggle with identity. We want to stay in with the med techs so we get their pay raises and so we keep in touch with our roots. However, we contrast the long hours, weekend pagers, increased responsibility, and completely different level of judgement required to perform our duties. Therefore, we argue, we should receive a premium. Since some of us are under the pathology medicine groups and some are not, this requires individual attention. Perhaps a unique position title or more accurate job description is all that is required to cure what ails us.

Some fields have gone to a skill based pay approach, similar to production workers and manufacturing. In this pay plan, employees are compensated for skills they can use rather than specific jobs they may be performing. Supervisors and coworkers certify mastery. This structure is associated with supporting new technologies and has received positive feedback according to Worldatwork's website on compensation and benefits. There are some drawbacks though, including increased training costs, ceiling limits, and design. Finally, it may outgrow its usefulness at smaller institutions. Regarding a salary survey, one was attempted by Adrian Gee in *Cytotherapy* last year (vol. 2, no. 3, 247-253) and was so poorly responded to that the results could not be published. This is attributable to a variety of reasons but justifies the lack of this data.

## **Career Advancement**

Finally, we address the issues of career advancement. Many want to have a long term plan. Additionally, it seems important to these authors that there is a sense of mission. After all, most of us entered this field with the hopes of doing good for humanity, fully aware that another industry might pay better. It is the responsibility of the organization and our larger working groups to demonstrate how our work contributes on a daily basis. The career ladder is a complex issue as this is intricately intertwined in our place within the organization and how we approach it depends on our addressing the issues mentioned above. At one of our institutions, we have redesigned our job descriptions, modeling the nursing career ladder. In this case, there are several layers of competency and responsibility (twice as many as previously held). In this case, employees are brought in at appropriate levels and then promoted once they have mastered the specific criteria for their job and are demonstrating most of the qualities at the next level. Our thoughts were that this would provide our valuable employees a place to go after a few years, other than... somewhere else! In this system, promotions are based on individual performance and not tenure. There are no quotas on each level so the more we have at the higher levels, the higher quality our lab will be. It is viewed as a win-win situation. This is new so check back in a few years and we will let you know how it goes!

## **Stepping up to the Challenge**

In closing, the unfortunate truth is that we don't have all of the answers. Our field is small but growing and that brings about its own challenges. Each setting is different with different employees having unique assets and goals. One successful approach has been focus groups in the hospital setting where benefits, attitude and perceptions are discussed. This permits the identification of problems, changing paradigms (such as those 20-somethings' goals) and reinforces the things that work. Just as importantly, if we get one of our staff on those committees, we take a small step in resolving our identity crisis! If you would like to share your successes, please post them on the ISHAGE website discussion lounge at [as we too, look for ways to improve and to maintain our most precious and valuable resource... our staff!](#)

*Kathy Loper and Diane Kadidlo*

### **References**

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## FAHCT Standards Update

The Second Edition of the FAHCT Standards for Hematopoietic Progenitor Cell Collection, Processing and Transplantation is scheduled to be circulated in the fall for general comments. The draft Standards will be posted on the ISHAGE website for review and comment by the ISHAGE membership.

Minor changes to the NETCORD-FAHCT Standards for International Standards for Cord Blood Collection, Processing, Testing, Banking, Selection and Release have resulted in a Second Edition. Copies of the cord blood Standards are available to ISHAGE members at a discounted price of \$50.00 from the FAHCT Accreditation Office at (402) 561-7555.

## 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

Fifteen additional BMT centers have gained FAHCT accreditation since the last issue of the *Telegraft*. FAHCT has now accredited 84 centers. There are 114 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:

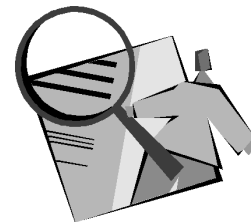
### *Autologous peripheral blood progenitor cell transplantation, including collection and laboratory processing:*

- Greater Baltimore Medical Center, Baltimore, MD  
Program Director: Gary Cohen, MD
- Methodist Medical Center of Illinois, Peoria, IL  
Program Director: John Kugler, MD
- Response Oncology, Inc. IMPACT Center of Abington, Abington, PA  
Program Director: John Redmond III, MD
- Saint Luke's Mountain States Tumor Institute, Boise, ID  
Program Director: William Kreisle, MD
- The Cancer Center of Providence Hospital, Mobile, AL  
Program Director: Thaddeus A. Beeker, MD

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

- Mayo Clinic/Saint Luke's Hospital Blood & Marrow Transplantation Program, Jacksonville, FL  
Program Director: Lawrence Solberg, MD
- USC/Norris Cancer Center Hospital, Los Angeles, CA  
Program Director: Daniel Douer, MD

# Just the FAHCTs



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

- Beth Israel Deaconess Medical Center, Boston, MA  
Program Director: David Avigan, MD
- Blood and Bone Marrow Transplant Program at University Hospitals of Cleveland and Case Western Reserve University, Cleveland, OH  
Program Director: Hillard Lazarus, MD
- Indiana Blood & Marrow Transplantation, Indianapolis, IN  
Program Director: Luke Akard, MD
- Indiana University Bone Marrow and Stem Cell Transplantation, Indianapolis, IN  
Program Director: Kenneth Cornetta, MD
- University of Nebraska Medical Center Transplant Program, Omaha, NE  
Program Director: Elizabeth Reed, MD
- Vanderbilt University Medical Center/Nashville Veteran's Administration Medical Center, Nashville, TN  
Program Director: Friedrich Schuening, MD
- Wake Forest University Baptist Medical Center, Winston-Salem, NC  
Program Director: David Hurd, MD

### *Autologous peripheral blood progenitor cell collection, processing and storage.*

- Greater Chesapeake and Potomac Region American Red Cross Blood Services, Baltimore, MD  
Program Director: Paul Ness, MD

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

Linda Miller



FAHCT Accreditation Office: (402) 561-7555  
[www.fahct.org](http://www.fahct.org)

Facilities Registered	198
Facilities Inspected	138
Accredited	84
Inspected/Pending Accreditation	54
Inspections in Process	11
Facilities Completing Checklists	49
Inspectors Trained	306

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