FDA Minutes/Summary of March 17, 1997 Open Public Meeting on the Proposed Approach to Regulation of Cellular and Tissue-Based Products.

FDA Opening Remarks:

Ms. Mary K. Pendergast, Esq., Deputy Commissioner/Senior Advisor to the Commissioner, welcomed those attending and briefly explained how and why FDA is proposing the new framework for cells and tissues. She discussed how the December 1993, Interim Rule for Tissue for Transplantation took provided oversight for some of the infectious disease problems for conventional tissue, and how after many interactions with Congress last year, FDA recognized that it needed a new approach that could regulate all tissues and cells in a way that would make sense with limited resources while triaging requirements based on risk.

Ms. Amanda Bryce Norton Esq. , Chief Mediator and Ombudsman, discussed how her Office has been addressing jurisdictional concerns for the past 5 years, as described in 21 CFR Part 3, involving tissue and cellular therapies, and how the newly formed Tissue Reference Group (TRG) will interact with her Office (OCMO) in the future. She introduced the members of the Group: from the Center for Biologics Evaluation and Research (CBER), Dr. Philip Noguchi (chair), Dr. Joy Cavagnaro, and Dr. Antonio Pereira; from the Center of Devices and Radiologic Health (CDRH), Dr. Claudia Gaffey, Dr. Celia Witten and Mr. Gene Berk. This group has met and is developing procedural and administrative strategies to address how to operate efficiently and expeditiously, and how to insure that decisions are not only prompt but thorough, consistent and reliable.

Dr. Kathryn Zoon, Director of CBER, emphasized that the purpose of this meeting was to listen to the public comment and recommendations on the proposal, and to answer questions that might clarify concerns with the requirements. She stated that this approach offers greater flexibility for the regulation of tissue-related products, but is based on strong scientifically sound principles that will assure public health safety. For CBER, the proposed approach will minimize the number of pre-market submissions and allow standard setting approaches for a number of products. CBER has been active in this area of regulation for a long time and has published several policy statements related to cellular and gene therapies, and for human tissue for transplantation. CBER will be actively interacting with CDRH as we develop this framework.

Dr Kimber Richter, Deputy Director, Office of Device Evaluation, CDRH, focused her comments on emphasizing CDRH's commitment to continue working with CBER to assure consistency and appropriate oversight of these products.

Ms Pendergast then presented an overview of the proposed regulatory framework that explained the basis of the tables accompanying the Rego document and the proposed approach document, that were made public in February. She discussed how the current regulatory approach was a patchwork quilt of regulatory policies that recognized a different approach for product classes, and that the new proposal will have one scheme that will cover all cellular and tissue-based products. Exempted from the new proposal, are vascularized organs, bone marrow, transfusable blood products, xenotransplants and secreted or extracted products such as collagen, growth

factors and breast milk. She focused her remaining comments on the 5 areas of product concern addressed by the framework and the product characteristics identified in the documents to determine the regulatory oversight necessary. She concluded by noting that besides listening to comment today, that comment to the docket will also be considered before FDA engages in notice and comment rulemaking.

Session addressing remarks concerned with General/Conventional, Eye and Reproductive Tissue Therapies:

This session was convened by Dr. Jay Epstein, Director of CBER's Office of Blood Research and Review (OBRR) who reminded participants that the docket was open through April 17 and the docket number was 97N-0068.

Ms. Martha Wells of FDA's Human Tissue Program, OBRR, CBER described how the new proposal specifically effected tissues for transplantation, those previously regulated under the Interim Regulation of December 1993, and those tissues that would be added to the regulatory framework. The proposal would add reproductive tissues such as oocytes, sperm and embryos, allograft heart valves, and dura mater under the same level of regulation as other tissues for transplantation. These tissues would be subject to requirements for control of transmission of communicable disease such as donor testing and screening for high risk behaviors, for complying with the proposed good tissue practice requirements, establishment registration and listing, and for compliance with labeling restrictions as tissues. They would also be required to submit reports of adverse events related to transmission of communicable disease to FDA. She requested specific comment on the use of accrediting bodies instead of FDA investigators for inspection of establishments for compliance with the regulation and what regulatory mechanism FDA could use to address this requirement. She noted that regulation of demineralized bone (DMB) will be addressed separately, because it is considered to be more than minimally manipulated. FDA will propose that it be classified as a Class I medical device exempted from premarket notification and device good manufacturing practices.

Dr. Antonio Pereira, Acting Director of the Human Tissue Program discussed the requirements for communicable disease control as specified in Table 2 of the proposed approach document. He indicated that allogeneic donors, living or cadaveric will be required to be screened for infectious disease risk factors either by direct questions or by a next of kin interview. The proposed requirements for donor testing varied depending on issues of autologous/allogeneic and whether the tissue is viable or not. The rationale for testing autologous banked tissue he explained is to protect laboratory personnel and health care workers. For those banked tissues where donor screening and testing is only recommended and not performed, such as for autologous banked tissue and stem cells, and for reproductive tissue from sexually intimate partners, the banked tissue must be identified as being "untested for biohazards" or if tested and positive, then identified as a "biohazard". He emphasized that the Agency will not intervene with the decisions between a family and their physicians or between sexually active partners and their physicians.

Dr. Ruth Solomon of the Human Tissue Program provided a more detailed explanation of what

good tissue practices (GTP) FDA was proposing to address processing controls. She defined GTPs as the processing and handling procedures aimed at preventing contamination and preserving integrity and function of cellular and tissue-based products. These will be the minimal baseline requirements to provide consistency across all products, will be general and flexible, enlist a quality assurance (QA) approach and will require no application to FDA. FDA has reviewed current voluntary standards and found that all encompass the elements that FDA is considering such as: a QA approach; specification of organization, personnel and facility; equipment, supplies and reagents; process controls over written procedures, tissue identification, process changes, and quarantine; labeling process controls; tissue storage and distribution; record maintenance; tissue tracking; errors and accidents; transmission of communicable disease reporting; and the keeping of complaint files for adverse reactions. The proposed approach will indicate what operations an establishment needs to document in order to comply with the regulation, but the establishment will have to determine how they will comply by developing their own SOP's and standards or using those developed by industry associations.

The open public presentations for this session were initiated by Mr. Gerald J. Cole, Executive Vice President of Tissue Banks International (TBI) a non-profit organization of eye and tissue banks with 26 locations in the US. He stated that TBI has found that its operating expenses have increased 20% since the Interim Rule went into effect in 1993, because of having to comply with additional technical and laboratory requirements. He also noted a flat to lower volume in the number of young donors qualifying because of new interpretations of high risk such as obtaining a recent tattoo, and because of additional FDA interpretations for issues such as hemodilution, and donor screening. Regarding the proposed framework, he expressed concern with implementation of the proposal adding regulatory burden for traditional tissue establishments without an expressed public health concern. He sees a need to clarify what is meant by minimal manipulation, homologous use, labeling for intended use, and good tissue practices. On questioning, he agreed to submit to the docket a list of specific examples of uses of tissues and manipulations that would be considered minimal

Dr. Richard J. Davey, Chief Medical Officer from the American Red Cross's (ARC) Biomedical and Tissue Services addressed issues related to banked human tissue and for peripheral and cord blood stem cells. He stated 4 positions/concerns: (1) demineralized bone (DMB) should be regulated as a tissue not a device; (2) ARC supports FDA's position on reduced regulation of autologous or family related stem cells; (3) FDA should use industry developed consensus standards and professional organizations to certify establishments; (4) seek clarification of the role of the TRG and relationship to the OCMO is needed. In response to a panel question, he stated that his reasoning for regulation of DMB as tissue is based on the fact that the processing involved removing elements that might impair the bones therapeutic effectiveness, not adding, changing, or enhancing its characteristics, and therefore is minimally manipulated. He called on Dr. May to address a question concerning whether ARC has noticed a decrease in young donors as TBI has since the Interim Dr. May responded that a smaller percentage of initially identified donors is accepted after screening but didn't know how that might be broken down by age group

Dr. Jur Strobos of the law firm Greenberg and Traurig and representing Biocoll, Inc. focused his comments on issues related to the border between minimal and extensive processing of structural human tissues. To encourage innovations in processing, he suggested that bone production or osteogenesis be considered an appropriate endpoint to demonstrate effectiveness, rather than controlled clinical trials when evaluating structural tissues that are more than minimally manipulated. For more than minimally manipulated tissue, imposition of the new device GMPs such as the design controls would be unworkable. He also stated that collagen derived from human tissue and used homologously should be regulated as tissue in that it should be considered minimally manipulated and that most bone, tendon, cartilage, corneas and dermis are also comprised primarily of Type 1 collagen. To this effect the acid washing of connective tissue should be determined to be minimal manipulation. In response to a panel question, he suggested that the TRG besides assessing levels of manipulation also determine what kind of data is required so the approach to data requirements is also coordinated at one level. He also elaborated on his request that acid washing of connective tissue be considered minimal manipulation by saying that this process has historically been used by surgeons and a number of premarket applications have been evaluated related to this process and the manufacture of collagen.

Ms. Mary Beth Dannefel, Chair of the Eye Bank Association of America (EBAA) a nonprofit organization consisting of 112 eye banks, focused her presentation on the premise that the EBAA standards are sufficient to monitor eye banks given the fact that based on the record of safe transplants, there is no identified threat to public safety and that FDA oversight is not needed until such a threat is identified. Though EBAA supports registration, the proposed framework addressing other aspects of regulatory oversight would be costly to eye banks to implement with no clear benefit or enhancement of safety. Responding to panel questions concerning the issue that the controls FDA is proposing would make the voluntary controls mandatory, Ms Dannefel indicated that her concern is with the GTP's being generalized to all tissue and the details not specified with the resulting possibility of additional costs to eye banks to implement them.

Dr. S. Randolph May, President of the American Association of Tissue Banks (AATB) representing 60 accredited tissue banks, noted his organization supported the framework, specifically the labeling provision , inclusion of reproductive tissue, and electronic registration . AATB has concerns with requiring tissue banks to determine whether a use is homologous or not since they have no authority over how the tissue will be used by a physician once they have distributed it. Non-homologous use, more than minimal manipulation, and non-tissue components need to be better defined. AATB also recommended better inter-center coordination to ensure consistent review and time frames for review. On questioning he agreed to submit a proposal concerning AATB's recommendation on timetables for review of various applications. He also responded to a question concerning minimal manipulation and the promotion and use of bone screws for a function that is not as a bone, and indicated that there needs to be a continuum in determining the regulatory oversight needed. Concerning demineralized bone he expressed concern that this is reversing a previous FDA decision to regulate DMB as a tissue and that taking out calcium should be determined to be minimal manipulation as is cutting of connective tissue to make it fit. Therefore, removing something from a naturally acquired tissue is minimal and adding

something is not. AATB also endorsed use of accrediting bodies for compliance with the regulations.

Mr. Richard Russo, Senior Vice President of Osteotech, Inc which processes bone for [redacted] and the [redacted] reported that there have been 455,000 transplants of Osteotech's demineralized bone (DMB) products in the last several years and that there is a greater than 30 year history of use of DMB. He requested that FDA reconsider its intent to regulate DMB as a Class 1 device and instead as suggested in the proposal, that it now consider demineralization as minimal manipulation based on knowledge of the extensive clinical experience with DMB. Mr. Russo also commented that promotion of DMB's osteoinductive and osteoconductive characteristics should be allowed in that these characteristics are the basis for demineralization of bone. Concerning GTP requirements, he suggested that errors and accidents in screening, testing or processing not be reportable as was suggested in earlier FDA discussions of GTPs and that there needs to be a mechanism established for requesting a variance or waiver from specific GTP requirements, and not left to on-site review by field inspectors. Concerning process validation, FDA should consider the adequacy of retrospective validation data wherever possible. He also suggested that FDA allow a flexible approach to clinical data requirements for non-viable allogeneic structural tissues that are more than minimally processed and allow laboratory in-vivo or in-vitro performance data. On questioning from the panel, he clarified his remarks concerning retrospective or surrogate material validation of processes as being based on the shortage of donated tissues and the stated purpose of the donation as given in informed consent for transplantation not for process validation. He also clarified that the variance he was proposing, would be to address that the GTP requirement could be met some other way and could be demonstrated through process validation to be as good as if not better. He discussed that error and accident reports are important for a firm's quality assurance program in order to assess the quality of their operation and should be kept on file at the firm.

Additional questions to the panel followed, first from Dr. Strobos who noted that it needs to be clarified as to whether DMB as a Class 1 exempt device would still be subject to the device reporting requirements. CDRH thought not. He also wanted to know if adding something such as glycerol to DMB would require a 510k modification- how will this be addressed? Dr. Richter responded that this will be addressed by the TRG on a case by case basis and would depend on what the material was that was being added. Mr Schweikert of Theracel that make cell based products for neurological diseases expressed concern that enzyme disruption of a tissue into a suspension without a change in function, shouldn't make it more than minimally manipulated and Dr. Siegel concurred. Dr. May and Mr. Tayo of AATB commented that their standards require the maintenance of an error and accident log which is examined during inspection, and though not mandated in the standards, many banks require assessments of actions taken to resolve incidents. Ms. Margery Moogk from Northwest Tissue Center ended this session with a comment supporting the recommendation to regulate allograft heart valves as tissue.

Session addressing remarks on Autologous and other Cell Therapies:

Dr. Jay Siegel, Director, Office of Therapeutics Research and Review, CBER moderated this session, and Dr. Philip Noguchi, Director of the Division of Cellular and Gene Therapies, OTRR provided an introduction to the issues relevant to evaluation of clinical safety and effectiveness as described in the proposed approach. He also provided a description of what procedures would constitute minimal manipulation and function as homologous use for cell and tissue products and gave examples of tissues combined with non-tissue elements. He elaborated on the fact that FDA has now determined that cell selection is minimal manipulation based on evaluation of considerable amount of data and clinical results in pre-market applications. Concerning flexibility in requirements related to pre-market approval, there will always need to be a baseline understanding on how the product will perform in a patient.

Dr. Siegel followed up with information concerning the availability of 2 new Agency released guidances to industry regarding providing clinical evidence of effectiveness and requirements for FDA approval of new cancer treatment uses for original and new indications.

Ms. Lisa Raines, Vice President of Government Relations for Genzyme Corp. specifically addressed the problems with requiring the 7 day general safety test for toxicity in mice and guinea pigs before releasing a product, as an unworkable requirement for such autologous products as cultured cartilage cells. She proposed that an exemption be made for this type of product as has been made for others products such as blood and gene therapies. Responding to questions from the panel, she clarified that all cellular and gene therapies whether autologous or not should be exempted from this requirement.

Dr Thomas McKearn, CEO of the Cytogen Corp, that has 2 FDA approvals for oncology products. ___ has performed over 5,000 autologous lymphocyte therapies and has documented less than 10 incidents of bacterial contamination. He questioned the definitions for structural and metabolic products and stated a need to regulate products based on scientific understandings. He requested clarification on the relationship of this framework with other recent guidances published by FDA on primary end points for cancer therapies. He was informed that he should follow the rules in place now, and FDA will be glad to discuss this further with Cytogen. He questioned what "policy" was being referred to on p. 18 referring to premarket submissions and exemption of autologous and family related donor cells and tissues. FDA's response is that there is not a distinction between stem cells and other cells on this point but on the extent of processing and that FDA is consciously not planning to regulate family decisions to use their own body parts.

Dr. Frederick Miesowicz, Vice President and General Manager of Cellcor Inc. discussed the fact that they have experience with hundereds of patients receiving autologous lymphocyte therapies that have well characterized phenotypes, and the homologous function is to restore immunity. These should be considered minimal manipulation based on process validation and product characterization. He also indicated that for some cultured cell therapies that have a 48 hour outdate where they lose their viability and ability to function, the 7 day general safety test would not be possible. He suggested that flexibility be built into the framework to allow for

supplemental indications and also proposed the use of surrogate markers for clinical efficacy for cancer therapies. He concluded with a discussion on the financial problem for small firms with obtaining reimbursement under IND, whether for accelerated approval or expanded access under a treatment IND. Dr Siegel clarified that lymphocytes used as lymphocytes to fight infection or tumor would be considered to have homologous function, however it is the activation with cytokines, or antigens that would be considered more than minimal manipulation and would trigger a higher regulatory requirement.

Dr. Alan Goldhammer, Director of Technical Affairs, Biotechnology Industry Organization (BIO) addressed concern that there is ambiguity as to how certain cell products and processes will be regulated and expressed willingness to assist FDA develop GTP's. He also said that expansion and activation of cells should be considered minimal manipulation, if cell function is not changed. Dr. Noguchi commented on the necessity to treat the regulatory requirements for cell propagation in highly structured facilities with good GMP's the same as those for cells grown by a surgeon. Additional discussion ensued as to where to draw the line concerning minimal manipulation or whether there needs to be cases by case decisions based on the scientific literature. The need for flexibility by FDA was emphasized. Dr. Siegel pointed out that many premarket applications for expanded cell therapies for cancer have been submitted to FDA for evaluation and they appeared safe but not efficacious. Ms. Pendergast added that the manufacture of all cell and tissue products should include process validation which it will be the industry's responsibility to oversee, while FDA's focus based on a resource standpoint will concern clinical validation. Ms. Raines pointed out that possible down-regulation of more than minimally manipulated products for which pre-market application are required would reduce incentive for innovation. FDA's Dr. Flamm explained that down regulation of more than minimally manipulated processes is only possible when it does not alter relevant biological characteristics, otherwise it will be possible to establish standards when enough is know as is being proposed for stem cells

Additional comment Pendergast/McKearn/Goldhammer/Raines- elaborate

Concluding comments in this session were presented by Dr. Robert Stillman a professor of obstetrics and gynecology at George Washington University who represented the board of the American Society for Reproductive Medicine (ASRM), and who couldn't be present at the morning session concerning reproductive tissue. He requested clarification concerning the 6 month quarantine provision for tissues that can be stored. He emphasized that oocytes can not be frozen and there is a reduced viability after freezing for embryos. He also addressed the problem of biohazard labeling because of the size of the vials for semen storage and suggested that another way of identifying them as such would be feasible. Retrospective relabeling would also be a problem and requires FDA clarification as do the definition of minimally manipulated as related to reproductive tissue such as assisted hatching He discussed the concept that infertility treatments should be considered a medical procedure and not be required to have premarket clearance, for these practices of medicine. On questioning from the panel he agreed to provide FDA with a list of examples of types of manipulations considered minimal

Session addressing remarks concerning Stem Cell Therapies:

This session was moderated by Dr. Curtis Scribner, Deputy Director of OBRR, CBER and introductory comments on the issues concerning peripheral blood and cord/umbilical blood stem cell regulation were provided by Dr. Liana Harvath, Chief, Laboratory of Cellular Hematology, Division of Hematology, OBRR, CBER. She described the proposed donor testing and screening that will be required for all allogeneic donors and recommended for autologous donors. She also detailed the labeling requirements as provided in Table 2 of the proposed approach document that are recommended if the donor is either not tested, or tested and found to be positive for an infectious agent. The appropriate level of requirements for processing controls and clinical safety and efficacy for stem cells will be determined based on the factors previously outlined for other therapies such as the amount of manipulation, and homologous use. It is the Agency's intent to promulgate product standards for these products and to phase in requirements for clinical evaluation if sufficient data is not available to develop processing and product standards after a specified period of time. FDA will first publish a Federal Register notice describing the relevant questions which need answers for inclusion in standards such as criteria for acceptance of a stem cell unit and procedures for handling, transporting, storing and thawing.

Public comment was initiated by Ms. Cynthia Fisher, President and CEO of Viacord, Inc. who stated that she thought the regulatory framework was appropriate and would allow the development of future therapies. On questioning reported that Viacord has had only 1 cord blood stem cell unit transplanted to date. On further questioning to determine whether the transplant outcome data was reported to the International Bone Marrow Transplant Registry (IBMTR) or any other bone marrow transplant registry, Ms. Fisher stated that the transplanter had intended to report the outcome data to IBMTR, and she believed that he did so. She said that ViaCord was on record as supporting the registration of transplant outcome data, but that she would prefer to defer to the advice of transplanters as to the organization where transplant outcome data should be reported.

Ms. Emily Rossiter presented the prepared remarks from Mr. Philip Coelho, President and CEO of ThermoGenesis Corp. who asserted that FDA should reconsider the decision to not require INDs for cord blood banks. Thermogenesis has invested in the development of processing and storage equipment for cord blood banks and is concerned that the lack of regulation with no IND exemptions, as proposed would result in legal claims on the manufacturers of the equipment used to process and store the product. He discussed that fact that not much is known about the efficacy of use of these cells, or of the quality and number needed. He was further concerned with advertising practices that are not backed up with data supporting successful use of this product. Of particular concern, he cited that commercial firms have given the impression that numerous successful transplants have been performed with cord blood units from their facility, when, in fact, their firms do not provide any information regarding the number of units used or the outcome data from transplants performed with units from their firms. Thermogenesis strongly

recommended and supports the inclusion of IND, GMP, and premarket application requirements in the regulatory plan for commercial operations which intend to market related allogeneic stem cell products. They strongly support FDA oversight and enforcement of labeling standards.

Dr. Rebecca Haley, Chair of the Hematopoietic and Cellular Therapies Committee of the American Association of Blood Banks (AABB.) addressed such concerns as: (1) a similar framework of regulation based on risk also needs to be developed for blood products; (2) clarity is needed to assure that banks collecting for autologous use are aware of additional requirements if they offer units for allogeneic use; (3) labeling should allow electronic labeling and the role of the TRG in evaluating promotional claims needs to be clarified; (4) clarify requirements for a test positive unit such as CMV; (5) should consider adding bone marrow stem cells to proposal since product and uses the same; (6) indicated the development of standards for stem cells is feasible and is being addressed by AABB in conjunction with FAHCT; (7) endorses use of private organizations for compliance activities. When questioned regarding cord blood collection experience, Dr. Haley stated that the American Red Cross is currently in the research phase and anticipates collection of cord blood for allogeneic use to begin soon. She said that she was unaware of the number of transplants of cord blood performed by AABB members, but thought that most of the unrelated allogeneic cord blood transplants performed by AABB members were reported to the transplant registries. When questioned regarding her comments on biohazard labeling of products she stated that placement of specific test results on the product label creates an invasion of privacy problem. She cited her experience of nurses refusing to transfuse platelets collected from a CMV positive donor, and recommends that CMV positive labels should not be required to be placed on the product.

Ms. Marie Staie filled in for Mr. Paul Billings, President and CEO of the International Cord Blood Foundation and questioned when informed consent needs to be given. ICBF requests 60 days pre-birth for cord blood, not at the time of collection. When questioned regarding the number of units collected by ICBF that have been used in a transplant, Ms. Staie replied that 1 unit had been used in an unrelated recipient. She through, but was not sure whether the outcome data had been reported to the transplant registry.

Mr. Thomas Moore, Chairman and CEO of Cord Blood Registry, Inc. (CBR) presented a model by which his company targets cord blood collection; the "very high risk patient" or "high-risk" category, and the low risk category of people who just want to save their cord blood. Mr. Moore stated that CBR has collected approximately 6,000 cord blood samples, which has involved more than 2,000 doctors who have collected samples in over 1,100 different birthing hospitals. When questioned regarding the number of units collected by CBR that have been used in transplantation, Mr. Moore stated that 2 transplants had occurred: the first was performed in late November of 1995 and the second was performed in late February 1997. He stated that CBR protocols require that the transplant physician is to report the outcome data to the marrow transplant registry; and CBR also has reported back to them at 3, 6, and 18 months, and each year thereafter for 5 years.

Dr. Nancy Collins of the Sloan Kettering Cancer Center Allogeneic Stem Cell Facility filled in for

Dr. Elizabeth Shpall and represented the Foundation for the Accreditation of Hematopoietic Cell Therapy (FAHCT) as well as the International Society for Hematotherapy and Graft Engineering (ISHAGE) and the American Society for Blood and Marrow Transplantation (ASBMT). She reported that FAHCT has developed standards for stem cell collection, processing, and transplantation and will soon start an inspection and accreditation program that will satisfy FDA requirements. Her major concerns related to: (1) requirements for an IND/PLA would hamper a bank from adapting new processing techniques, (2) the definition of family related should also include cousins, grandparents, aunts or uncles because the infectious disease risk is no different from where the donor is a parent, child or sibling. (3) clarification of regulation of intended use, and (4) theirneed to clarify regulation of ancillary devices and reagents used in processing. When questioned regarding the number of units collected and transplanted by members of FAHCT, ISHAGE, and ASBMT, Dr. Collins said she did not know the answer and did not want to guess. She said that the FAHCT standards encourage, but do not require the reporting of transplant outcome data. She was further questioned regarding her comments of opposition to an IND. She sated that it is their perception that an IND impedes research. Further questions regarding the exact reasons for this perception were focused on who pays)the patient of the institution) for experimental therapies, as the possible major reason for opposition to the IND.

Dr Pablo Rubenstein, Director of the Cord Blood Bank of the New York Blood Center was the final public speaker and stated that he believes the IND mechanism is the only way to guarantee that all the information generated in the course of study of a technology will be available to evaluate its potential for good and bad. He said that the development of specific standards for a product for which the causal element for hematopoiesis remains undefined, is a serious problem. He expressed his concerns that cord blood units collected for family use, which are not subject to an IND, may be used in the future in manipulated cell therapies. He asked the agency to clarify its position as to whether minimal manipulation also applies in a prospective sense. He also expressed his concerns regarding the labeling and promotion of materials by commercial firms who base their claims on data collected by others who have been using different methods and procedures that the firm making the claims. When questioned regarding the number of cord blood units from the NY Blood Center cord blood bank, he stated that 357 cord blood units from their bank have been used in transplants. He stated that he believes it is the cord blood bank's responsibility to collect the transplant outcome data. He did not oppose sharing the data with transplant registries, but believes the primary responsibility is with the cord blood bank providing the units.

The meeting was adjourned by Ms. Pendergast at 4:45.