BEFORE THE
SCIENTIFIC AND MEDICAL ACCOUNTABILITY STANDARDS
WORKING GROUP
TO THE INDEPENDENT CITIZENS' OVERSIGHT COMMITTEE
TO THE
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE
ORGANIZED PURSUANT TO THE
CALIFORNIA STEM CELL RESEARCH AND CURES ACT

ANNUAL MEETING

LOCATION: SAN FRANCISCO MARRIOTT
UNION SQUARE
480 SUTTER STREET
SAN FRANCISCO, CALIFORNIA

DATE: WEDNESDAY, MAY 26, 2010
10 A.M.

REPORTER: BETH C. DRAIN, CSR
CSR. NO. 7152

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I N D E X

SAN FRANCISCO, CALIFORNIA; WEDNESDAY, MAY 26, 2010

10 A.M.

CHAIRMAN LO: GOOD MORNING. WHY DON'T WE GET SETTLED. EVERYBODY SORT OF GRAB YOUR LAST CUP OF COFFEE FOR THE MORNING. WE HAVE A REALLY INTERESTING AND PACKED AGENDA THIS MORNING. WE'RE REALLY GLAD TO HAVE EVERYONE HERE. WE'RE LOOKING FORWARD TO A GREAT MEETING. SHERRY LANSING IS GOING TO SORT OF START US OFF BY SETTING THE TONE.

MS. LANSING: FIRST OF ALL, I WANT TO WELCOME ALL OF YOU AND THANK YOU FOR WAITING. I LEFT LOS ANGELES VERY EARLY THIS MORNING AND CIRCLED SAN FRANCISCO FOR OVER AN HOUR AND 15 MINUTES BECAUSE THE PRESIDENT WAS HERE. SO EVEN THE PRESIDENT -- UNFORTUNATELY THERE WAS NOTHING WE COULD DO, SO I APOLOGIZE FOR STARTING THIS MEETING TEN MINUTES LATER.

BUT I REALLY WANT TO WELCOME ALL OF THE STANDARD WORKING GROUP MEMBERS AS WELL AS WELCOME THE INVITED PANELISTS, THE GRANTEES, AND MEMBERS OF THE PUBLIC. THIS IS REALLY KIND OF A HISTORIC MEETING FOR US BECAUSE THIS IS THE FIFTEENTH MEETING OF THE STANDARD WORKING GROUP IN THE PAST FIVE YEARS. AND I WANT TO SAY WHEN WE STARTED THIS

GROUP, WE SAID THAT WE WERE GOING TO BE A WORK IN PROGRESS, THAT WE WERE CONSTANTLY GOING TO MONITOR WHAT WAS GOING ON IN THE WORLD, AND WE'VE BEEN QUITE TRUE TO OUR WORD. AND WE ADJUST AS THE TIMES CHANGE. AND THAT'S REALLY WHAT THIS MEETING IS ABOUT.

AS YOU KNOW, THIS IS THE 2010 ANNUAL MEETING OF THE STANDARDS WORKING GROUP. AND THE ANNUAL MEETING IS TYPICALLY DEDICATED TO EXPANDING OUR UNDERSTANDING OF EMERGING ISSUES IN STEM CELL SCIENCE. THIS MEETING ACTUALLY PROVIDES AN OPPORTUNITY FOR THE STANDARD WORKING GROUP TO DEVELOP AN UNDERSTANDING OF THE ISSUES ON WHICH IT MAY BE CALLED UPON TO MAKE POLICY RECOMMENDATIONS TO THE ICOC IN THE FUTURE.

SO THIS YEAR WE APPROACHED DR. TROUNSON AND WE ASKED HIM WHAT HE CONSIDERED TO BE THE IMPORTANT ETHICAL POLICY ISSUES THAT MIGHT BE FACING CIRM. HE INDICATED THAT THERE WERE A SET OF SCIENTIFIC, ETHICAL, AND INTELLECTUAL PROPERTY ISSUES RELATED TO STEM CELL BANKING THAT HE WOULD LIKE TO EXPLORE IN A WORKSHOP FORMAT. DR. TROUNSON IS ACTUALLY GOING TO EXPAND ON THESE QUESTIONS AT THE BEGINNING OF OUR WORKSHOP. SO WE THANK YOU, ALAN, FOR YOUR INPUT.

AS A POINT OF CLARITY, I JUST WANT TO SAY FOR THOSE OF YOU WHO MIGHT NOT BE AWARE THAT THE STANDARD WORKING GROUP IS CHARGED WITH RECOMMENDING TO THE ICOC STANDARDS FOR THE ETHICAL CONDUCT OF CIRM-FUNDED RESEARCH. THIS MANDATE ACTUALLY INCLUDES PROCEDURES FOR THE SAFE AND ETHICAL PROCUREMENT OF CELLS FOR RESEARCH AND CLINICAL EFFORTS. GIVEN THIS MANDATE, WE ARE EXTREMELY PLEASED TO HAVE OUR ANNUAL MEETING AS A VENUE TO DISCUSS ISSUES RELATED TO THE COLLECTION AND DISTRIBUTION OF RESEARCH MATERIALS.

I WOULD LIKE ALSO TO EXTEND A SPECIAL THANKS TO OUR INVITED PANELISTS WHO WILL INTRODUCE THEMSELVES SHORTLY TO YOU. OUR PANELISTS RANGE FROM SCIENTISTS THAT CREATE STEM CELL LINES FOR RESEARCH TO MANAGERS OF STEM CELL BANKING AND DISTRIBUTION ORGANIZATIONS. I CANNOT TELL YOU HOW GRATEFUL WE ARE TO ALL OF YOU FOR TAKING TIME OUT OF YOUR EXTREMELY BUSY SCHEDULES TO JOIN US HERE TODAY.

AND FINALLY, I WOULD LIKE TO RECOGNIZE OUR NEWEST WORKING GROUP MEMBER, PATRICK TAYLOR. PATRICK COMES FROM HARVARD MEDICAL SCHOOL CHILDREN'S HOSPITAL IN BOSTON. PATRICK HAS BEEN DEALING WITH THE RANGE OF LEGAL AND POLICY ISSUES RELATED TO HUMAN STEM CELL RESEARCH. HE HAS DIRECT OPERATIONAL

EXPERIENCE WITH THE IMPLEMENTATION OF STEM CELL RESEARCH OVERSIGHT PROGRAMS, AND WE REALLY WELCOME YOUR PRACTICAL EXPERIENCE AND ARE VERY GRATEFUL THAT YOU HAVE JOINED THIS COMMITTEE.

DR. TAYLOR: THANK YOU.

MS. LANSING: AGAIN, I WOULD LIKE TO WELCOME EVERYBODY. AND I LOOK FORWARD TO AN EXTREMELY PRODUCTIVE MEETING. AND WITH THAT, BERNIE, I'LL TURN IT BACK TO YOU.

CHAIRMAN LO: THANKS, SHERRY. I THOUGHT MAYBE WE'D FIRST GO AROUND THE ROOM AND HAVE EVERYONE INTRODUCE THEMSELVES. WE HAVE A LOT OF PEOPLE HERE, AND WE WANT TO HAVE A GOOD DIALOGUE GOING. I'LL START. I'M BERNARD LO FROM UCSF HERE IN SAN FRANCISCO. I CO-CHAIR THIS PANEL WITH SHERRY.

MS. LANSING: I'M SHERRY LANSING. I CO-CHAIR THE PANEL WITH BERNIE. I'M THE PATIENT ADVOCATE FOR THE CANCER COMMUNITY ON THE CIRM BOARD.

DR. TAYLOR: I'M PAT TAYLOR. I'M REALLY DELIGHTED TO BE HERE. NOTICE THAT SHERRY DIDN'T SAY I HAD EXPERIENCE WITH DOING THEM CORRECTLY, SO I'M ACTUALLY HERE TO LEARN AS MUCH AS ANYTHING ELSE AND DELIGHTED TO BE HERE.

MS. FEIT: I'M MARCY FEIT AND I'M BOARD

MEMBER ON CIRM, AND I'M A PATIENT ADVOCATE FOR DIABETES.

DR. CIBELLI: JOSE CIBELLI, MICHIGAN STATE UNIVERSITY.

DR. KIESSLING: ANN KIESSLING, HARVARD MEDICAL SCHOOL.

(INTRODUCTION OF CIRM STAFF OFF MICROPHONE.)

DR. ISASI: ROSARIO ISASI, CENTER OF GENOMICS AND POLICY AT MCGILL UNIVERSITY AND INTERNATIONAL STEM CELL FORUM WORKING PARTY SECRETARY.

MR. TORRES: FORMER SENATOR ART TORRES, COLON CANCER SURVIVOR, PATIENT ADVOCATE, AND VICE CHAIRMAN OF THE GOVERNING BOARD OF CIRM.

DR. ROBSON: I'M JOHN ROBSON. I'M VICE PRESIDENT OPERATIONS AT CIRM.

MS. BAUM: I'M ELONA BAUM, THE GENERAL COUNSEL OF CIRM.

DR. TROUNSON: ALAN TROUNSON, PRESIDENT OF CIRM.

DR. COUTURE: I'M LARRY COUTURE FROM CITY OF HOPE NATIONAL MEDICAL CENTER AND BECKMAN RESEARCH INSTITUTE.

DR. OLSON: PAT OLSON, EXECUTIVE DIRECTOR

AT CIRM.

DR. FORSBERG: ERIK FORSBERG. I'M COMING FROM MADISON, WISCONSIN. I REPRESENT WICELL RESEARCH INSTITUTE AS THE EXECUTIVE DIRECTOR.

DR. LORING: I'M JEANNE LORING. I'M THE DIRECTOR OF THE CENTER FOR REGENERATIVE MEDICINE AT THE SCRIPPS RESEARCH INSTITUTE, THE STEM CELL CENTER WHICH IS SPONSORED BY CIRM AND I'M ALSO A CIRM GRANTEE.

DR. CYPRESS: RAY CYPRESS. I'M CHAIRMAN, PRESIDENT, AND CEO OF AMERICAN TYPE CULTURE COLLECTION.

CHAIRMAN LO: AGAIN, OUR GRATITUDE AND THANKS FOR OUR SCIENTIFIC PANELISTS FOR COMING.

DR. PRIETO: FRANCISCO PRIETO. I'M ALSO A BOARD MEMBER OF THE ICOC AS A PATIENT ADVOCATE.

DR. PETERS: TED PETERS FROM THE GRADUATE THEOLOGICAL UNION IN BERKELEY. I'M HERE AS A BIOETHICIST.

DR. ROBERTS: I'M DOROTHY ROBERTS. I'M A PROFESSOR AT NORTHWESTERN LAW SCHOOL AND A FACULTY FELLOW AT THE INSTITUTE FOR POLICY RESEARCH.

CHAIRMAN LO: SO I'M GOING TO TURN IT OVER TO GEOFF LOMAX, TO WHOM WE OWE A GREAT DEAL OF THANKS FOR PUTTING THIS PROGRAM TOGETHER, TO DO A

STAFF REPORT.

DR. LOMAX: THIS WILL BE VERY BRIEF AND WE'LL MOVE QUICKLY INTO THE WORKSHOP. I'D ALSO LIKE TO RECOGNIZE PAT BECKER AND NINI GABRA AT THE BACK OF THE ROOM. THEY REALLY ARE THE WORKHORSE IN TERMS OF THE FACT WE'RE ALL HERE TODAY ORGANIZED AND PREPARED.

I ALSO WANTED TO CHECK. WE HAVE SOME FOLKS ON THE PHONE LINE. SO WE DO HAVE ROB TAYLOR ON THE PHONE LINE AT THE MOMENT. I KNOW, ROB, IF YOU CAN HEAR US ALL RIGHT, FEEL FREE TO CHIME IN AT ANY MOMENT BECAUSE WE KNOW WE CAN'T SEE YOUR HAND.

DR. TAYLOR: I CAN HEAR YOU. THANKS, GEOFF.

DR. LOMAX: I THOUGHT WE WOULD START WITH THE UPDATE. THIS IS A NICE IMAGE OF THE NEWEST CIRM FACILITY THAT'S COME ONLINE. IT'S THE STEM CELL CENTER AT THE UNIVERSITY OF CALIFORNIA IRVINE. I HOPE FOLKS HAVE BEEN SEEING SOME OF THE REPORTS THAT OUR FACILITIES ARE UP AND RUNNING, AND IT'S VERY EXCITING TO SEE ALL THIS NEW CAPACITY COMING ONLINE IN THE STATE.

QUICKLY TO REMIND YOU ON THE SORT OF POLICY SIDE, THIS WAS THE TIMELINE FOR THE LAST SET OF REVISIONS WE DID TO OUR REGULATIONS. THE

SECTIONS WERE 170, 80, AND 90. AND THE LAST TIME WE CONSIDERED THESE SECTIONS WAS LATE NOVEMBER, I BELIEVE, OR EARLY DECEMBER. IN FEBRUARY OF 2010, THE ICOC APPROVED THE LANGUAGE WE PUT FORTH, AND WE ARE AS OF THIS DATE STILL WAITING FINAL WORD FROM THE OFFICE OF ADMINISTRATIVE LAW BEFORE ACTUALLY POSTING THAT REGULATORY LANGUAGE.

HOWEVER, IN ANTICIPATION OF THE APPROVAL FROM THE OFFICE OF ADMINISTRATIVE LAW, WITH DID FEEL IT WAS IMPORTANT TO GET OUT EARLY THIS YEAR AND ADVISE OUR GRANTEE INSTITUTIONS ON THESE AMENDMENTS. SO WE HELD A SERIES OF WORKSHOPS IN NORTHERN CALIFORNIA, LOS ANGELES, AND SAN DIEGO TO REVIEW THE AMENDMENTS. WE ALSO COVERED THE CIRM COMPLIANCE PROGRAM WHICH I'VE DESCRIBED TO YOU PREVIOUSLY. THAT'S THE PROGRAM WHERE WE DO SITE VISITS AND EVALUATE GRANTEE COMPLIANCE WITH OUR VARIOUS PROCEDURES AND POLICIES. AND ALSO DISCUSS NEW ISSUES THAT HAVE EMERGED, PARTICULARLY ISSUES THAT COME UP IN MULTI-INSTITUTIONAL COLLABORATIONS.

AS YOU MAY BE AWARE, WE'VE INITIATED A NUMBER OF DISEASE TEAM PROJECTS WHICH INVOLVE MULTIPLE INSTITUTIONS, HUMAN SUBJECTS ISSUES, ANIMAL CARE ISSUES. SO WE'VE BEEN OUT DESCRIBING SORT OF HOW WE'D LIKE TO SEE THE ASSURANCES AND OTHER

COMPLIANCE DOCUMENTS COME TO CIRM.

AND IN ADDITION, THIS TIME WE ALSO INCLUDED DISCUSSION OF FINANCIAL ADMINISTRATION ISSUES. THESE DON'T BEAR DIRECTLY ON THE MEDICAL AND ETHICAL STANDARDS, BUT WE THOUGHT IT WAS A USEFUL TOPIC TO AT LEAST BRING TO THIS MEETING. IT CERTAINLY WAS A TOPIC OF INTEREST TO A LOT OF THE INSTITUTIONAL OFFICIALS. SO WE FEEL IT WAS JUST A WAY TO COMBINE REGULATORY COMPLIANCE WITH SORT OF ADMINISTRATIVE COMPLIANCE. AND IT SEEMED TO BE A GOOD FORMAT. WE HAD 42 PARTICIPANTS AND VERY SORT OF LIVELY DISCUSSION, GOOD Q AND A.

WE HAVE INCLUDED A REPORT IN YOUR PACKET, AND THERE'S COPIES OF THE REPORT ON THE TABLE THAT SORT OF SUMMARIZE SORT OF INSIGHTS THAT WE'VE GAINED AND SOME MODEST RECOMMENDATIONS, PARTICULARLY IN RELATION TO CALIBRATING CIRM STANDARDS WITH STATE GUIDELINES.

AND HERE'S A COPY OF THE COVER OF THE REPORT AND YOURS TRULY AT ONE OF THE WORKSHOPS. THIS IS THE ONE HELD IN SAN FRANCISCO. AGAIN, A VERY SORT OF LIVELY TURNOUT, GOOD DISCUSSION FORMAT.

ANOTHER ITEM, AGAIN JUST TO REPORT BACK ON, WE HAD DR. JOHN GALLAND OF THE OFFICE OF RESEARCH INTEGRITY TALK TO US ABOUT FEDERAL POLICY

REGARDING RESEARCH INTEGRITY. IN PARTICULAR, ONE OF THE ISSUES THAT WE WERE INTERESTED IN HEARING ABOUT IS HOW THEY ADDRESS ISSUES OF SCIENTIFIC MANIPULATION OF IMAGES. WE THOUGHT IT WOULD BE HELPFUL, GIVEN THAT IMAGING IS SUCH AN IMPORTANT PART OF PUBLISHING THESE DAYS, HOW WE SORT OF UNDERSTAND THE FRAMEWORK IN WHICH IMAGING IS EVALUATED, WHAT CONSTITUTES APPROPRIATE IMAGING, WHAT CONSTITUTES INAPPROPRIATE MODIFICATION OF IMAGES.

I THINK WE CAME AWAY FROM THAT SESSION REALIZING IT'S SORT OF COMPLICATED, BUT THE NICE PART ABOUT IT IS THAT ORI SORT OF SELF-IDENTIFIED AS A RESOURCE. TO THE EXTENT WE WOULD EVER HAVE QUESTIONS ABOUT THE APPROPRIATENESS OF ANY PARTICULAR SCIENTIFIC IMAGE, THEY WOULD BE HAPPY TO WORK WITH US TO EVALUATE THAT. THIS WASN'T DRIVEN BY ANY SORT OF PARTICULAR PROBLEM. IT WAS JUST REALLY ONE OF THOSE ITEMS THAT WE HAD BEEN READING A LOT ABOUT IN THE LITERATURE AND THOUGHT AS A STAFF WE SHOULD UNDERSTAND A BIT BETTER WHAT THE ISSUES WERE AND WHAT THE PROCESS IS FOR RESOLVING THOSE ISSUES.

AND THEN WE HAD A NICE SORT OF MORE GENERAL DISCUSSION ABOUT THE ROLE OF FUNDING

ORGANIZATIONS, PUBLISHERS, AND INSTITUTIONS, AND JUST PROMOTING GOOD RESEARCH PRACTICE OVERALL. IT WAS ATTENDED BY THE MAJORITY OF OUR SCIENTIFIC STAFF. AND, AGAIN, IT WAS SORT OF A REALLY NICE SORT OF GIVE-AND-TAKE. I THINK WE GOT SOME GOOD INSIGHTS ABOUT HOW ONE SORT OF PROMOTES BEST RESEARCH PRACTICE.

WE HAVE, AGAIN, A REPORT WHICH I BELIEVE WE PROVIDED A LINK AND DIDN'T WANT TO REPRODUCE IN THE INTEREST OF SAVING PAPER, BUT THE CIRM DIVERSITY WORKSHOP, WHICH WAS HELD AT DREW UNIVERSITY IN SOUTHERN CALIFORNIA. AND ONE OF THE ISSUES THAT CAME UP AT THE WORKSHOP WAS DISCUSSION OF THE NEED FOR GREATER DIVERSITY OF DONORS OF HUMAN EMBRYONIC STEM CELL LINES AND INDUCED PLURIPOTENT CELLS. AND THAT'S DIVERSITY IN BOTH SORT OF THE ETHNIC AND DISEASE CHARACTERISTICS OF LINES.

AND THEN THERE WAS EXTENSIVE DISCUSSION ABOUT STRATEGIES FOR RECRUITING PARTICIPANTS BOTH IN BASIC RESEARCH AND CLINICAL TRIALS. OBVIOUSLY THE ABILITY TO SUCCESSFULLY RECRUIT PARTICIPANTS HAS DIRECT BEARING ON YOUR ABILITY TO DIVERSIFY WHAT MATERIALS ARE AVAILABLE FOR RESEARCH.

AND THEN WE HAD SOME ADDITIONAL DISCUSSIONS ABOUT HOW SMALLER RESEARCH INSTITUTIONS

COULD BE INVOLVED IN CIRM RESEARCH. AND WE HAD A VERY INTERESTING DISCUSSION AT THE END ABOUT MODELS FOR USING PRACTICE-BASED NETWORKS TO SUPPORT RECRUITMENT IN CLINICAL TRIALS. AND, AGAIN, IN INTEREST OF TIME, I WON'T GO INTO DETAIL THERE, BUT I THINK IT'S WELL DEVELOPED IN THE REPORT. AND WE GOT SOME VERY INTERESTING DATA IN TERMS OF IF YOU HAVE A PRIMARY CLINIC AND YOU'RE ASKING THEM TO HELP WITH RECRUITMENT OF DONORS IN CLINICAL TRIALS, WHAT THE IMPACTS OF THAT WOULD BE ON THE SORT OF CLINICAL PRACTICE BOTH IN TERMS OF COST AND TIME COMMITMENT.

WE THINK THAT WAS VERY VALUABLE DATA BECAUSE IT SORT OF GIVES US A SENSE THAT IF YOU WERE GOING TO SORT OF FUND A PROGRAM LIKE THAT, WHAT THE FINANCIAL IMPACTS WOULD BE.

AGAIN, SOME IMAGES FROM THE WORKSHOP. AND I BELIEVE THAT IS THE LAST SLIDE. SO IF THERE ARE ANY QUESTIONS, I'LL TAKE THEM.

DR. PETERS: WITH REGARD TO ETHNIC DIVERSITY, HOW DID YOU FORMULATE YOUR MOTIVATION FOR MOVING IN THAT DIRECTION? WAS IT GENOMIC IN ORDER TO GET A MORE COMPREHENSIVE COLLECTION OF GENOMES, OR WAS IT IMPORTANT SOCIALLY TO DO THAT?

DR. LOMAX: I THINK IT WAS -- MY SENSE WAS IT WAS DRIVEN PRIMARILY BY THE SCIENCE, BUT I

BELIEVE DR. TROUNSON WILL SORT OF TOUCH ON THIS POINT IN SOME OF HIS OPENING REMARKS. THE INITIAL IMPETUS, AS I UNDERSTOOD IT, WAS DO OUR STOCKS OF RESEARCH MATERIALS, ARE THEY SUFFICIENT BOTH FOR BASIC RESEARCH; AND IN THE EVENT WE WERE DEVELOPING A THERAPEUTIC PRODUCT AND WITH THE UNDERSTANDING THAT WE WOULD WANT THAT PRODUCT TO BE AVAILABLE TO THE DIVERSITY OF THE CALIFORNIA POPULATION, DO WE HAVE THE RIGHT STUFF? IT WAS REALLY WITH AN AYE TOWARDS THAT DELIVERY OF CLINICAL PRODUCT THAT IS AVAILABLE TO EVERYONE WHICH HAS ALWAYS BEEN A GOAL OF THIS ORGANIZATION.

THANK YOU FOR YOUR TIME.

CHAIRMAN LO: DO YOU WANT TO GET US STARTED ON THE BANKING WORKSHOP?

DR. LOMAX: SURE. LET ME COME BACK OVER THERE, IF I MAY, AND SHUFFLE A FEW NOTES.

MR. TORRES: MR. CHAIRMAN, FOR THE MOMENT, I REALIZE THAT THE BEAUTY OF CIRM IS THAT WE ALWAYS BRING IN INTERNS FROM UNIVERSITIES THROUGHOUT THE COUNTRY DURING THE SUMMER. I'M VERY PROUD TO HAVE IN THE CHAIR'S OFFICE A YOUNG WOMAN I RECRUITED FROM BRANDEIS UNIVERSITY. AND BRANDEIS IS FULLY FUNDING HER PARTICIPATION WITH US THIS SUMMER, DANIELLE WOLFSON.

CHAIRMAN LO: THANK YOU. WELCOME.

DR. LOMAX: BEST THINGS ABOUT THESE MEETINGS IS YOU GET A LOT OF EXERCISE. SO I'D LIKE TO INVITE DR. TROUNSON TO COME TO THE PODIUM. HE'S GOING TO MAKE SOME BRIEF REMARKS ABOUT SORT OF THE WORKSHOP AND SOME OF HIS THINKING. AND I JUST NEED TO FIND THOSE SLIDES.

DR. TROUNSON: THANK YOU, GEOFF, SHERRY, BERNIE, ALL MEMBERS OF THE STANDARDS WORKING GROUP, ALL OUR VISITORS, ALL OUR FRIENDS, AND MEMBERS OF STAFF. IT'S ONE OF THE ENJOYABLE, REALLY ENJOYABLE WORKING GROUPS, I HAVE TO SAY.

MS. LANSING: WE HAVE FUN AS WELL AS DO WORK.

DR. TROUNSON: IT'S A COOL THING.

MS. LANSING: I JUST WANT TO SAY THERE'S A CONSISTENCY. A LOT OF US HAVE BEEN HERE SINCE THE VERY BEGINNING, SO IT'S A GROUP THAT PEOPLE LIKE TO SERVE ON.

DR. TROUNSON: EVEN PRESIDENTS WON'T STOP US GETTING HERE. SO AS SHERRY SAID, I HAVE SOME VIEWS ABOUT WHAT WE SHOULD BE DOING IN THE SENSE OF BANKING. AND I WANTED TO TRY AND DESCRIBE TO YOU WHAT I HAD IN MIND AND WHAT MAYBE THE AGENCY WOULD BE PROGRESSING IN BECAUSE THERE ARE SOME ISSUES THAT

HAVE COME OUT OF THE UTILIZATION OF PATIENT CELLS FOR DISCOVERY PURPOSES, VERY IMPORTANT DEVELOPMENTS IN MEDICINE, BUT ALSO COMMERCIAL ISSUES. AND IT RAISED MANY CONCERNS, AND I SUPPOSE THAT'S BEST EXPRESSED BY THE PROBLEMS THAT CAME OUT OF THE HELA CELL LINE WORK, WHICH HAS BEEN VERY, VERY IMPORTANT FOR SCIENCE AND MEDICINE.

BUT WHETHER WE REALLY EVER HAD PROPER CONSENT, BERNIE, I THINK IN THAT PARTICULAR EXAMPLE, WE'RE TRYING TO AVOID SOME OF THIS BY SORT OF THINKING FORWARD. SO I HAD ASKED GEOFF AND BERNIE TO SORT OF THINK ABOUT THIS AND THEN BRING THIS PROPOSAL TO SHERRY TO SEE IF WE COULD SORT OF START TO THINK INTO THIS SPACE. AND IT'S A LITTLE DIFFERENT, I THINK, THAN WHAT WE'VE BEEN THINKING OF BEFORE.

SO I WANT TO START WITH THERE ARE TWO ENDS OF THIS. THERE ARE RESEARCH TOOLS AND CORE PROGRAMS, AND I WANT TO LOOK AT THE CLINICAL END FIRST BECAUSE I THINK IN SOME RESPECTS IT'S A BIT SIMPLER. THE USE PARTICULARLY OF IPS CELLS AND EMBRYONIC STEM CELLS FOR CLINICAL RESEARCH REALLY SORT OF FITS PRETTY MUCH IN WHAT LARRY AND OTHERS HAVE BEEN DOING IN DEVELOPING CELLS THAT REALLY COME FROM A BACKGROUND WHERE THERE'S BEEN A LOT OF CARE

IN DEVELOPING THEM. AND PARTICULARLY NOWADAYS WE ARE DEVELOPING CALIFORNIA EMBRYONIC STEM CELL LINES WHICH REALLY EVOLVE INTO CLINICAL USEFULNESS BECAUSE THEY'VE BEEN DERIVED THROUGH GMP FACILITIES. NOT THE ACTUAL EMBRYO, BUT THE MATERIAL THAT COMES FROM THOSE EARLY EMBRYOS AND THEN GROWN UP AND LOOKED AFTER IN VERY SPECIAL FACILITIES.

AND, THEREFORE, THESE STOCKS OF EMBRYONIC STEM CELLS AND I THINK IN THE FUTURE IPS CELLS, THE INDUCED PLURIPOTENTIAL STEM CELLS, WILL PROBABLY BE USED BY SPECIFIC COMPANIES AND ACADEMIC UNITS FOR CLINICAL PURPOSES BECAUSE THEY'LL BE SUCH A VALUABLE STOCK THAT I THINK THAT THOSE STOCKS WILL BE SORT OF MANAGED VERY CAREFULLY AND PROVIDED FOR THE PURPOSES OF THE PEOPLE WHO ARE DERIVING THEM RATHER THAN BEING BROADLY USED. IT'S POSSIBLE THAT THEY MIGHT BE BROADLY USED, BUT I THINK THE TEAMS THAT DEVELOP THOSE PARTICULAR GMP LINES WANT TO MAINTAIN THEM SO THEY CAN USE THEM OVER A LONG PERIOD OF TIME BECAUSE THEY'RE NEEDED FOR THE REGULATORY REQUIREMENTS BY FDA AND OTHER REGULATORY BODIES TO HAVE SOME CONSISTENCY.

AND SO IF THE PRODUCT COMES FROM A BANK AND THE BANK IS KNOWN AND HAS A HISTORY AND THOSE CELLS HAVE BEEN MANAGED IN A CERTAIN WAY, THEN IT'S

CLEARLY BETTER FOR THE COMPANY OR FOR THE UNIT THAT'S DEVELOPING THOSE CLINICAL PROCEDURES TO BE ABLE TO ALWAYS GO BACK TO THAT BANK. AND IT HELPS THEM IN THEIR PROCESSES GOING FORWARD.

SO IN SOME RESPECTS, I THINK THE CLINICAL UTILIZATION OF CELLS WILL BE VERY SPECIFIED, VERY WELL-MANAGED, VERY CAREFULLY MANAGED, WILL BE MAINTAINED, I THINK, IN UNITS WHERE THEY'RE DERIVED, AND THEY'LL BE MAINTAINED UNDER STRICT VIGILANCE THAT WON'T ALLOW THOSE CELLS TO BE INTERFERED WITH IN ANY WAY. SO THEY WILL IN MANY RESPECTS BE THE PRODUCT, THE COMMERCIAL PRODUCT, THAT IS THE REALLY VALUABLE THING FOR COMPANIES. ONCE YOU'VE GOT A CELL LINE THAT WILL PRODUCE AN INSULIN-PRODUCING CELL THAT WILL CORRECT DIABETES, YOU WON'T WANT TO MOVE AWAY FROM IT IF YOU CAN HELP IT.

SO IN THAT RESPECT, THE CELLS THAT ARE GOING TO BE USED CLINICALLY, I THINK, HAVE BEEN CONSIDERED VERY CAREFULLY AND PARTICULARLY EMBRYONIC STEM CELLS. I THINK WE HAVE A VERY GOOD UNDERSTANDING OF HOW THEY'LL BE MANAGED, AND THE CONSENTS AND SO FORTH ARE FAIRLY WELL STANDARDIZED.

WHEN IT COMES TO IPS CELLS, THERE'S MUCH LESS STANDARDIZATION, AND I DON'T THINK THAT WE'VE GOT REALLY ANY UNDER GMP PRODUCTION AS YET, ALTHOUGH

I SUPPOSE IT MUST BE GETTING CLOSE. THERE IS. CLOSE. SO GETTING CLOSE MEANS THAT THAT COULD BE IMPORTANT. NOW, IPS CELLS CLINICALLY YOU WOULD EXPECT TO BE USED FOR THE PATIENT WHO DONATED THE CELL. SO ONE MIGHT EXPECT THAT THE BENEFIT OF IPS CELLS IS BECAUSE THEY'RE GENETICALLY COMPATIBLE WITH THE PATIENT. SO YOU WON'T HAVE THE CHALLENGE OF IMMUNE SUPPRESSION OR AT LEAST NOT THE LEVEL OF IMMUNE SUPPRESSION THAT YOU WOULD USE IF THE CELLS WERE COMPLETELY ALLOGENEIC AND COMPLETELY FOREIGN, BUT IT'S POSSIBLE THAT THEY COULD BE USED IN A GENERAL WAY AS WELL.

AND SO IN SOME RESPECTS WE NEED TO MAKE SURE THAT THEY FIT INTO THE SAME KIND OF FORMAT AS EMBRYONIC STEM CELLS. I DON'T THINK THE KIND OF CONSENTS THAT ARE SET UP FOR IPS CELLS YET HAVE BEEN INCLUDED IN THAT. I MIGHT BE WRONG, SHERRY, BUT I THINK IT'S NOT THERE. WE DON'T KIND OF DEMAND THE SAME DETAILS UNDER OUR CONSIDERATIONS AS WE WOULD FOR EMBRYONIC STEM CELLS. AND SO I THINK PERHAPS WE SHOULD FOR THE CLINICAL PURPOSES MAKE SURE THAT THEY FIT TOGETHER SO THAT WE'VE GOT THE SAME KIND OF CONSENT FOR THEIR USE THAT WE WOULD FOR EMBRYONIC STEM CELLS, PARTICULARLY IF THEY'RE GOING TO BE USED IN AN ALLOGENEIC SENSE.

SO THESE ARE THE DISEASE TEAM CLINICAL TRIALS. I WANT TO SORT OF BRING YOU INTO LINE WHERE OUR FRONT LINE IS. AND CLEARLY SOME OF THIS WORK IS EMBRYONIC STEM CELLS, AND THE TYPE I DIABETES REQUIRES EMBRYONIC STEM CELLS. AND, OF COURSE, IN THAT PARTICULAR COMPANY, NOVOCELL HAS A BANK OF A SPECIAL CELL LINE. AND I THINK THEY'LL MAINTAIN THAT AS LONG AS THEY CAN. I THINK IT WILL BE THE CASE FOR SOME OF THE OTHER STUDIES IN MACULAR DEGENERATION. ALTHOUGH IT'S POSSIBLE THAT SEVERAL LINES, EMBRYONIC STEM CELL LINES, WILL BE USED THERE OR STROKE, THESE KIND OF CELL LINES WILL BE THE GENERAL EMBRYONIC STEM CELL LINES THAT ARE BEING DEVELOPED THAT HAVE ALREADY BEEN DEVELOPED THROUGH THE GMP FACILITIES OR ARE UNDER PRODUCTION IN THOSE FACILITIES AT THE PRESENT TIME.

MS. LANSING: HOW MANY OF THESE LINES DO WE HAVE?

DR. TROUNSON: FOR EMBRYONIC STEM CELLS, I THINK THERE ARE FOUR, PAT; IS THAT RIGHT, THERE ARE FOUR OF THEM, AND THERE'S ONE IPS CELL. SO FOUR OF THEM ARE EMBRYONIC STEM CELLS. THERE ARE SEVERAL WHICH ARE NEURAL STEM CELLS WHICH ARE IN THE CANCER CATEGORY WHERE THEY'RE GOING TO BE DEVELOPED FOR USE FOR GLIOMAS, BUT THEY ARE FETAL-DERIVED CELLS.

AGAIN, THERE ARE ISSUES CLEARLY FOR THE DERIVATION OF THOSE CELL LINES. THEY COME FROM FETAL MATERIAL. AND FOR HIV/AIDS AND SICKLE CELL ANEMIA AND THE LEUKEMIAS, THEY'RE COMING FROM THE PATIENT'S OWN HEMATOPOIETIC STEM CELLS, BLOOD STEM CELLS THAT ARE TAKEN FROM THE PATIENTS. AND THE HEART WORK IS, AGAIN, AN AUTOLOGOUS STUDY WHERE THEY'RE TAKING THE PATIENT'S OWN HEART TISSUE AND THEN GENERATING IT. SO REALLY THE ONES THAT I THINK WE'RE CONCERNED ABOUT ARE THE EMBRYONIC STEM CELLS PARTICULARLY AND THE IPS CELLS.

THE IPS CELLS ARE BEING DEVELOPED FOR EPIDERMOLYSIS BULLOSA, THAT TERRIBLE SKIN CONDITION SHOWN UP RIGHT-HAND TOP THERE, WHERE THERE'S A COLLAGEN DEFECT, AND TO TAKE THE CELLS FROM THE PATIENTS, CONVERT THEM INTO IPS CELLS. AND THERE ARE GOOD METHODS FOR THAT THAT DON'T REALLY REQUIRE THAT YOU HAVE INTEGRATION OF YOUR VIRUSES OR YOUR GENES INTO THE GENOME THESE DAYS.

DR. PETERS: JUST A QUICK QUESTION. DO WE ACTUALLY HAVE IPS CELL LINES THAT ARE NOT CARCINOGENIC SO THAT THAT CAN GO FORWARD?

DR. TROUNSON: WELL, YOU KNOW, THERE'S NO PARTICULAR EVIDENCE THAT THEY ARE CARCINOGENIC, THAT THEY PRODUCE ANY CANCERS AT THIS STAGE. THEY DO

PRODUCE TERATOMAS, AND THAT'S THE SAME AS EMBRYONIC STEM CELLS. AND SO ONCE YOU DIFFERENTIATE THOSE CELLS, HOPEFULLY YOU CAN SEPARATE OUT OR COMPLETELY DIFFERENTIATE THE CELLS, SEPARATE OUT THE UNDIFFERENTIATED CELLS THAT WOULD PRODUCE A TERATOMA. THAT'S A SOLID TUMOR, BUT IT'S NOT A CANCER. OKAY. IT'S NOT A GOOD OUTCOME BECAUSE IT MIGHT DEPEND WHERE THAT TUMOR IS, BUT IT'S NOT A MALIGNANCY AS YOU WOULD GET IN A CANCER. SO NONE OF THESE CELLS HAVE REALLY GOT ANY CANCER BASIS. IN FACT, A LOT OF THE STRATEGIES ARE HERE KNOCKING OUT CANCER CELLS, CANCER STEM CELLS.

BUT THE IPS CELLS FOR EPIDERMOLYSIS BULLOSA COME FROM THE PATIENT, FROM THE PATIENT WHO'S GOING TO BE TREATED. SO I THINK THAT WILL BE PRETTY CLEAR-CUT. IT'S BASICALLY AN AUTOLOGOUS PROCEDURE. BUT LET'S SAY THAT YOU GOT THESE CELLS AND THOSE CELLS FROM THOSE PATIENTS, IT'S A GENETIC DISEASE, EPIDERMOLYSIS BULLOSA, SO YOU'RE GOING TO HAVE TO CORRECT THE GENETIC DISEASE. SO YOU WOULDN'T WANT TO USE THOSE CELLS FOR ANY OTHER PATIENT. WE'RE VERY PATIENT SPECIFIC BECAUSE YOU NEED TO THEN INTRODUCE THE CORRECT GENE INTO THE CELL LINE AND THEN GROW IT OUT INTO DERMIS, SKIN, WHICH YOU CAN THEN UTILIZE FOR TRANSPLANTATION ON

THE PATIENT.

BUT BECAUSE WE GOT IPS CELLS NOW MOVING INTO THE FRONT LINE CLINICALLY, I THINK THERE'S AN ONUS ON US TO MAKE SURE THAT WE'VE GOT ALL OF THESE IN THE CORRECT CATEGORIES AND WE KNOW THE KIND OF CONSENTS THAT WE WANT TO USE AND WE UNDERSTAND WHAT WE NEED OF THE STANDARDS MOVING FORWARD.

SO WHERE IT'S MORE COMPLEX AND MORE IN A SENSE, I THINK, A LITTLE MORE INTERESTING FROM MY POINT OF VIEW RIGHT AT THE MOMENT, AND I SHOULDN'T SAY IT'S MORE INTERESTING THAN THE CLINICAL WORK, BUT BECAUSE WE HAVEN'T REALLY SORT OF MADE OUR WAY INTO THIS AREA, I THINK HERE'S A GREAT OPPORTUNITY FOR CIRM TO UTILIZE IPS CELLS IN PARTICULAR FOR TOOLS FOR BASIC RESEARCH. AND THE REASON FOR THIS IS THAT IPS CELLS CAN BE TURNED INTO CLOSE TO THE EQUIVALENT OF EMBRYONIC STEM CELLS. I DON'T THINK IT REALLY MATTERS IF THEY ARE EQUIVALENT OR NOT. I THINK IT MATTERS WHETHER THEY DO THE JOB MEDICALLY THAT WE WANT THEM TO DO BECAUSE WHILE AN EMBRYONIC STEM CELL IS A GOLD STANDARD FOR UNDIFFERENTIATED CELLS, THEY'RE NOT NECESSARILY GOLD STANDARD FOR USE IN TRANSPLANTATION OR FOR MEDICAL THERAPIES AS YET.

NOW, WHAT WE'VE GOT, OF COURSE, IN AN IPS CELL IS THE ABILITY TO TAKE CELLS FROM PATIENTS IN A

POPULATION. SO LET'S SAY IN THIS ROOM WE'VE GOT TWO DISEASES OR THREE DISEASES, AND ONE WOULD BE TYPE I DIABETES, ONE MIGHT BE TYPE II DIABETES, ONE MIGHT BE A CANCER. NOW, IN THOSE POPULATIONS OF THOSE HUMAN DISEASES, THERE'S A LOT OF HETEROGENEITY. THAT IS, WE'RE NEVER EXACTLY THE SAME AS ONE ANOTHER. SO EVEN IF WE'VE GOT TYPE I DIABETES, WE'LL BE DIFFERENT ONE TO ANOTHER.

SO THE PROBLEM WITH MOUSE MODELS IS THAT WE KNOCK OUT A GENE OR TREAT AN ANIMAL AND WE GET ONLY PARTIAL MODELING OF THE HUMAN DISEASE. IT NEVER ACCURATELY REFLECTS THE HUMAN DISEASE. THE HUMAN DISEASE IS MADE UP WITH GENETIC EFFECTS, ENVIRONMENTAL EFFECTS, A WHOLE LOT OF THINGS WHICH WILL COME IN A PERSONALIZED WAY. AND THERE MAY BE MULTIPLE GENETIC EFFECTS AND EPIGENETIC EFFECTS THAT ARE RESIDENT IN A PATIENT. SO IN ANY ONE POPULATION THERE ARE GOING TO BE PATIENTS WHO RESPOND TO THERAPY, A DRUG THERAPY, PATIENTS WHO DON'T RESPOND, NOTHING HAPPENS WHEN YOU GIVE THEM THE DRUG, AND SOME THERE ARE GOING TO BE SOME PATIENTS WHO RESPOND ADVERSELY.

AND THIS IS WHAT COSTS AN ABSOLUTE FORTUNE FOR THE DRUG INDUSTRY BECAUSE IF YOU'VE GOT SOME PEOPLE IN THE POPULATION THAT REACT ADVERSELY AND

YOU CAN'T PICK THEM, YOU WON'T GIVE THE DRUG TO THE WHOLE POPULATION EVEN THOUGH, SAY, THE MAJORITY WOULD HAVE AN INCREDIBLE BENEFIT. SO THERE'S A BIG PROBLEM OF, IF YOU LIKE, PERSONALIZED MEDICINE THAT THIS AREA OF RESEARCH COULD START TO CLICK INTO AND START TO SATISFY.

AND IT'S AN ENORMOUS POTENTIAL, I THINK. I THINK ONE DAY SOMETIME LONG IN THE FUTURE WE'LL POSSIBLY TAKE INDIVIDUAL CELLS FROM INDIVIDUAL PEOPLE AND WORK IT ALL OUT, BUT RIGHT NOW WE CAN LOOK AT THE POPULATION, SEE IF WE CAN CATEGORIZE THE POPULATION INTO THOSE THAT RESPOND, DON'T RESPOND, AND RESPOND ADVERSELY, AND THAT WOULD BE A TREMENDOUS OUTCOME. THERE ARE POSSIBLY MORE DEATHS FROM ADVERSE RESPONSES TO DRUGS THAN TO CAR ACCIDENTS. AND THIS IS A HUGE PERSONAL HUMAN TRAGEDY ASSOCIATED WITH MEDICINE BECAUSE SOME PEOPLE RESPOND IN A WAY WHICH IS UNPREDICTABLE. IF WE COULD FIGURE THAT OUT, NOT ONLY THE COST OF THE DRUGS WOULD BE REDUCED DRAMATICALLY, BUT, OF COURSE, THE HARM THAT WE DO IN AN UNPREDICTED WAY TO PATIENTS WOULD BE DRAMATIC.

SO THE IPS CELLS CAN BE CONVERTED FROM A SKIN CELL OR ANY CELL OF THE BODY, FAT CELLS. I UNDERSTAND IT'S PREFERABLE NOT TO DERIVE THEM FROM

BLOOD CELLS. THERE'S A PAPER THAT'S STILL NOT PUBLISHED, BUT I UNDERSTAND IT'S AN IMPORTANT PAPER THAT SAYS BLOOD CELLS ARE NOT THE PREFERRED WAY OF DERIVING THEM. BUT ANY OTHER CELLS, IT SEEMS THAT YOU CAN DERIVE THEM. YOU CAN DERIVE THEM IN A RANGE OF SPECIES. SO THERE'S A LOT OF WORK NOW GOING ON IN DIFFERENT SPECIES AS WELL AS THE HUMAN. THERE'S A LOT OF WORK NOW SHOWING THAT YOU CAN DERIVE THEM, AS I SAID, WITHOUT LEAVING THE GENES OR THE VIRAL PRODUCT IN THE GENOME.

WHAT NORMALLY HAPPENS WHEN YOU USE A VIRUS TO INSERT THESE TRANSCRIPTION FACTORS IS THEY INSERT IN UNPREDICTABLE PLACES, BUT THEY STAY THERE. THEY GET TURNED ON FOR A PERIOD OF TIME AND THEY GET TURNED OFF. BUT BECAUSE THEY MAY BE CLOSE TO ANOTHER GENE, THEY CAN HAVE AN EFFECT ON OTHER GENES OR OTHER SET OF GENES, OR THEY CAN TURN ON IN AN UNPREDICTABLE WAY. THIS COULD BE A REALLY SERIOUS PROBLEM BECAUSE SOME OF THOSE GENES ARE ONCOGENES OR CANCER-RELATED GENES. AND YOU DON'T WANT THEM TURNING ON. YOU WANT THEM TURNED OFF. YOU NEED TO STAY OFF. SO BETTER THAT THEY BE OUT. AND THERE ARE NOW WAYS, REALLY CLEVER WAYS, OF DOING THIS WITHOUT HAVING THE GENES INSERTED INTO THE GENOME.

SO WE'VE GOT IPS CELLS AND YOU CAN MAKE

THEM FROM ANY PERSON, EQUIVALENT, ROUGHLY EQUIVALENT TO EMBRYONIC STEM CELLS. THEY PRODUCE TERATOMAS. IF YOU CAN GET A SAMPLE FROM THE WHOLE POPULATION AND THEN CREATE THE DISEASE IN A DISH, SO THIS IS WHAT THE CLEVER SCIENTISTS DO, AND YOU'VE GOT PH.D. STUDENTS AND POST DOCS WORKING MADLY ON THIS ALL THE TIME. THERE ARE DISEASE IN A DISH THAT'S COMING THROUGH ALL THE TIME. YOU CAN SHOW, IF YOU TAKE A CELL FROM A PATIENT WITH A CANCER OR WITH A NEURAL DEGENERATIVE DISORDER, YOU CAN ACTUALLY SEE SOME SORT OF TEST IN A DISH. THE CELLS WILL BE DIFFERENT TO THOSE CELLS THAT COME FROM A PATIENT THAT DO NOT HAVE THE DISEASE. SO YOU CAN GET A DISEASE IN A DISH.

ONCE YOU'VE GOT A DISEASE IN A DISH, YOU CAN THEN SUBJECT THAT TO HIGH THROUGHPUT OR MEDIUM THROUGHPUT SCREENING WITH THE LIBRARIES OF SMALL MOLECULES OR BIOLOGICS THAT ARE AVAILABLE IN THE ACADEMIC INSTITUTIONS AND IN THE DRUG COMPANIES. AND, OF COURSE, THEN WHAT IT DOES IS IT OPENS UP A WHOLE LOT OF NEW DRUGS THAT COULD BE USEFUL FOR TREATING THOSE DISEASES.

SO THEN WE CAN ACTUALLY CATEGORIZE SOME OF THESE IF WE'VE TAKEN THE SAMPLES FROM DIFFERENT MEMBERS OF THE POPULATION THAT ARE RESPONSIVE TO THE

DRUG, UNRESPONSIVE TO THE DRUG, OR RESPOND ADVERSELY, AND THEN WE CAN WORK OUT THE DIAGNOSTICS TO KEEP THE ADVERSE PATIENTS OUT OF IT. NO USE GIVING A DRUG TO A PATIENT WHO'S TOTALLY UNRESPONSIVE. HOPEFULLY REMOVE THOSE AS WELL AND LEAVE THE POPULATION THAT WILL BE RESPONSIVE TO THE DRUG.

SO I THINK AN IDEAL IPS CIRM CELL BANK IN THIS AREA WOULD BE ONE THAT, LET'S SAY, OUR 70 DISEASES THAT WE'RE INTERESTED IN CIRM, YOU NEED A SAMPLE FROM THE POPULATION. SO WHAT'S THE NUMBER FOR EACH AND EVERY DISEASE WILL PROBABLY BE DIFFERENT. SOME DISEASES A SMALLER NUMBER WILL REPRESENT THE POPULATION, AND OTHERS WILL PROBABLY BE A LARGER NUMBER. I'VE JUST SORT OF CHOSEN 50 AS AN OVERALL NUMBER, SAMPLES FROM 50 PATIENTS IN THAT POPULATION, AND CLEARLY WE'RE GOING TO HAVE THE CLINICIANS INVOLVED IN IDENTIFYING WHO THOSE PEOPLE ARE. AND IF YOU'RE IN A TYPE II DIABETES POPULATION, IT WOULD BE TERRIFIC TO HAVE SOME SAMPLES FROM THOSE PATIENTS WHO SHOULD HAVE THE DISEASE AND DON'T. SO THAT YOU'VE HAVE GOT A VARIETY HERE THAT HAVE A PHENOTYPE, WHAT WE CALL A PHENOTYPE AND A MEDICAL HISTORY, THAT THEN WE CAN RELATE TO THE DISEASE AND THE RESPONSIVENESS THAT WE

SEE.

AND AT LEAST FROM A SCIENTIFIC POINT OF VIEW, YOU'D WANT THREE CLONES OF EACH INDIVIDUAL JUST TO TAKE CARE OF THE WITHIN PATIENT VARIABILITY. THAT'S THE TECHNICAL ISSUES THAT RESULT THAT WILL BE PRESENT WHEN YOU MAKE THESE CELL LINES. FROM ONE TO ANOTHER THEY WILL VARY, AND YOU WANT TO TAKE CARE OF THAT VARIANCE SO THAT YOU'VE GOT THAT UNDER CONTROL. AND I THINK THEY NEED TO BE MADE EXACTLY THE SAME WAY, AND PREFERABLY MADE BY THE SAME GROUP OF PEOPLE, THE SAME UNIT SHOULD MAKE THEM ALL, SO THAT YOU REDUCE THE TECHNICAL VARIANCE OF MAKING THEM.

CURRENTLY THERE ARE BANKS TAKING IN IPS CELLS, BUT THEY'RE ALL MADE IN ALL SORTS OF DIFFERENT WAYS. AND, OF COURSE, THAT WILL CREATE A VARIANCE WHICH WILL IMPEDE YOU TO LOOK AT THE SPECIFIC VARIANCE THAT YOU WANT TO LOOK BETWEEN PATIENTS. IF YOU ADD A LOT OF TECHNICAL VARIANCE, IT BECOMES INSENSITIVE, THE TEST. SO YOU WANT TO GET THEM MADE BY THE SAME PEOPLE.

AND IF WE DID THIS, WE MIGHT WANT 10,000 LINES BECAUSE 70 BY 50 BY 3 IS 10,000. SO THIS IS A BIG DEAL, BIG DEAL. AND I THINK CALIFORNIA RESEARCHERS WOULD LOVE TO HAVE THESE CELLS AVAILABLE. I THINK THE INSTITUTIONS I TALKED TO

WOULD LOVE TO HAVE, ALL OF THE COMPANIES I'VE TALKED TO WOULD LOVE TO HAVE ACCESS TO THIS. SO THERE'S BOTH ACADEMIC AND BIOTECH INTEREST. AND INTERNATIONAL COLLABORATIVE PARTNERS WOULD LOVE TO HAVE THIS, AND I THINK THE PHARMACEUTICAL COMPANIES WOULD LOVE TO HAVE ACCESS TO THIS. THIS WOULD BE A HUGE AND IMPORTANT RESOURCE, AND I THINK IT'S SOMETHING THAT'S DEFINITELY WORTH US CONSIDERING. AND I'M CERTAINLY TRYING TO CREATE A VISION FOR IT. IT WILL RESULT IN DECADES OF RESEARCH.

SO IF WE DO SOMETHING LIKE THIS, THEN WE'VE GOT TO FIGURE OUT WHAT IS REQUIRED IN THE SENSE OF CONSENT, THE WAY IN WHICH WE TAKE THESE CELLS, BECAUSE THEY'RE GOING TO COME FROM PATIENTS. SOME PATIENTS WILL RESPOND, OTHERS WILL NOT RESPOND, AND SO ON. DO THEY GET THAT INFORMATION BACK? THERE ARE A WHOLE LOT OF IMPORTANT THINGS THAT ARE DWELLING IN CREATING A BANK THAT'S GOING TO BE USED FOR DECADES THAT I THINK DESERVES THINKING ABOUT.

SO THERE ARE ISSUES OF DIVERSITY AND QUALITY. WE WANT THE IPS TO ENCOMPASS THE DISEASE SPECTRUM. WE WANT POPULATION DIVERSITY, AND CLEARLY THERE ARE POPULATION SUBSETS IN OUR COMMUNITY AND IN COMMUNITIES OVERSEAS WHICH WILL HAVE A VARIABLE INCIDENCE OF THE CERTAIN DISEASES. THAT'S

IMPORTANT. THAT'S A VERY IMPORTANT COMPONENT PART TO CREATE -- MAKE SURE WE CREATE THE DIVERSITY THAT COVERS ALL OF OUR PEOPLE AND IS EFFECTIVELY ADDRESSING THOSE PARTICULAR ISSUES.

THE ETHICAL CONSIDERATIONS IS ABOUT THE ADEQUACY OF THE CONSENT PROCESS AND THE PROVENANCE DATA. AND, OF COURSE, IF WE HAVE INTERNATIONAL COLLABORATIONS WHERE WE WOULD GET, SAY, CELLS THAT WE WOULD THEN TO MAKE UP THE IPS CELLS FROM OVERSEAS, WE NEED TO BE ABLE TO INCORPORATE ALL OF THAT THINKING INTO SOME APPROPRIATE CONSENT AND PROVENANCE FOR THAT.

FOR THE PROGRAM EFFICIENCY AND EFFECTIVENESS, I THINK WE WANT NATIONAL AND INTERNATIONAL PARTNERSHIPS. AND I THINK PEOPLE WOULD BE VERY WILLING TO CONTRIBUTE IN SOME WAY TO THIS, IF NOT DOLLARS, IN TERMS OF MATERIALS. I THINK THIS IS A CRITICAL NICHE FOR THE FIELD, AND I THINK WHAT WOULD COME FROM THIS WILL BE AN EXTRAORDINARY, I THINK A REAL EXTRAORDINARY DEVELOPMENT IN HUMAN MEDICINE.

SO UNDERSTANDING OUR ROLE IN THIS I THINK IS VERY IMPORTANT. WE'VE GOT IN THE CLINICAL SIDE NIH AND FDA. THERE ARE IMPORTANT CONSIDERATIONS AS WELL AS THE TEAMS THAT HAVE GOT THE GMP FACILITIES

DEVELOPING THE BANKS. WE'VE GOT CIRM GRANTEES. WE'VE GOT, IF WE'RE GOING TO CREATE A CELL BANK FOR THE RESEARCH THAT I TALKED ABOUT, IT WOULDN'T HAVE TO BE GMP BECAUSE IT WOULD PROBABLY BE MORE SUITABLE AND LESS COSTLY TO DO IT IN A NON-GMP WAY. AGAIN, I'D BE OPEN TO THOUGHTS ABOUT THIS, BUT IT SOUNDS LIKE PUTTING THAT THROUGH A GMP FACILITY WOULD BE INCREDIBLY EXPENSIVE. WHEN YOU WANT TO USE IT FOR RESEARCH PURPOSES, I DON'T THINK IT'S NECESSARY TO MAKE THEM IN A GMP WAY, BUT IT WOULD NEED TO BE A VERY STANDARDIZED WAY OF MAKING THEM.

SO SHERRY, BERNIE, MEMBERS OF THE TEAM, I HOPE THAT GIVES YOU SOME IDEA OF THE KIND OF THOUGHTS THAT I HAVE IN THIS AREA. AND THE FACT THAT WE HAVEN'T REALLY THOUGHT VERY DEEPLY IN OUR IPS CELL AREA FOR ETHICS AND STANDARDS, BUT I THINK IT'S TIME TO DO THAT. AND ANY GUIDANCE THAT CAN COME FROM THIS MEETING, I THINK, WOULD BE VERY WELCOME TO BE INPUTTED INTO OUR SCIENCE PROGRAM AND INTO THE BOARD FOR THEIR CONSIDERATION WHEN WE BRING THIS MATERIAL FORWARD. SO THANK YOU VERY MUCH.

MS. LANSING: THANK YOU. THAT WAS GREAT. THAT ANSWERS YOUR QUESTION ABOUT WHY WE WENT TO THE DIVERSITY?

DR. PETERS: OH, YEAH.

DR. ROBERTS: I HAVE MORE QUESTIONS ABOUT THAT. AND ACTUALLY IT COMPLICATED, I THOUGHT, THE ISSUE. SO IT SOUNDED AS IF THERE ARE A COUPLE POINTS IN THE PROCESS WHERE DIVERSITY AND CATEGORIZATION WOULD BE IMPORTANT. ONE WAS WITH RESPECT TO PERSONALIZED MEDICINE, WHICH IS SORT OF AT THE END OF THE WHOLE PROCESS WHEN SOME PRODUCT IS GOING TO BE PRODUCED FROM ALL OF THIS RESEARCH. AND SO THAT -- YOU TALKED ABOUT CATEGORIZING POPULATION, THOSE WHO WOULD RESPOND WELL AND WOULDN'T. AND I'M NOT -- SO THERE I'M NOT SURE WHAT THOSE CATEGORIES WOULD LOOK LIKE BECAUSE, AS YOU MENTIONED, PEOPLE'S RESPONSE TO ANY KIND OF MEDICINE IS GOING TO BE VERY PERSONAL. IT WILL DEPEND ON ALL SORTS OF THINGS, THEIR GENES, THEIR ENVIRONMENT, YOU MENTIONED EPIGENETICS, WHAT THEIR MOTHER'S ENVIRONMENT, ALL SORTS OF THINGS, AND WHAT THOSE CATEGORIES WOULD LOOK LIKE.

AND THEN THERE'S ANOTHER PART WHERE YOU MENTIONED CATEGORIZATION, WHICH IS AT THE BEGINNING RECRUITING PEOPLE WHO WILL DONATE TO THIS BANK. AND THERE -- AND IT SEEMS TO ME THAT THOSE COULD BE TWO COMPLETELY DIFFERENT KINDS OF CATEGORIES, BUT THAT WAS WHERE YOU MENTIONED DIVERSITY WITH THE RECRUITMENT. AND IT SOUNDED LIKE THE REASON FOR IT

IS MORE OF A SCIENTIFIC REASON IN THE SENSE THAT THERE'S AN ASSUMPTION THAT PEOPLE FROM DIFFERENT POPULATIONS HAVE A DIFFERENT INCIDENCE OF DIFFERENT DISEASES. SO IF YOU WANT TO GET THE 70 DISEASES REPRESENTED, YOU MAY WANT TO RECRUIT MORE FROM ONE POPULATION THAN ANOTHER BECAUSE OF THE INCIDENCE OF DISEASE.

SO THERE I WAS WONDERING HOW THOSE POPULATIONS WOULD BE DEFINED, AND ALSO HOW YOU WOULD TAKE INTO ACCOUNT THE SOCIAL WAYS WE DEFINE POPULATIONS IF YOU'RE TALKING ABOUT ETHNIC AND RACIAL, BUT ALSO THE COMPLEXITY OF WHY CERTAIN POPULATIONS HAVE HIGHER INCIDENCE OF DISEASE WHICH MAY BE, I THINK IT IS FOR SOCIAL REASONS, FOR THE KINDS OF DISEASES YOU ARE TALKING ABOUT, DIABETES AND CANCER, NOT GENETIC, PURELY GENETIC DISEASES.

SO I JUST WONDERED IF YOU WOULD TALK ABOUT -- I KNOW IT'S A LOT, BUT I THOUGHT IT'S VERY COMPLICATED.

MR. TORRES: MADAM CHAIR, IF I MAY, DR. ROBERTS. DR. TROUNSON REALLY HAS BEEN INNOVATIVE IN REACHING OUT TO DIFFERENT COMMUNITIES ACROSS THE STATE. AND THE WORKSHOP THAT I HELPED CHAIR WITH DR. TROUNSON AT DREW UNIVERSITY WAS ESPECIALLY HELPFUL BECAUSE WE HAD A SOCIAL SCIENTIST WHO HAD

COMMISSIONED A REPORT. I'LL TALK ABOUT THE RECRUITMENT. I'M CURRENTLY A BOARD MEMBER OF ONE LEGACY, WHICH IS AN ORGAN TRANSPLANT FOUNDATION IN SOUTHERN CALIFORNIA.

WE HAD GREAT DIFFICULTY REACHING OUT TO AFRICAN-AMERICAN AND LATINO FAMILIES TO DONATE. SO IT TOOK A VERY CONCERTED RECRUITMENT EFFORT TO DO THAT.

THE OTHER ISSUE THAT CAME TO MIND DURING THIS WORKSHOP WAS I DIDN'T KNOW THAT WE HAD AN INCIDENCE OF LATINOS WITH SICKLE CELL ANEMIA. AND SO FOR ME AS A LATINO, HAVING BEEN ONE ALL MY LIFE, WE DECIDED TO MOVE INTO THIS DIRECTION BECAUSE WE NEEDED TO HAVE A SPECIFIC RECRUITMENT AREA.

SO WHAT WE ARE LOOKING AT NOW IN TERMS OF THAT ISSUE, BECAUSE OF DR. TROUNSON'S LEADERSHIP ON THIS ISSUE OF DIVERSITY, IS HOW DO WE REACH OUT TO THOSE COMMUNITIES.

THE SECOND ISSUE WHICH WAS IMPORTANT, AND I'LL END WITH THIS, WAS WHAT DR. NORRIS, HEAD OF DREW UNIVERSITY, SAID TO US AS WELL. 48 PERCENT OF AMERICANS ARE FUNCTIONALLY ILLITERATE. SO WHEN YOU GET TO THE POINT OF CONSENT FORMS, WHICH IS VERY CRUCIAL, AS YOU WELL KNOW, WE HAVE TO BE VERY CAREFUL OF HOW THOSE CONSENT FORMS ARE TRANSLATED IN

SOME CASES, BUT EVEN FOR THOSE PEOPLE WHO ARE FUNCTIONALLY ILLITERATE WHO WANT TO PARTICIPATE AND BE PART OF OUR RECRUITMENT EFFORT, WE HAVE TO BE ESPECIALLY CAREFUL IN THOSE AREAS AS WELL.

SO I JUST WANTED TO LET YOU KNOW THAT THAT'S VERY MUCH AT THE TOP OF OUR AGENDA, THE SOCIAL, ECONOMIC, AND DIVERSITY ISSUES IN TERMS OF RECRUITMENT AND CONSENT. I CAN'T SPEAK BECAUSE I'M NOT A SCIENTIST. I WOULD DEFER BACK TO THE PRESIDENT.

DR. ROBERTS: I THINK THIS IS A BIG ISSUE THAT WE CAN TALK ABOUT OVER TIME. BUT ONE OF MY CONCERNS IS THE CONFUSION OF SOCIAL GROUPS, LIKE LATINOS, AFRICAN-AMERICANS, ASIANS, NATIVE AMERICANS, ALL DEFINED SOCIALLY BEING CONFUSED WITH A BIOLOGICAL CATEGORY. AND I KNOW THERE'S A HISTORY OF WANTING TO INCREASE DIVERSITY FOR A NUMBER OF REASONS, BOTH JUST TO HAVE MORE PEOPLE HAVE THE BENEFITS OF RESEARCH GIVEN TO EVERYONE ON AN EQUAL BASIS, IN ADDITION TO THE SCIENTIFIC OR BIOLOGICAL REASONS OF HAVING DIVERSITY IN TERMS OF BIOLOGY. BUT MAKING SURE THAT THERE ISN'T A CONFUSION THAT PEOPLE OF DIFFERENT SOCIAL GROUPS ARE DISCRETE BIOLOGICAL GROUPS.

AND SO THAT'S -- I THINK IT'S IMPORTANT AS

WE LOOK AT DIVERSITY TO MAKE SURE THAT THAT DISTINCTION IS MADE AND ALSO THAT THERE'S AN UNDERSTANDING THAT THE REASON WHY CERTAIN GROUPS HAVE HIGH RATES OF -- HIGHER RATES OF DISEASE MAY ALSO AND DOES INCLUDE SOCIAL REASONS AS WELL AS BIOLOGICAL REASONS.

DR. TROUNSON: SO, YOU KNOW, OF COURSE, YOU ARE CORRECT. WE DO KNOW FROM SINGLE-GENE DISEASES THAT THEY ACCUMULATE MORE IN SOME GROUPS THAN OTHERS BECAUSE THERE'S A HIGHER MUTATION RATE IN SOME POPULATIONS THAN OTHERS. SO A HIGH PROPENSITY TO A DISEASE COULD WELL BE MULTIGENIC OR IT COULD BE RELATED TO THE GENOME. IN THAT PARTICULAR GROUP OF PEOPLE, THERE'S MORE -- MAKES THEM MORE SUSCEPTIBLE. THAT'S A POSSIBILITY.

THERE MAY BE EPIGENETIC EFFECTS WHICH ARE ACCUMULATED BECAUSE OF THE ENVIRONMENT OR REALLY BY EFFECTS OF BEING IN THAT POPULATION. STRICTLY ENVIRONMENTAL EFFECTS, LIKE NUTRITION, MAY NOT BE REFLECTED IN THESE PARTICULAR TESTS, BUT THEY MIGHT BE BECAUSE THEY MIGHT HAVE AN IMPACT ON THE EPIGENOME OR PART OF THE HIGHER ORDER THAT REGULATES SOME OF THE GENES.

SO WHAT WE WANT TO DO IS SEE IF WE CAN FIND MEMBERS OF THE POPULATION WHO DO RESPOND, WHO

DON'T RESPOND, OR WHO RESPOND ADVERSELY. AND IT DOESN'T MATTER WHAT POPULATION, BUT YOU WANT TO PROTECT THOSE PEOPLE IF YOU CAN. SO I DON'T THINK AT THIS POINT IN TIME WE'RE TRYING TO INDIVIDUALIZE THE MEDICINE DOWN TO THE INDIVIDUAL BECAUSE I THINK THAT WILL COME IN 20, 30 YEARS TIME, BUT MAYBE BEYOND THE TIME THAT WE'RE HERE, CHAIR. BUT I THINK THE OPPORTUNITY TO LOOK DIAGNOSTICALLY AT THE GROUPS WHEREVER THEY COME FROM WOULD BE GOOD. AND IT MAY BE IN SOME POPULATIONS THAT THERE WILL BE MORE OF THE PATIENTS WHO ADVERSELY RESPOND OR DO RESPOND. IN THAT CASE IT WOULD BE AN ADVANTAGE TO THAT POPULATION TO HAVE THE DRUG OR NOT HAVE THE DRUG, IF YOU UNDERSTAND. OR WE CAN CREATE SOME SORT OF DIAGNOSTIC THAT WILL SEPARATE THOSE PEOPLE WHO RESPOND BADLY OR DO RESPOND WELL.

SO I THINK THAT THE SCIENCE IS TRYING TO LOOK DEEPLY INTO THAT MATTER. OF COURSE, WE HAVE TO HAVE THE INVOLVEMENT OF THE CLINICIANS. AS MR. TORRES SAID, WE'VE BEEN WORKING OUR WAY INTO SOME OF THE CLINICAL -- INTO SOME OF THE PRIMARY AND TERTIARY CLINICIANS IN SOME OF THESE PLACES TO GET AN IDEA OF WHETHER THEY COULD SAMPLE. AND CLEARLY THERE ARE COMPLEX ISSUES ABOUT THAT, BUT THEY'RE NOT IMPOSSIBLE.

CHAIRMAN LO: SO WE HAVE A NUMBER OF PEOPLE ALREADY WANTING TO JUMP IN. SO I HAVE DR. PRIETO, DR. CIBELLI, MS. LANSING, AND THEN DR. TAYLOR.

DR. PRIETO: FIRST, I GUESS RESPONDING TO SOME OF DOROTHY'S QUESTIONS, I THINK I SORT OF SEE THIS THROUGH THE LENS OF DIABETES BECAUSE IT'S HOW I LOOK AT THE WORLD, I THINK. ACTUALLY MORE SO WITH TYPE II THAN TYPE I, THAT THERE'S THIS TREMENDOUS HETEROGENEITY OF DISEASE EXPRESSION. AND I THINK ONE OF THE THINGS THAT A LARGE GENETIC POOL CAN TELL US IS HOW MUCH OF THIS IS GENETICALLY DETERMINED, HOW MUCH OF IT IS SOCIALLY AND ENVIRONMENTALLY DETERMINED. HOW ARE WE SIMILAR AND HOW ARE WE DIFFERENT?

I THINK FOR DR. TROUNSON A COUPLE QUESTIONS I'D HAVE RELATING TO THAT AND CELL BANKING, WE'RE TALKING ABOUT HUGE NUMBERS OF CELL LINES. I GUESS I'M WONDERING WHERE YOU WOULD SEE A CELL BANK PHYSICALLY RESIDING AND WHAT THE ROLE OF CIRM WOULD BE IN FACILITATING THAT, SETTING THE STANDARDS, ETC.

DR. TROUNSON: WELL, AT THIS POINT I THINK THEY'RE VERY IMPORTANT ISSUES, AND WE'VE BEEN -- I'VE BEEN THINKING ABOUT, WITHOUT SORT OF BRINGING

ANYTHING FORWARD TO THE BOARD OR REALLY TO THE COMMUNITY, BUT I WOULD LIKE TO HAVE ONE GROUP DERIVE THE IPS CELLS IN ORDER TO REDUCE THE VARIATION IN THE DERIVATION OF THE CELLS. AND I'VE ACTUALLY INQUIRED, AND THERE ARE A NUMBER OF COMPANIES OR, IN FACT, PEOPLE WHO WOULD LOVE TO START UP A COMPANY TO DO THAT. AND CLEARLY THERE ARE INSTITUTIONS WHO WOULD LOVE TO BE INVOLVED. I THINK, FOR EXAMPLE, THERE JUST WAS ONE INSTITUTION, THE BUCK INSTITUTE, WOULD LOVE TO BE INVOLVED.

SO I THINK THERE ARE A LOT OF PEOPLE WHO WOULD LIKE TO BE INVOLVED. AND SO THE DERIVATION, I THINK, WOULD BE IDEAL IF IT WAS DONE BY ONE GROUP. AND THE BANK, THEN, WOULD BE SITUATED WHEREVER THAT WAS. BUT, OF COURSE, YOU HAVE TO PROTECT THE BANK BY PUTTING SAMPLES IN AT LEAST TWO PLACES. SINCE WE LIVE IN EARTHQUAKE LAND, YOU DON'T WANT THEM ALL TO BE LOST IN ONE MOMENT.

WHAT WOULD CIRM'S ROLE BE IN IT? I THINK, AS WE NORMALLY DO, FACILITATING SOMETHING WHICH WILL MAKE A LONG-TERM DIFFERENCE. I THINK THAT THIS AREA IS RIPE FOR TREMENDOUS RESEARCH FOR DECADES. AND, OF COURSE, IT WON'T ALL COME -- THERE WILL BE SOME DISEASES OR SOME CONDITIONS THAT WON'T TURN OUT TO BE A GOOD DISEASE IN A DISH OR WE WON'T BE ABLE TO

FIND A DISEASE IN A DISH BECAUSE IT'S GENERALLY A SOCIAL DISEASE, AND IT DOESN'T REFLECT IN A DIFFERENCE IN THE DIFFERENTIATION OF THE CELLS. THAT WILL HAPPEN. BUT THE MORE THAT THE SCIENTISTS ARE LOOKING AT THE CURRENT DISEASES THAT WE HAVE, THE 70, THEY'RE FINDING MORE AND MORE DISEASE IN A DISH ASSAYS. AND THESE ASSAYS CAN BE TURNED INTO HIGH THROUGHPUT SCREENS.

AND SO WHETHER THEY THEN TURN OUT MOLECULES WHICH WILL BE EFFECTIVE IN TREATING THOSE DISEASES, BUT IF YOU CAN IMAGINE IN THE CASE OF HUNTINGTON'S DISEASE, IF YOU COULD FIND SOME MOLECULES THAT WILL PUT THAT DISEASE OFF FOR 20 YEARS, IT WOULD BE INCREDIBLY IMPORTANT TO THOSE PATIENTS. OR IF THOSE KIND OF THINGS START TO EVOLVE FROM THESE STUDIES, I THINK THAT COULD BE TERRIBLY IMPORTANT. SO CIRM I SEE AS AN ENTITY THAT WOULD ENCOURAGE THAT, WOULD TRY AND BRING SOME OF THE PARTNERS TOGETHER SO THAT WE GET CLINICAL TEAMS WORKING IN CALIFORNIA. MAYBE IT WOULD INCLUDE OUR COLLEAGUES IN OTHER STATES AND MAYBE DRAW IN THE NIH INVOLVEMENT INTO THIS, MAYBE DRAW OUR INTERNATIONAL PARTNERS. OUR INTERNATIONAL PARTNERS HAVE RESPONDED AT LEAST IN THE DISCUSSION AS REALLY WANTING TO BE INVOLVED.

SO I THINK WE'RE THE CATALYST, I THINK, AT THIS POINT, AND I THINK THAT'S WHERE WE SHOULD BE IN DERIVING A RESOURCE THAT WILL BE AVAILABLE HOPEFULLY FOR AN IMPORTANT LONG-TERM MEDICAL DISCOVERY.

DR. PRIETO: DO YOU THINK -- IS IT POSSIBLE FOR ONE OR TWO INSTITUTIONS TO GENERATE THE NUMBER OF CELL LINES THAT WE'RE TALKING ABOUT?

DR. TROUNSON: I THINK YOU TURN SCIENTISTS ONTO THIS, AND I THINK THEY CAN DO IT. IT'S AN AWFUL LOT OF CELL LINES, AND I WANTED TO GET THAT MULTIPLE THERE. ONCE YOU LOOK AT DISEASES BY LARGE NUMBER OF SAMPLES IN THE POPULATION, BY THREE CLONES YOU SUDDENLY SORT OF GET OUT VERY WIDE. THERE WOULD BE ARGUMENTS THAT YOU WOULDN'T NEED THE THREE CLONES; BUT AS A SCIENTIST, I WOULD FEEL THAT THAT WOULD NOT BE A WISE MOVE NOT TO HAVE THE INTERNAL CONTROL. BUT, YEAH, IT WILL BE CHALLENGING, AND IT WILL BE TIME-CONSUMING AND IT WON'T HAPPEN ALL AT ONCE. BUT THE WHOLE IDEA WOULD BE TO BE ABLE TO CREATE THIS SAMPLE OVER A NUMBER OF YEARS. AND IF IT TAKES US FIVE TO SIX YEARS TO GET IT ALL DONE, THEN I THINK THAT WOULD BE REASONABLE.

I DON'T KNOW WHAT OTHER SCIENTISTS THINK, BUT THIS IS CHALLENGING. BUT IT'S SOMETHING THAT WHEN I TALKED TO DR. LOVE, HE THOUGHT THAT HE AND I

WOULD LOVE TO GO OFF AND TRY AND DO IT. SO THE ENTHUSIASM FOR CREATING SOMETHING LIKE THIS, I THINK IS RESIDENT. AND IF THERE'S FUNDING AVAILABLE, OF COURSE, THAT USUALLY IS THE STOPPER FOR THESE THINGS. BUT I WOULD LIKE TO BE ABLE TO TALK TO NIH AND OTHER PEOPLE TO REALLY HELP IN THIS.

AND IT MAY BE THAT THIS LITTLE GRAIN OF AN IDEA MIGHT BE ABLE TO GROW INTO SOMETHING ELSE. AND IT MAY BE ABLE TO INCORPORATE MORE VARIANCE FROM MAKING IT UNDER DIFFERENT WAYS. BUT I WOULD HAVE A PREFERENCE TO MAKE IT THE SAME WAY, WHICH COMES DOWN TO SORT OF WANTING TO DO IT IN ONE GROUP. AND THAT MIGHT BE THE BIGGEST CHALLENGE IS TO GET IT ALL DONE BY ONE TEAM, BUT IT'S GOOD STUFF FOR SCIENTISTS. THEY WOULD LIKE TO DO THIS. AND WHEN I STARTED IVF, TO THINK OF THE NUMBERS THAT THE CLINICS TREAT NOW, IT WAS TOTALLY OUT OF PROPORTION OF WHAT I THOUGHT WAS POSSIBLE. THINGS ARE POSSIBLE IF YOU SET IT UP THE RIGHT WAY.

CHAIRMAN LO: I'M GOING TO STEP IN HERE AS SORT OF MODERATOR AND CO-CHAIR AND TRY AND BRING US BACK TO OUR SCHEDULE. LET ME SEE IF I CAN SORT OF PUT A FRAME AROUND WHAT ALAN HAS DONE. HE'S REALLY GIVEN US A VERY NICE START TO THE WORKING GROUP -- WORKSHOP.

SO THIS IS AN IDEA OF SORT OF AN IDEA IN PROGRESS, SORT OF SETTING UP A STEM CELL BANK THAT CIRM WOULD BE VERY MUCH INVOLVED WITH. AND THERE'S A LOT OF DETAILS THAT NEED TO BE SORT OF THOUGHT THROUGH.

I THINK OUR TASK TODAY AS THE STANDARDS WORKING GROUP IS TO IDENTIFY ETHICAL ISSUES THAT WE NEED TO ADDRESS RIGHT FROM THE ONSET AS WE'RE DEVELOPING THESE IDEAS SO THAT THEY CAN BE BUILT INTO THE DEVELOPMENT OF THE PLAN, WHICH REALLY THEN HAS TO GO BACK TO THE ICOC FOR APPROVAL.

I WANT TO TRY AND GET TO OUR FOUR GUEST SPEAKERS WHO HAVE A LOT OF EXPERTISE IN THE DETAILS OF SORT OF HOW WE MIGHT ACTUALLY DO THAT AS WELL AS LESSONS LEARNED I THINK THEY WANT TO IMPART TO US. SO I'M GOING TO ASK THE PANEL, UNLESS IT'S DIRECTLY RELATED TO ALAN. A LOT OF ISSUES, I THINK, WILL COME UP AS OUR FOUR GUESTS ADDRESS US. I WANT TO REALLY BRING THEM INTO THE DISCUSSION BECAUSE THEY'VE HAD THE EXPERIENCE DERIVING LINES, BANKING THEM, AND ALSO DISTRIBUTING THEM TO OTHER SCIENTISTS. I JUST WANT TO SORT OF GO THROUGH. JOSE, SHERRY, AND PAT.

DR. CIBELLI: I JUST WANT TO CONGRATULATE ALAN FOR THIS. I GUESS THIS IS PROBABLY GOING TO BE

YOUR BIGGEST LEGACY AS THE PRESIDENT OF CIRM. IT COULD BE THE BIGGEST LEGACY OF CIRM, PREPARING THE TOOLS FOR THE FUTURE OF MEDICINE. AND I THINK THAT WHAT YOU ARE TALKING ABOUT, WORKING GMP CONDITIONS PRODUCING ALL THESE CELL LINES IS A VERY EXPENSIVE PROPOSITION. AND STEP NO. 1 IS TO COME UP WITH THE PRIORITIES OF WHAT ARE THE PEOPLE THAT YOU ARE GOING TO HAVE DONATING THE CELLS FOR THE BANK. I'M NOT TALKING ABOUT ETHICAL ISSUES. I'M TALKING ABOUT MOSTLY RELATED TO WHETHER THIS IS GOING TO TRANSLATE IN A DISH OR NOT.

SO MAYBE THERE'S ROOM FOR AN RFA WHERE YOU ARE GOING TO HAVE BIOINFORMATICIANS WORKING WITH STATISTICIANS TO COME UP WITH WHAT ARE THE BEST CANDIDATES. THAT'S ALL.

DR. TAYLOR: I'LL TURN MY COMMENTS, WHICH WILL IN ANY EVENT BE BRIEF, INTO A QUESTION THAT WE CAN INVITE THE PANELISTS TO RESPOND TO. IT'S A TERRIFIC PRESENTATION. THANK YOU SO MUCH. I THINK IT EFFECTIVELY SHOWED EXACTLY THAT THERE ARE SOME ETHICAL ISSUES WE NEED TO ADDRESS ACROSS THE BOARD.

SO THE QUESTION IS REALLY THIS. RECOGNIZING THAT GENOMIC DIVERSITY IS ESSENTIAL FROM THE SCIENTIFIC PERSPECTIVE, RECOGNIZING THAT POPULATION DIVERSITY IS ESSENTIAL FROM THE

PERSPECTIVE OF JUSTICE AND REALLY BENEFITING PEOPLE, AND IF THE TWO WORLDS HAVE TO BE CONNECTED IN WAYS THAT DON'T USE REALLY PERNICIOUS CLASSIFICATIONS, YET THE PEOPLE HAVE HUGE CONCERNS ABOUT HOW THEIR TISSUES WILL BE USED WHICH MAP ONTO SOME OF THOSE SOCIAL CONCERNS, HERE'S THE QUESTION. WHAT DO YOU RECOMMEND THAT CIRM DO IN THE CONTEXT OF RFA'S OR INFORMED CONSENTS TO ADDRESS THOSE KINDS OF CONCERNS, SUCH AS HOW TISSUES AND DATA AND SO ON MIGHT BE MISUSED FOR PEOPLE WHO ARE LATINO OR AFRICAN-AMERICAN DESCENT? HOW DO RECOMMEND THAT ISSUE BE SPECIFICALLY ADDRESSED?

IN MY OWN EXPERIENCE, ALTHOUGH IT MAY COME UP, PEOPLE TALK ABOUT IT, PEOPLE ARE AWARE OF IT, I HAVE YET TO SEE AN INFORMED CONSENT PROCESS THAT TAKES IT HEAD-ON AND SAYS TO PEOPLE HERE'S WHAT WILL HAPPEN. WE KNOW YOUR CONCERN AND HERE'S HOW IT WILL BE ADDRESSED.

CHAIRMAN LO: THIS IS EXACTLY THE QUESTION I'M GOING TO PUT FRONT AND CENTER. I THINK SOME OF OUR PANELISTS HAVE HAD SOME EXPERIENCE DEALING WITH THAT BECAUSE THEY'VE BEEN GETTING DONATIONS, DERIVING THE LINES, AND SORT OF DISTRIBUTING THEM. SO THIS IS SOMETHING TO KEEP IN MIND AND WE'RE GOING TO COME BACK TO. LET'S NOW --

MS. LANSING: IT'S FINE. I ACTUALLY AM GLAD YOU SAID WHAT YOU SAID BECAUSE THIS IS WHY WE'RE HERE TODAY. I WAS JUST ACTUALLY GOING TO SAY IT'S CLEARLY OBVIOUS THAT AS A CANCER ADVOCATE, WITH THE BRCA GENE, IF YOU DIDN'T HAVE A VERY SELECT POPULATION IN THIS CASE OF JEWISH PEOPLE FROM A CERTAIN COMMUNITY, YOU WOULD NEVER HAVE LOCATED THAT GENE WHICH HAS A HIGH PROPENSITY. SO I THINK IT'S THE SCIENCE THAT IS DRIVING THIS AS WELL AS SOCIAL JUSTICE THAT WE GET A DIVERSE POPULATION.

CHAIRMAN LO: LET'S TURN TO OUR FIRST GUEST. JEANNE LORING IS THE FOUNDING DIRECTOR OF THE CENTER FOR REGENERATIVE MEDICINE AT SCRIPPS, AND SHE HAS A DISTINGUISHED SCIENTIFIC CAREER AND, IN FACT, HAS WORKED ON DIVERSITY WITHIN STEM CELL LINES AND HAS ALSO BEEN ACTIVE IN THE POLICY REALM. SO WE'RE LOOKING FORWARD TO YOUR TALK, WHICH IS GOING TO SORT OF AGAIN HELP -- I WANT TO JUST REMIND EVERYBODY WE HAVE SOME DISTINGUISHED SCIENTISTS ON OUR COMMITTEE HERE, BUT MOST OF US I THINK ARE NOT. SO WE'RE CERTAINLY GOING TO ASK QUESTIONS OF CLARIFICATIONS, AND WE ASK OUR PANELISTS TO SORT OF KEEP IT AT A LEVEL THAT THE EDUCATED LAYPERSON CAN UNDERSTAND. AND WE'LL ASK YOU A LOT OF QUESTIONS.

DR. LORING: I'D LIKE TO THANK THE

ORGANIZERS FOR INVITING ME. I WAS JUST AT A CONFERENCE IN WHICH ESSENTIALLY ALL THE SLIDES HAD WESTERN BLOTS GENOMIC SEQUENCE AND DIFFERENTIAL EQUATIONS, SO THIS IS A REALLY NICE CHANGE, I HAVE TO ADMIT.

SO I THINK THE REASON I WAS INVITED WAS BECAUSE OF A PILOT PROJECT THAT I HAVE DONE WITH THE BILL AND MELINDA GATES FOUNDATION. AND THE GOAL OF THAT PROJECT WAS TO CREATE MORE GENETIC DIVERSITY IN IPS CELL LINES OR PLURIPOTENT STEM CELL LINES THAT COULD BE USED FOR DRUG TESTING BECAUSE THERE ARE SOME VERY CLEAR ETHNIC ASSOCIATIONS WITH RESPONSES TO HIV AND TUBERCULOSIS DRUGS. SO WITH THAT FUNDING, WE CREATED THE FIRST NIGERIAN, COMPLETELY NIGERIAN IPS CELL LINE. WE HAVE ONE FROM KENYA AND WE HAVE ABOUT 30 AFRICAN-AMERICAN CELL LINES. SO WE'RE STARTING THAT AS THE BASIS FOR OUR DRUG SCREENING.

AND AS A LONG-TERM GOAL, WE HAVE A GOAL OF MAKING A HUNDRED CELL LINES THAT REPRESENT THE ENTIRE WORLD AS FAR AS THE PHARMACEUTICAL COMPANY VIEWS IT, IN WHICH WE HAVE SUFFICIENT ETHNIC OR GENETIC DIVERSITY SO THAT MOST OF THE DRUGS THAT ARE CURRENTLY ON THE MARKET, WE SHOULD BE ABLE TO PICK UP THE ADVERSE REACTIONS AND CERTAIN

GENOMIC-SPECIFIC BENEFITS OF DRUGS.

SO WITH THAT AS INTRODUCTION, I'M REALLY JUST GOING TO LAY OUT THE FRAMEWORK OF WHAT WE HOPE TO DISCUSS FROM MANY PERSPECTIVES IN THE NEXT FEW HOURS.

SO YOU'VE SEEN THIS SLIDE ALREADY, THE THREE STAGES OF CELL LINE DEVELOPMENT. YOU NEED TO OBTAIN THE CELLS OR THE TISSUES, YOU NEED TO DERIVE THEM, AND THEN YOU NEED TO BANK THEM AND DISTRIBUTE THEM, WHICH ARE ACTUALLY TWO DIFFERENT THINGS. THE OBJECT HERE IS TO DISCUSS THE SEVERAL DIFFERENT TYPES OF SUBJECTS, INCLUDING THE MATERIAL QUALITY. WHETHER THE CELL LINE IS GROWN UNDER GMP-COMPLIANT CONDITIONS OR NOT IS EXTREMELY IMPORTANT, NOT ONLY IN THE POTENTIAL USE OF THOSE CELLS, BUT ALSO IN THE COST OF THE DERIVATION AND BANKING OF THOSE CELLS.

WE'RE PARTICULARLY INTERESTED RIGHT NOW IN NOMENCLATURE BECAUSE THERE ARE SO MANY CELLS BEING GENERATED, THAT WE CAN'T KEEP TRACK OF THEM. SO WE WANT TO ESTABLISH AT THIS RELATIVELY EARLY STAGE, IT MAY BE TOO LATE ALREADY, SOME KIND OF STANDARD NOMENCLATURE, LIKE A LICENSE PLATE WAS MENTIONED, IN WHICH YOU CAN UNIQUELY IDENTIFY A CELL LINE. AND ALSO, AS I MENTIONED, THE DIVERSITY FOR BOTH SCIENTIFIC AND SOCIAL REASONS IS REALLY IMPORTANT TO

ME.

SO SOME OF THE QUESTIONS WE WILL PROBABLY WANT TO DISCUSS IS IF THERE IS SUFFICIENT RACIAL, ETHNIC, AND DISEASE VARIABILITY IN EXISTING CELL LINES. I THINK THAT'S A PRETTY EASY ANSWER. THERE HAVE BEEN TWO STUDIES THAT LOOKED AT A CONGLOMERATE OF MAYBE 75 HUMAN EMBRYONIC STEM CELL LINES AND IPS CELL LINES AND DISCOVERED THAT THEY WERE UNIFORMLY EITHER EUROPEAN OR EAST ASIAN.

THE EAST ASIAN AND EUROPEAN ISSUE IS REALLY -- THE REASON FOR THAT IS THE PEOPLE WHO USE IVF CLINICS TEND TO BE PREDOMINANTLY UPPER MIDDLE CLASS; THEREFORE, THEY TEND TO BE EUROPEAN AND EAST ASIAN. IT'S JUST A MATTER OF CIRCUMSTANCES THE MATERIAL WE STARTED WITH WAS ALREADY BIASED.

SO LET'S ASSUME THAT THERE IS SUFFICIENT RACIAL AND ETHNIC AND DISEASE VARIABILITY IN EXISTING CELL LINES FOR SOME PROJECTS, CERTAINLY IN BASIC RESEARCH, DISEASE-IN-A-DISH MODELS. WE NEED TO REALLY JUST GATHER THAT INFORMATION, DISCOVER WHAT WE NEED TO FILL OUT THE REST OF THE BLANKS.

FOR CLINICAL USE, AS ALAN POINTED OUT, THAT'S GOING TO BE ANOTHER ENTIRE KETTLE OF FISH. WE'RE GOING TO HAVE TO LOOK AT A LOT OF OTHER ISSUES BESIDES THE -- IF YOU STOP IN A DISH, THEN THERE ARE

NOT A LOT OF PROBLEMS WITH PUTTING CELLS INTO PATIENTS. THOSE CELLS WILL NEVER GO INTO PATIENTS. THEY'RE USED FOR DRUG SCREENING. BUT IF YOU GO BEYOND THAT STAGE, YOU HAVE A WHOLE DIFFERENT GROUP OF CONSIDERATIONS.

SO WHAT ARE THE MILESTONES? WHAT SHOULD THEY BE? I TOLD YOU ONE SET OF MILESTONES, WHICH IS ESSENTIALLY PHARMACEUTICAL INDUSTRY BASED. THE REASON I CHOSE THAT ONE WAS BECAUSE IT WAS STRAIGHTFORWARD AND THERE WERE ONLY A HUNDRED LINES INVOLVED. IF WE'RE GOING TO MAKE 10,000 LINES OR SO, THE ANSWER IS, YES, ONE LAB CAN DO THAT. AS MANY OF YOU MAY KNOW, THERE'S GENOMIC-WIDE ASSOCIATION STUDIES THAT HAVE LED TO A LOT OF KNOWLEDGE ABOUT DISEASE SUSCEPTIBILITY BASED ON THE GENOME. AND THOSE STUDIES USUALLY INVOLVE, IF THEY'RE GOING TO BE EFFECTIVE, AT LEAST A THOUSAND PATIENTS, USUALLY 10,000 PATIENTS.

AND JUST IN THE LAST MONTH THE NIH CAME UP WITH A REQUEST, CAME OUT WITH A REQUEST FOR APPLICATIONS FOR PEOPLE TO MAKE IPS CELL LINES FROM ENTIRE GWAS STUDIES. SO THEY'RE ALREADY THINKING ABOUT MAKING 10,000 IPS CELL LINES. SO THAT MEANS US AS SCIENTISTS ARE THINKING ABOUT HIGH THROUGHPUT METHODS FOR MAKING IPS CELL LINES. THAT IS IN THE

WORKS. I THINK YOU CAN DRAW ON EXISTING EXPERIENCE ALREADY IN THAT FIELD.

SO WHAT'S THE ROLE OF NOMENCLATURE? I THINK IT'S REALLY CRITICAL BECAUSE FROM A SCIENTIST'S POINT OF VIEW, IF YOU HAVE A REALLY KLUDGY NAME FOR A CELL, THEN PEOPLE AREN'T PROBABLY GOING TO USE THAT CELL LINE BECAUSE IT'S NOT SELF-EVIDENT WHAT IT IS. IF YOU NAME IT AFTER YOURSELF, THEN ALL YOUR FRIENDS WILL USE THE CELL LINE, BUT PEOPLE THAT DON'T KNOW YOU WON'T.

SO WHAT OTHER BOTTLENECKS ARE THERE FOR BANKING AND DISTRIBUTION? SO, OF COURSE, THERE'S THE REGULATORY ELEMENTS, THE HUMAN SUBJECTS AND CONSENT REQUIREMENTS, WHICH I THINK ARE GOING TO BE AN IMPORTANT PART OF THIS MEETING, THE PRIVACY PROTECTIONS, OR WITHDRAWAL OF MATERIALS. THIS IS ESPECIALLY IMPORTANT BECAUSE WE'RE NOW DOING WHOLE GENOME SEQUENCING OF SAMPLES FROM IPS CELLS AND ES CELLS. AND THIS IS A WHOLE DIFFERENT TYPE OF INFORMATION THAT WE NEED TO INDEPENDENTLY CONSENT IN PATIENTS.

AND THEN, OF COURSE, WE NEED TO PAY ATTENTION TO FDA REGULATIONS, WHICH ARE IN SOME SENSE UNCHANGING AND IN SOME SENSE MUTABLE. I THINK WE CAN HAVE AN INFLUENCE ON THE FDA BY EDUCATING

THEM, BUT WHAT IS REQUIRED.

SO HERE'S SOME QUESTIONS ABOUT PRIVACY AND PROVENANCE, REGULATORY CONSIDERATIONS. WHAT PROPORTION OF THE CELL LINES, LET'S SAY THE ONES WE HAVE NOW, HOW MANY OF THEM ARE DERIVED FROM ANONYMOUS SOURCES OR IDENTIFIABLE SOURCES? DO WE HAVE A COMMON CONSENT DOCUMENT? DO THE DOCUMENTS -- ARE THE DOCUMENTS THAT WE USE REALLY COVERING EVERYTHING, ALL THE POSSIBLE USES OF THESE CELLS? ARE THE MATERIALS PROCURED UNDER IRB PROTOCOLS? THAT'S ALWAYS AN INTERESTING SUBJECT BECAUSE IT DEPENDS ON YOUR IRB. AND THIS IS A VERY IMPORTANT ISSUE. SHOULD CIRM BE ABLE TO HAVE A LITTLE CLOUT HERE? SHOULD CIRM BE ABLE TO DECIDE OR TO REGULATE NON-CIRM RESEARCH USING BANKED MATERIALS THAT CIRM BANKS? SHOULD THERE BE SOME KIND OF A BAR THAT PEOPLE HAVE TO PASS IN ORDER TO USE THOSE CELLS BECAUSE IF WE MAKE BANKS, AS ALAN SUGGESTED, THEY'RE GOING TO BE EXTREMELY VALUABLE, AND PEOPLE FROM OTHER FUNDING ORGANIZATIONS WILL WANT TO USE THEM.

AND THEN THE QUESTION ABOUT THE EXISTING STOCKS OF CELLS COMPLYING WITH FDA REGULATIONS. THE ANSWER IS, OF COURSE, YES BECAUSE THERE ARE CLINICAL TRIALS GOING ON RIGHT NOW. BUT THAT HAS BEEN PRETTY DIFFICULT BECAUSE OF NOT ONLY THE INFORMED CONSENTS,

BUT ALSO THE HISTORY OF THE CELLS AND THE CONDITIONS UNDER WHICH THEY WERE DERIVED. SO THIS IS A BRAVE NEW WORLD. WE CAN START OVER AND DO EVERYTHING RIGHT.

FINALLY, THE MATERIALS AND SHARING REQUIREMENTS. HOW DO YOU BANK AND DISTRIBUTE THESE CELLS FAIRLY? WE WILL HAVE SOME DISCUSSION ABOUT THE IMPACT OF INTELLECTUAL PROPERTY RULES ON MATERIALS SHARING AND DISTRIBUTION. THIS IS SOMETHING WE DON'T REALLY LIKE TO THINK ABOUT AS RESEARCHERS, BUT UNFORTUNATELY IT DOES HAVE A RATHER LARGE IMPACT ON OUR LIVES.

SO FOR BASIC RESEARCH THAT'S RELATIVELY SIMPLE; BUT COMMERCIALIZATION, PATENTS ARE, IN FACT, FILED BY COMPANIES OR PEOPLE WHO WANT TO MAKE MONEY OFF THEM. SO THE VISAGE OF COMMERCIALIZATION, WE HAVE TO DEAL WITH IT BECAUSE THE PEOPLE WITH PATENTS WILL WANT TO GET SOME RETURN ON THEIR INVESTMENT.

ARE THERE SUFFICIENT STOCKS OF GMP-COMPLIANT MATERIALS FOR COMMERCIAL DEVELOPMENT? I DON'T KNOW THE ANSWER TO THAT. MAYBE SOMEBODY ELSE KNOWS THIS. ARE EXISTING REQUIREMENTS AND MTA'S COMPATIBLE WITH CIRM IP POLICIES? I THINK THE REQUIREMENT FOR SHARING OF CIRM-DERIVED LINES IS SOMETHING THAT IS ACTUALLY A VERY GOOD MODEL FOR THE

REST OF THE FUNDING AGENCIES.

SO THIS SUMMARIZES ALL THE THINGS THAT I MENTIONED. NOW, WHEN WE'RE TALKING ABOUT COSTS, NOT ONLY IN DOLLARS, BUT ALSO IN HOW MANY SKILLED LABORERS, HOW MANY PEOPLE DO YOU NEED TO BE WORKING ON A PROJECT. THE PROCUREMENT IS RELATIVELY EASY. AND ACTUALLY IT'S USEFUL TO BE INVOLVED WITH PEOPLE WHO ARE IN PUBLIC HEALTH WHO ARE USED TO RECRUITING PEOPLE FOR OTHER TYPES OF STUDIES. THAT'S PROVED TO BE VERY VALUABLE FOR US, HAVE PEOPLE WHO ARE EXPERIENCED ACTUALLY WORK ON THIS.

THE DERIVATION IS EXTREMELY EXPENSIVE, AND I'LL SHOW YOU AN OUTLINE OF ONE COST ESTIMATE I'VE MADE. AND THEN DISTRIBUTION IS NOT MY AREA OF EXPERTISE, BUT I UNDERSTAND THERE ARE COST SAVINGS ASSOCIATED WITH ONCE YOU ESTABLISH BANKS, DISTRIBUTING IS LESS EXPENSIVE. SO WE WANT TO DISCUSS THAT.

SO WHAT ARE THE COSTS FOR MATERIALS PROCUREMENT FROM GETTING THE CELLS TO DISTRIBUTING THEM? AND WHAT COST-EFFECTIVE OPTIMAL RETURN ON INVESTMENT APPROACHES CAN WE TALK ABOUT? WHAT'S THE BEST WAY TO MOVE FORWARD? AND THEN I THINK IMPORTANTLY IS THERE ANY WAY THAT CIRM CAN TAKE ADVANTAGE OF ESTABLISHED BANKS? IS THERE ANY WAY TO

BE ABLE TO LEVERAGE CIRM WITH OTHER FUNDING ORGANIZATIONS IN ORDER TO PROVIDE A WIDE VARIETY OF CELLS AND A LOT OF EXPERTISE?

SO HERE'S MY ESTIMATES. I USED THESE IN SEVERAL GRANTS I'VE APPLIED FOR. THIS IS THE ACTUAL COST OF MAKING IPS CELLS THAT REPRESENT ONE INDIVIDUAL. SO THIS GOES FROM THE RECRUITMENT TO FIRST-PHASE BANKING, AND THEN I'VE ADDED A MASTER BANK COST WHICH I HAVE NOT ACTUALLY BEEN ABLE TO CALCULATE BECAUSE I HAVEN'T DONE IT YET. BUT THE RECRUITMENT MATERIALS, IF YOU'RE DOING A RELATIVELY LARGE STUDY, LIKE YOU WANT A HUNDRED INDIVIDUALS, ARE RELATIVELY CHEAP. THAT'S EDUCATIONAL. MOST OF IT IS EDUCATIONAL AND A LOT OF ONE-ON-ONE NETWORKING WITH COMMUNITY GROUPS AND DISEASE ORGANIZATIONS.

THE BIOPSY MATERIALS, YOU TAKE A LITTLE SKIN PUNCH, THAT DOESN'T COST VERY MUCH, AND THE CLINIC IS USUALLY WILLING TO DO THAT EITHER FOR FREE OR MINIMUM COST.

THE BANKING OF FIBROBLASTS, YOU JUST GROW UP A LOT OF CELLS AND FREEZE THEM DOWN SO YOU CAN GO BACK TO THAT BANK. THIS IS SOMETHING I THINK A LOT OF PEOPLE DON'T INCLUDE, BUT I THINK IS REALLY CRITICAL; THAT IS, GENOTYPING THE FIBROBLAST LINE. THE GENOTYPING WILL TELL YOU THE ETHNICITY OF THAT

FIBROBLAST LINE. IT WILL ALSO TELL YOU WHETHER YOU GENERATED ANY GENOMIC ABNORMALITIES DURING THE GROWTH OF THAT FIBROBLAST LINE. SO THIS WOULD BE A WAY OF FILTERING OUT CELLS THAT YOU REALLY DON'T WANT TO MOVE FORWARD BECAUSE YOU'LL JUST BE AMPLIFYING THOSE PROBLEMS.

SO THERE'S THE FIRST PHASE. SO REPROGRAMMING TO IPS CELLS IS NOT THAT EXPENSIVE. THREE CONES PER INDIVIDUAL, WE AGREE ABOUT THAT, ALAN. THE RUNNING COSTS ARE ACTUALLY ON THE FAR RIGHT OVER THERE. YOU CAN SEE THE COST OF STOPPING AT WHATEVER STAGE. THE FIRST PHASE, QUALITY CONTROL, THEY NEED TO BE STERILE, YOU NEED TO SHOW THAT THEY'RE PLURIPOTENT, AND THAT THEY CAN DIFFERENTIATE. THESE ARE REALLY VERY SIMPLE ASSAYS, NOT TOO EXPENSIVE.

THEN THERE'S THE EXPANSION AND BANKING OF THE IPS CELLS USING THREE CLONES PER INDIVIDUAL, WHICH IS THE MOST EXPENSIVE PART OF THE PROCESS. THE COST OF CULTURE MEDIA, THE DISHES, IT ADDS UP. IT'S A HUGE AMOUNT OF MONEY.

AND THEN AFTER YOU -- I DECIDED THAT I CAN ONLY AFFORD TO DO QUALITY CONTROL WITHOUT PEOPLE GETTING STICKER SHOCK ON ONE OF THOSE THREE CELL LINES, ONE OF THOSE THREE CLONES FROM EACH PERSON.

AND THEN PRESUMABLY I CAN GO BACK AND REPEAT THAT PROCESS IF THAT PARTICULAR CLONE TURNS OUT TO BE A BAD ONE FOR SOME REASON.

SO, AGAIN, WE GO THROUGH THE SECOND PHASE: STERILITY, PLURIPOTENCE, MARKER ASSAY, GENOTYPING AGAIN. AND THE GENOTYPING AT THIS STAGE IS ESPECIALLY IMPORTANT BECAUSE ONCE YOU MAKE CELLS PLURIPOTENT AND IMMORTAL IN CULTURE, THEY START PICKING UP GENOMIC ABNORMALITIES, INCLUDING SOME EXTRA CHROMOSOMES. YOU DON'T WANT TO USE THOSE CELLS IN PATIENTS. AND THESE ARE CHANGES THAT ARE UNIQUE TO PLURIPOTENT STEM CELLS. SO WE KNOW THEY'RE GOING TO HAPPEN. THE QUESTION IS IF WE AVOIDED THEM, WE WANT TO KNOW. IF WE HAVEN'T AVOIDED THEM, WE WANT TO KNOW.

SO THAT ALL ADDS UP TO $7,830 PER INDIVIDUAL PATIENT TO CAPTURE THEIR GENOTYPE IN CELLS IN A FREEZER, AND THEN AN UNKNOWN AMOUNT IF YOU WANT TO DISTRIBUTE THOSE CELLS.

SO OUR GOAL, ONE OF OUR GOALS, AND I THINK THE GOAL OF A LOT OF PEOPLE IS TO BRING THAT COST DOWN CONSIDERABLY SO THAT WE CAN ACTUALLY DO THIS, WE CAN DO A HUNDRED OR A THOUSAND IPS CELL LINES AT REASONABLE COST.

SO I'M GOING TO LEAVE THIS NOW. THIS IS

THE LAST SLIDE. SO THE QUESTION IS WHETHER THE COSTS, AND I'VE GIVEN YOU AN ESTIMATE FOR BASIC RESEARCH, MAYBE $10,000 PER LINE. I DON'T MEAN -- I MEAN PER PATIENT ESSENTIALLY COMING UP, AND I REALLY DO MEAN CAPTURING THE GENOME OF THAT PATIENT IN A PLURIPOTENT CELL LINE. SO ONCE YOU'VE DONE THAT, EVERYTHING ELSE IS POSSIBLE. BUT UP TO THAT STAGE, IT COSTS QUITE A BIT.

AND TO TAKE GMP-COMPLIANT CELL LINES, THE SAME SORT OF THING. I HAVE HEARD MANY ESTIMATES, BUT WE HAVE AN EXPERT HERE ON THE PANEL, SO I'M GOING TO LET LARRY ACTUALLY COMMENT ON THAT.

ANY QUESTIONS?

CHAIRMAN LO: THANK YOU VERY MUCH. IT WAS A VERY LUCID AND COMPREHENSIVE OVERVIEW. AS I WAS LISTENING TO YOU, I WAS JUST TRYING TO CHECK OFF. YOU JUST RAISED A WHOLE BUNCH OF ETHICAL ISSUES. I JUST WANT TO MARK THEM BECAUSE I THINK THESE ARE THINGS WE'RE GOING TO NEED TO THINK ABOUT AS A GROUP. SO ETHNIC DIVERSITY, PRIVACY PROTECTIONS, ETHICAL ISSUES REGARDING WHOLE GENOME SEQUENCING, WITHDRAWAL OF MATERIALS, USE OF ANONYMOUS SOURCES OR DONORS WHO MAY HAVE GIVEN MATERIALS FOR CLINICAL USE OR FOR ANOTHER RESEARCH PROJECT, TO NOW USE THEM FOR THIS NEW ENDEAVOR OF DERIVING IPS LINES, CONSENT

REQUIREMENTS.

AND AT SOME POINT I'M GOING TO ASK GEOFF OR PAT TO SORT OF WALK US THROUGH THE EXCEPTIONS TO CONSENT THAT APPLY TO ANONYMIZED TISSUE, AND THEN HOW YOU DISTRIBUTE THE CELL LINES FAIRLY ONCE YOU HAVE A BANK AMONG THE RESEARCHERS THAT WANT THEM, AND HOW DO YOU SETTLE INTELLECTUAL PROPERTY CONCERNS?

A LOT OF ISSUES THAT WE'RE GOING TO HAVE TO SINK OUR TEETH INTO. I'M GOING TO ACTUALLY ASK OUR OTHER GUESTS TO ALSO GIVE US SOME REMARKS PARTICULARLY TO HELP US WHO ARE NOT REALLY FAMILIAR WITH STEM CELL DERIVATION AND BANKING, AS PROFESSOR LORING DID, TO SORT OF HIGHLIGHT FOR US THE ISSUES THAT YOU THINK WE NEED TO BE THINKING ABOUT AS WE THINK ABOUT ETHICAL AND POLICY STANDARDS FOR THIS PROJECT THAT ALAN HAS PUT BEFORE US.

UNLESS THERE ARE QUESTIONS SPECIFICALLY ABOUT PROFESSOR LORING'S PRESENTATION, I'D LIKE TO SORT OF HOLD MORE GENERAL QUESTIONS TILL WE'VE HEARD FROM ALL OUR PANELISTS BECAUSE I THINK WE'RE GOING TO GET A MUCH RICHER PICTURE FROM THE TOTAL OF FOUR.

DR. PRIETO: I JUST HAVE A QUESTION ABOUT YOUR COMMENTS ABOUT NOMENCLATURE. I WAS THINKING ABOUT THAT AND THE HISTORY, HOW IMPORTANT

NOMENCLATURE OR STANDARDIZED NOMENCLATURE HAS BEEN IN THE HISTORY OF BIOLOGY. NOT MUCH ATTENTION HAS BEEN PAID TO THIS.

DR. LORING: I AGREE.

DR. PRIETO: IT COULD BE VERY IMPORTANT. I WONDER WHERE WE ARE AND WHO'S ADDRESSING THIS.

DR. LORING: SO WE'RE JUST STARTING TO ADDRESS THIS. WE INSERTED A SMALL WORKSHOP INSIDE ANOTHER WORKSHOP FOR THE ISSCR MEETING IN A COUPLE OF WEEKS. THERE'S A SMALL GROUP OF US WHO ARE DISCUSSING THIS. I THINK THE ANALOGY REALLY COMES FROM THE HUMAN GENOME PROJECT IN WHICH PEOPLE CALLED A CERTAIN GENE BY MAYBE 20 DIFFERENT NAMES. IT'S SORT OF LIKE THE ELEPHANT AND ALL THE BLINDFOLDED PEOPLE.

AND SO THE NIH STEPPED IN AND SAID WE ARE GOING TO CALL THIS GENE BY THIS NAME. THIS IS THE OFFICIAL NAME. IF YOU WANT TO LOOK UP ANYTHING ABOUT THIS GENE, YOU WILL HAVE TO USE THIS NAME. I DON'T KNOW IF WE REALLY HAVE THE CLOUT TO IMPOSE THAT SORT OF NOMENCLATURE, BUT I THINK WE CAN ARGUE THAT IT'S GOING TO BE MORE VALUABLE TO THE FIELD IF THE CELLS ARE SORT OF UNIQUELY IDENTIFIABLE AND THEY'LL BE USED -- THE SAME TITLE WILL BE USED, THE SAME NAME WILL BE USED BY EVERYONE WHO USES THOSE

CELLS FROM NOW ON.

SO THERE'S BENEFIT TO RESEARCHERS, AND THERE'S OBVIOUSLY BENEFIT TO A LOT OF THESE DATA BANKS NOW THAT ACTUALLY DO TEXT SEARCHING. SO THEY FIND ALL SORTS OF INFORMATION BASED ON A WORD OR A NAME OF SOMETHING.

I THINK IT'S REALLY CRITICAL. THE GREAT THING ABOUT THIS IS THAT WE HAVE THE POSSIBILITY OF DOING SOMETHING ABOUT IT NOW. AND PRETTY SOON IT'S GOING TO BE TOO LATE.

SO IF YOU HAVE ANY GOOD IDEAS, I WOULD LOVE TO HEAR THEM BECAUSE RIGHT NOW WE'RE JUST BRAINSTORMING.

DR. PRIETO: I'M JUST WONDERING WHO HAS THE CLOUT TO IMPOSE IT, AND MAYBE THE ISSCR IS THE BODY TO PUSH THIS FORWARD.

DR. LORING: I'M HOPING THE NIH --

DR. PRIETO: YOU HAVE TO GET BUY-IN FROM NIH AND INTERNATIONALLY.

DR. LORING: I'M HOPING THE NIH WILL GIVE OUT A SMALL GRANT. IF YOU HAVE ANY INFLUENCE WITH THOSE GUYS, I'D APPRECIATE IT. A SMALL GRANT SPECIFICALLY FOR THIS BECAUSE I KNOW THE NCBI, INFORMATION IS REALLY IMPORTANT TO THEM. SO WHY NOT ACTUALLY PAY TO HAVE SOMEBODY DO THIS? RIGHT NOW

WE'RE ALL VOLUNTEERS.

ANY OTHER SPECIFIC QUESTIONS?

CHAIRMAN LO: I WANT TO SORT OF TRY AND KEEP US FROM GETTING INTO AN IN-DEPTH DISCUSSION OF A PARTICULAR ISSUE LIKE NOMENCLATURE, PARTICULARLY IF IT'S NOT AN ETHICS ISSUE.

DR. KIESSLING: I JUST HAVE A REALLY QUICK QUESTION. THANK YOU, DR. LORING, FOR THAT NICE PRESENTATION. I WANT TO POINT JUST FOR EVERYBODY'S THINKING THAT I THINK YOUR CELL LINE DERIVATION IS HIGHLY EFFICIENT. I THINK MOST LABORATORIES IT'S GOING TO COST A GREAT DEAL MORE THAN THAT PER CELL LINE. I THINK THAT'S ONLY IN LABORATORIES THAT ARE PROBABLY DOING MULTIPLE CELL LINES AT A TIME. FOR LABORATORIES THAT ARE DOING SMALLER NUMBERS, THE NUMBERS ARE MUCH HIGHER THAN $10,000 A LINE.

DR. LORING: I THINK YOU'RE RIGHT, ALTHOUGH IT'S BEEN HARD TO GET THAT INFORMATION BECAUSE MOST PEOPLE DON'T ACTUALLY ADD UP ALL THE COSTS.

CHAIRMAN LO: THANKS AGAIN. I'M GOING TO CALL ON ANOTHER PANELIST. DR. LARRY COUTURE IS THE DIRECTOR OF THE CENTER FOR APPLIED TECHNOLOGY DEVELOPMENT AND ALSO DIRECTOR OF THE CENTER OF BIOMEDICINE AND GENETICS AT THE CITY OF HOPE. AND

HE'S ALSO BEEN INVOLVED IN WITH A NUMBER OF START-UP BIOTECH COMPANIES IN THE SOUTHERN CALIFORNIA AREA. SO PLEASE SET MORE THINGS BEFORE US FOR ISSUES WE NEED TO BE THINKING ABOUT.

DR. COUTURE: SO FIRST LET ME START BY THANKING GEOFF AND JEANNE FOR ACTUALLY INVITING ME TO COME AND GIVE A FEW WORDS ON OUR BANKING ACTIVITIES AND SOME THOUGHTS WE HAVE. FIRST I JUST WANT TO THANK GEOFF AND JEANNE FOR ASKING ME TO COME UP AND GIVE A FEW COMMENTS ON OUR THOUGHTS ON BANKING, GMP BANKING PARTICULARLY, FOR THE STEM CELL LINES. I WANT TO APOLOGIZE FOR NOT GETTING THE SLIDES OUT. THANKS TO ONE PARTICULAR AIRPLANE, I SPENT EIGHT HOURS FROM L.A. TRYING TO GET HERE. I DIDN'T GET HERE UNTIL TWO IN THE MORNING LAST NIGHT FROM DELAYED FLIGHTS AND CANCELED FLIGHTS AND MISDIRECTED FLIGHTS AND ALL SORTS OF THINGS, SO UNFORTUNATELY I COULDN'T GET THE SLIDES OUT LAST NIGHT.

MS. LANSING: AND THE PRESIDENT OF THE UNITED STATES.

DR. COUTURE: AND IT WAS ALMOST CERTAINLY OBAMA'S FAULT. IT WAS WEATHER UNFORTUNATELY THAT CANCELED A LOT OF FLIGHTS OUT OF LAX. SO ANYWAY, WHAT I'M GOING TO TALK ABOUT IS NOT THE STEM CELL,

THE BANKS FOR RESEARCH PURPOSES FOR SCREENING, OR NECESSARILY THE AUTOLOGOUS USE OF IPSC, BUT RATHER THE ALLOGENEIC, WHICH MEANS THE BROAD USE OF A PARTICULAR CELL BANK FOR MULTIPLE PROJECTS OR MULTIPLE DISEASE INDICATIONS FOR PATIENTS, AND PARTICULARLY EMBRYONIC STEM CELLS AND IPSC. SO MY COMMENTS KIND OF APPLY TO BOTH.

SO WHAT SOME OF YOU PROBABLY DON'T KNOW IS I RUN A LARGE BIOLOGICS MANUFACTURING FACILITY AT THE CITY OF HOPE NATIONAL MEDICAL CENTER. IT'S AN ACADEMIC INSTITUTION. WE ACTUALLY HAVE TWO FACILITIES, AND WE'RE KIND OF AN ECLECTIC FACILITY. WE PRODUCE VIRTUALLY ANYTHING YOU CAN IMAGINE IN TERMS OF BIOLOGICS. WE'VE BEEN A NATIONAL RESOURCE AND WE ARE FOR ABOUT A DECADE NOW TO PRODUCE LENTIVIRUSES, ANTIBODIES, AND CELL PRODUCTS.

SO ABOUT THREE YEARS AGO, WE STARTED FOCUSING HEAVILY ON EMBRYONIC STEM CELL TECHNOLOGY TO ALLOW US TO PRODUCE BANKS AND WHATNOT IN LARGE PART IN ANTICIPATION OF PROJECTS COMING THROUGH CIRM AND THE FUNDING MOVING TO THIS PRECLINICAL TRANSLATIONAL PHASE WHICH IT HAS.

OVER THE SIX OR EIGHT MONTHS OR SO, BECAUSE OF THAT ACTIVITY AND BECAUSE OF WHAT'S GOING ON IN CIRM, WE ARE ACTUALLY NOW EITHER CO-PI,

CO-INVESTIGATOR, OR A SUBCONTRACTOR ON A NUMBER OF THE CIRM DISEASE TEAM GRANTS, AND WE'VE ALSO RECENTLY BEEN AWARDED ONE OF THE NATIONAL HEART, LUNG, AND BLOOD INSTITUTE'S PACT CENTER CONTRACTS, WHICH IS PROGRAMS FOR ACCESS TO CELLULAR THERAPIES, AND SPECIFICALLY TO FOCUS ON PRODUCING EMBRYONIC STEM CELL PRODUCTS.

WE'RE NOT THE ONLY PACT CENTER. IN FACT, WISCONSIN IS ALSO A PACT CENTER AND PRODUCES EMBRYONIC STEM CELL LINES, BUT WHAT MAKES US SOMEWHAT UNIQUE IS THAT WE'RE AT THE NEXUS HERE OF A MULTIPLE PUBLIC FUNDING ORGANIZATION, CIRM AND THE NHLBI. IN FACT, WE NOW HAVE RUN INTO THE DILEMMA THAT WE KNEW WAS PROBABLY GOING TO COME OUR WAY, BUT WE DIDN'T ANTICIPATE IT COMING SO SOON. AND THAT IS WE'RE GETTING MULTIPLE REQUESTS TO PRODUCE EXACTLY THE SAME MASTER CELL BANK, EXACTLY THE SAME CELL LINE FOR EITHER MULTIPLE AGENCIES OR WITHIN ONE PROGRAM FOR MULTIPLE INVESTIGATORS.

AND TO CUT TO THE CHASE, THIS IS SOMEWHAT OF A WASTE OF RESOURCES AND NOT A VERY EFFICIENT USE OF OUR FISCAL RESOURCES WHERE WE'D MUCH PREFER TO BE SPENDING TIME ON DEVELOPING DIFFERENTIATION STRATEGIES AND PRODUCING ACTUAL CLINICAL PRODUCTS.

SO JUST QUICKLY, THIS WILL ONLY TAKE A

COUPLE OF MINUTES TO TALK ABOUT WHAT THE CURRENT PARADIGM IS, AND WE KIND OF SUGGEST FOR A PARADIGM THAT NEEDS TO BE CONSIDERED RIGHT NOW AS WE'RE FACING THE PRODUCTION OF THESE DIFFERENT CELL BANKS. AGAIN, JUST A BIT OF A TANGENT, BUT SAY WE ARE CURRENTLY LOOKING AT PRODUCING THREE DIFFERENT EMBRYONIC STEM CELL BANKS FOR MULTIPLE INVESTIGATORS, AND ACTUALLY PROBABLY FOUR BY THE END OF THIS YEAR, AND WE ALREADY KNOW THROUGH AT LEAST THE PACT PROGRAM THAT MULTIPLE INVESTIGATORS ARE GOING TO BE REQUESTING EXACTLY THE SAME STEM CELL BANK. SO THIS IS NOT A HYPOTHETICAL. THIS IS A REAL SITUATION.

SO, IN FACT, AS I SAID, THERE ARE MULTIPLE AGENCIES FUNDING THE PRODUCTION OF GMP BANKS, BOTH HESC'S, AND WE'RE ALREADY TALKING TO ONE GROUP TO DO AN IPSC PROBABLY LATER THIS YEAR OUTSIDE OF CIRM, BUT PROJECTS COMING OUR WAY. PART OF THE PROBLEM IS THE PARADIGM FOR OWNERSHIP AND CONTROL AND CUSTODY OF THESE BANKS THAT IS A LEGACY FROM GENERAL GRANT FUNDING; THAT IS, THE GRANTEE, THE PI, OWNS ALL THE MATERIALS PRODUCED THROUGH THE GRANT. SO THE EMBRYONIC STEM CELLS AREN'T NECESSARILY MATERIAL CREATED UNDER A BANK ALTHOUGH THERE COULD BE A NEW CELL LINE GENERATED. MOST ALL THE CELL LINES WE'VE

BEEN SPEAKING WITH INVESTIGATORS WITH NOW OR ARE CONTRACTING TO PRODUCE ARE ALL FROM THE NIH REGISTRY EXISTING EMBRYONIC STEM CELL LINES WITH THE EXCEPTION, OF COURSE, THIS IPSC THAT'S COMING OUR WAY.

THE PROBLEM IS THAT THESE EMBRYONIC PARENTAL CELL LINES THAT WE'RE BANKING, WE'RE NOT TALKING ABOUT THE DIFFERENTIATED PRODUCTS HERE. WE'RE TALKING ABOUT THE ACTUAL PARENTAL BANKS, BASICALLY THE SAME BANKS THAT ALAN HAS BEEN TALKING ABOUT EXCEPT FOR THIS IS FOR THERAPEUTIC USE, ARE NOT THERAPEUTIC PRODUCTS. THEY'RE REALLY MORE OR LESS JUST RAW MATERIALS. AND THOSE RAW MATERIALS AREN'T PROJECT SPECIFIC. THEY JUST HAPPEN TO NOW APPEAR TO BE PROJECT SPECIFIC BECAUSE NOBODY HAS REQUESTED THESE THINGS TO BE PRODUCED YET. SO THE FIRST INVESTIGATORS TAKING IT INTO THE CLINIC ARE THE FIRST INVESTIGATORS TO HAVE A NEED FOR THESE BANKS TO EXIST.

THERE'S SORT OF A TACIT UNDERSTANDING THAT, WELL, THEN, THE BANKS PROBABLY BELONG TO THAT GROUP. THOSE BANKS ARE ACTUALLY SUITABLE OR USEFUL TO PRODUCE A NUMBER OF DIFFERENT TYPE OF CELLULAR PRODUCTS, AS EVERYONE HERE, I THINK, UNDERSTANDS. ANY INDIVIDUAL EMBRYONIC OR IPS CELL LINE CAN BE

USED TO GENERATE EVERYTHING FROM, AS I THINK ALAN SAID, EVERYTHING FROM INSULIN-SECRETING CELLS TO NEURAL PROGENITORS TO CARDIOMYOCYTES, ETC. SO THEY'RE ACTUALLY A RESOURCE OR A TOOL THAT'S USEFUL FOR MULTIPLE INVESTIGATORS.

AND THEN TAKE INTO CONSIDERATION THE FACT THAT DESPITE THE NOTION THAT SOME OF THESE TRIALS WILL GO ON AND HAVE A DEMAND FOR A LARGE OF NUMBER OF CELLS FROM A LARGE BANK AND HAVE TO HAVE ACCESS TO COMMON, CONSISTENT BANK FOR THOSE TRIALS, A LOT OF EARLY PHASE CLINICAL TRIALS LIKE IN ANY FIRST-IN-MAN BIOLOGIC TECHNOLOGY WILL NOT PROCEED BEYOND PHASE I FOR A LOT OF POTENTIAL REASONS. HOPEFULLY SOME DO. INVESTIGATORS MAY MOVE ON TO A DIFFERENT DIRECTION, MAY CHOOSE A DIFFERENT CELL LINE, ETC. SO IF WE PRODUCE CELL BANKS ON A PROJECT-SPECIFIC BASIS, IT IS INEVITABLE THAT A LOT OF THOSE CELL BANKS WILL END UP JUST STAGNATING IN A FACILITY, OURS, WISCONSIN'S, OTHER FACILITIES OUT THERE, AND NOT BE USED AT ALL.

WE KIND OF CONSIDER, WOULD LIKE TO PROPOSE SORT OF DISCUSSION AROUND AN ALTERNATIVE APPROACH FOR FUNDING AND USE OR CONSIDERATION OF THESE CELL BANKS, ONE WHERE PRETTY IT'S SELF-EVIDENT THAT WHERE THERE'S COMMON CELL BANKS, SELF-EVIDENT FROM WHAT

I'VE BEEN SAYING WOULD BE COMMON CELL BANKS THAT WOULD BE AVAILABLE TO A NUMBER OF INVESTIGATORS AND ACROSS FUNDING AGENCIES. SO WE STILL SEE THAT A PRINCIPAL INVESTIGATOR SHOULD BE ABLE TO REQUEST WHATEVER CELL BANK HE OR SHE FEELS IS APPROPRIATE FOR THEIR STUDY. AND IF THAT CELL BANK EXISTS SOMEWHERE IN ONE OF THE FUNDED CENTERS, THAT INVESTIGATOR WOULD HAVE INSTANT ACCESS TO THAT CELL BANK.

BUT IF THE CELL BANK HASN'T BEEN PRODUCED, THAT WE WOULD PRODUCE A NEW BANK. WE'RE ALREADY DOING THIS UNDER THE PACT PROGRAM WITH THE NHLBI IN ANTICIPATION OF A NUMBER OF PROJECTS COMING OUR WAY, FOR EXAMPLE, IN THE CARDIOMYOCYTE FIELD. WE'VE ACTUALLY WORKED WITH INVESTIGATORS, DECIDED WHAT A CELL LINE THAT A NUMBER OF THEM WOULD BE INTERESTED IN, AND THEN WE ACTUALLY SERVED AS THE PRINCIPAL INVESTIGATOR AND PROPOSED TO THE PACT PROGRAM THAT THEY FUND US TO PRODUCE AN EMBRYONIC STEM CELL BANK THAT THEY WOULD USE, AND THEY'VE AGREED THAT THAT'S THE APPROACH TO USE. SO WE WILL ONLY BE PRODUCING ONE OF THIS MASTER CELL BANK FOR A NUMBER OF INVESTIGATORS COMING TO THE TABLE TO USE IT.

SO IT WORKS. WE CAN DO THAT. AND WHAT I WOULD LIKE TO SUGGEST IS CIRM CONSIDER SOME FUNDING

MECHANISM TO ALLOW THAT TO TAKE PLACE HERE. IT IS A CHANGE OF PARADIGM BECAUSE IT ACTUALLY PUTS OWNERSHIP, CONTROL OF THAT CELL BANK WITHIN THE CENTER THAT DOES THE PRODUCTION OSTENSIBLY ON BEHALF OF THE FUNDING AGENCY.

SO IN ADDITION, I'D LIKE TO RAISE THE BAR JUST ONE LITTLE NOTCH, AND INSTEAD OF SIMPLY JUST CIRM OR PACT LOOKING TO KIND OF ECONOMIZE WITHIN THEIR OWN RESPECTIVE PROGRAMS, THE H1, H7, OR H9 CELL BANKS THAT WE'VE PRODUCED FOR PACT IS EXACTLY THE SAME THE CELL BANK THAT WILL BE REQUESTED FOR CIRM. SO THERE'S REALLY NO REASON FOR THE SAME CENTER TO BE PRODUCING TWO DIFFERENT H1 CELL BANKS FOR TWO DIFFERENT FUNDING AGENCIES OR FOR TWO DIFFERENT INVESTIGATORS WITHIN THE SAME FUNDING AGENCY. WE'D LIKE TO SEE THERE BE SOME COLLABORATION AMONG THESE TWO, RIGHT NOW TWO, BUT THERE IS ALMOST CERTAINLY TO BE MORE FROM THE NATIONAL INSTITUTES OF HEALTH IN THE COMING YEARS, TO COLLABORATE AND ALLOW FOR RECIPROCAL ACCESS TO FUNDED INVESTIGATORS TO THOSE MASTER CELL BANKS.

BECAUSE OF THAT, ALAN RAISED A REALLY GOOD POINT, AND THAT IS THESE ARE BIG PROGRAMS, THESE DISEASE TEAM, THERE'S A SIGNIFICANT AMOUNT OF MONEY GOING INTO THESE PROJECTS, AND A LOT OF THEM HAVE

EITHER DIRECTLY INVOLVEMENT IN COMPANIES OR THE ANTICIPATION IS THAT COMPANIES WILL GET INVOLVED AS SOME OF THESE PROJECTS PROGRESS. AND EVERY COMPANY UNDERSTANDS THAT, UNLIKE ACADEMIC INVESTIGATORS WHO ARE LOOKING FOR SCIENTIFIC SUCCESS IN AN EARLY PHASE CLINICAL TRIAL, THEY'RE LOOKING FOR CLINICAL SUCCESS AND, THEREFORE, FOR A PRODUCT OUT THE OTHER END AND ANTICIPATE THAT IN THEIR LOGISTICAL PLANNING UP FRONT AND CREATE LARGE MASTER CELL BANKS AND THEN USE WORKING CELL BANKS OFF OF THOSE. SO YOU MAKE A 3- TO 500-VIAL MASTER CELL BANK AND THEN FROM THAT CREATE ANOTHER 3 TO 500-VIAL WORKING CELL BANK, AND IT'S THE WORKING CELL BANK THAT YOU USE TO SUPPORT STUDIES.

LOT OF ACADEMICS IN FIRST-IN-MAN BIOLOGICS DON'T DO THAT. WE JUST MAKE MASTER CELL BANKS AND USE THE MASTER CELL BANK ITSELF. IT WORKS FOR SCIENTIFIC STUDIES AND PROOF OF PRINCIPLE AND CLINICAL TRIALS, BUT IT DOESN'T LEND ITSELF TO LONG-TERM COMMERCIAL DEVELOPMENT OF THE PRODUCT.

SO WE WOULD PROPOSE, IN ORDER TO MAKE SURE THAT THERE'S ENOUGH CELLS TO GO AROUND AND THAT THERE'S A LOT OF CONSISTENCY FOR A LONG TIME, A NUMBER OF PROJECTS BACK TO THE SAME MASTER CELL BANK, THAT WE ACTUALLY GO TO A MASTER CELL

BANK/WORKING CELL BANK MODEL AND CREATE THOSE WORKING CELL BANKS ON EITHER A MULTIPLE PROJECT BASIS. AGAIN, ONE WORKING CELL BANK CAN SERVE A NUMBER OF TRIALS. AS THOSE TRIALS PROGRESS, THEN THAT INVESTIGATOR COULD REQUEST TO HAVE A WORKING CELL BANK MADE SPECIFICALLY FOR THEIR PROJECT.

I'LL SHOW IN MY LAST SLIDE IN JUST A SECOND THAT IF IT ACTUALLY SHOWS A GREAT DEAL OF POTENTIAL THE WAY WE'VE KIND OF DONE THE LOGISTICS OF SETTING UP THESE BANKS, WE COULD THEN CREATE A NEW MASTER CELL BANK AND WORKING CELL BANK FOR A COMMERCIAL PARTNER OR EVEN AN ACADEMIC FACILITY THAT DECIDED TO TAKE THIS ALL THE WAY INTO MARKETING.

ANOTHER ADVANTAGE OF HAVING COMMON CELL BANKS IS THAT IT WOULD ADD FOR ADDITIONAL COMPARABILITY BETWEEN STUDIES OF PROJECTS ACROSS THE COUNTRY. SOMETHING THE FDA, I KNOW, APPRECIATES IN ALL OF THE BIOLOGICS THAT GO INTO THE CLINIC, WE CAN REMOVE SOME VARIABLES FROM ONE TRIAL TO THE NEXT, AND EVERYBODY HAS THE ABILITY TO COMPARE OUTCOMES AND RESULTS AS BEING MORE A FUNCTION OF HOW THE CELLS ARE DIFFERENTIATED OR HOW THEY'RE APPLIED OR ADMINISTERED RATHER THAN ALL THE WAY BACK TO THE RAW MATERIAL VARIABILITY.

SO THIS IS MY LAST SLIDE. I WON'T GO

THROUGH THIS IN DETAIL. IT BASICALLY JUST ILLUSTRATES HOW THIS COULD WORK VERY WELL, SAVE AN ENORMOUS AMOUNT OF MONEY IN THE LONG RUN BY ONLY MAKING A VERY SMALL NUMBER OF MASTER CELL BANKS OF VERY SPECIFIC CELL LINES, NOT JUST AT CITY OF HOPE, BUT WHEREVER THEY MIGHT BE MADE BY EITHER A PACT CENTER, A PACT PROGRAM, OR THE CIRM.

WE'D START WITH A SEED BANK OF JUST A SMALL NUMBER OF CELLS, THE EARLIER CELLS AVAILABLE FOR THAT PARTICULAR LINE, WHETHER IT'S A NEWLY CREATED LINE OR WHETHER IT'S ONE OF THE EXISTING REGISTRY LINES. AND FROM THAT YOU CREATE THE MASTER CELL BANK OF A RIGHT-SIZED BANK, WHATEVER THAT SEEMS TO BE, WHATEVER SEEMS TO BE APPROPRIATE, SOMEWHERE PROBABLY BETWEEN THREE TO 500 VIALS. FROM THAT YOU CAN PRODUCE IN THE GREEN IN THE CENTER THERE THE WORKING CELL BANK THAT WOULD SUPPORT MOST OF THE PHASE I TRIALS SUPPORTED BY EITHER FUNDING AGENCY AND BOTH FUNDING AGENCIES, BUT YOU COULD ALSO MAKE A RESEARCH BANK OF THE SAME PASSAGE NUMBER FROM THAT MASTER CELL BANK AND ALLOW IT TO BE DISTRIBUTED TO RESEARCHERS, WHO CAN THEN, THEREFORE, DO PRECLINICAL WORK FUNDED BY THE SAME ORGANIZATIONS WITH CELLS WITH THE PASSAGE NUMBER SO THAT THEY'RE, AGAIN, VERY COMPARABLE, THAT YOU'RE NOT EATING UP YOUR GMP

WORKING CELL BANKS.

AS THEY PROGRESS, YOU CAN EITHER MAKE MORE WORKING CELL BANKS, SO AGAIN THE SAME PASSAGE TO SUPPORT TRIALS AS THEY MOVE ON. AS I SHOW HERE, YOU CAN ALSO MAKE A NEW MASTER CELL BANK AND A NEW WORKING CELL BANK FOR A PRODUCT THAT'S ACTUALLY GOING TO BE VERY SUCCESSFUL AND COMPLETELY SUPPORT THAT PRODUCT ALL THE WAY THROUGH COMMERCIALIZATION AND MARKETING. THAT'S ALL I HAVE. THANK YOU.

CHAIRMAN LO: CAN YOU HIGHLIGHT FOR US ANY SORT OF ETHICAL ISSUES YOU WANT TO BE SURE TO THINK ABOUT AS WE CONSIDER THIS MODEL OF MASTER CELL BANK?

DR. COUTURE: AS A GMP MANUFACTURING FACILITY, FOR US THE ETHICAL ISSUES KIND OF COME UP UPSTREAM AND, OF COURSE, THE ISOLATION, DERIVATION, AND CHOICE OF A CELL LINE THAT'S USED. AT OUR INSTITUTION ANYWAY, WE'VE ADDRESSED THOSE, WE THINK, FAIRLY ADEQUATELY, NOT FOR IPSC'S OR HESC'S, BUT FOR ALL THE CELL PRODUCTS WE PRODUCE IN THE FACILITY, WHICH ARE COMPARABLE IN ETHICAL CONSIDERATION IF THEY COME FROM A PATIENT. WE'VE ADDRESSED ALL THOSE IN INFORMED CONSENT. I THINK THE INFORMED CONSENT MODELS THAT EXIST OUT THERE ARE ADEQUATE TO ADDRESS IPSC'S AND HESC'S, SO IT'S BEING DONE.

DR. TAYLOR: UNDER THE MODEL YOU PROPOSE,

WHAT WOULD BE THE DISTRIBUTION OBLIGATIONS OF ONE OF THE FUNDED CENTERS?

DR. COUTURE: AGAIN, AS I KIND OF TRIED TO DESCRIBE, THE OWNERSHIP OF THE BANK EFFECTIVELY STAYS WITH THE FUNDING INSTITUTIONS. THE CENTERS SORT OF BECOME CUSTODIANS FOR THOSE BANKS AND DISTRIBUTE THOSE UNDER DIRECTION FROM THE FUNDING AGENCY. THEY DON'T BECOME AVAILABLE TO EVERYBODY, BUT THAT'S ENTIRELY AT THE DISCRETION OF THE FUNDING AGENCY.

AGAIN, GMP BANKS TYPICALLY ARE MATERIALS RESERVED FOR FUNDED PROGRAMS THAT ARE REVIEWED AT SOME LEVEL. SO PROBABLY WOULD NOT JUST DISTRIBUTE THE CELLS TO ANYBODY WHO REQUESTED THEM, BUT WOULD DO SO UNDER THE DIRECTION OF THE FUNDING AGENCY AND/OR THE SAME CREATING BANKS. BUT THE CENTERS WOULD HAVE TO DISTRIBUTE THOSE CELLS.

ACTUALLY I DREW THIS HERE AS IT'S SHIPPED OUT TO THE BLUE ONE, TO A DISTRIBUTION CENTER. THE GMP PRODUCTION FACILITIES AREN'T NECESSARILY GOOD AT JUST BEING GENERIC DISTRIBUTION CENTERS, AND THERE ARE OTHER PROGRAMS AROUND THAT DO THAT VERY WELL FOR RESEARCH BANKS, AND THEY MIGHT BE TRANSFERRED.

DR. TAYLOR: SO LET ME SHARPEN MY QUESTION A LITTLE BIT TO MAKE IT MORE LIKE DR. LO'S QUESTION.

SO IF A CENTER, ONE OF THESE FUNDED CENTERS, IS ALSO NIH FUNDED AND, THEREFORE, FUNCTIONS UNDER CLASSIC BAYH-DOLE OBLIGATIONS ALSO TO DISTRIBUTE IN A WAY THAT MAXIMIZES UNDER WHATEVER METHODS SOCIAL BENEFIT AND CHOOSES TO DO SO NORMALLY THROUGH EXCLUSIVE LICENSES, WHAT ETHICAL ISSUES DO YOU SEE ARISING? HOW WOULD YOU THINK CIRM AND THIS GROUP SHOULD MAKE SPECIFIC RECOMMENDATIONS ABOUT THOSE DISTRIBUTION OBLIGATIONS THAT YOU ARE TALKING ABOUT AS AGAINST OTHERS THAT MIGHT BE INSTITUTIONAL NORMS OR CLASSIC BAYH-DOLE OBLIGATIONS? REALLY QUITE A SHARP QUESTION ABOUT CONFLICTING OBLIGATIONS TO MULTIPLE PEOPLE, THIS CONCEPT OF CUSTODIANSHIP, AND IT'S WHERE YOU GET INTO THE DETAILS THINGS GET A LITTLE BIT ROUGH.

DR. COUTURE: SO WE KIND OF DEALT WITH THAT A LITTLE BIT. WE'VE BEEN A NATIONAL GENE VECTOR LAB FOR PRODUCING PLASMA DNA'S AND VIRUSES AND WHATNOT, AND THOSE SAME KIND OF ISSUES COME UP. AND THE WAY THEY HAVE BEEN HANDLED IN THE PAST IS THE MATERIALS, BECAUSE THEY'RE GOVERNMENT OR PUBLICLY FUNDED, TEND TO HAVE SORT OF A CATCH THAT THEY HAVE TO BE SOMEWHAT AVAILABLE. AND I THINK CIRM WOULD AGREE THAT THAT'S TO SOME DEGREE THE CASE AS WELL. THAT WOULD BE NO DIFFERENT WHETHER THE

CENTER HAD CUSTODY/OWNERSHIP OF THE BANK OR WHETHER THE PI HAD CUSTODY/OWNERSHIP OF THE BANK. SO I DON'T THINK THE ETHICAL ISSUE ACTUALLY CHANGES. IT JUST SHIFTS FROM ONE PI TO ANOTHER PI, THE PI IN THIS CASE BEING THE PI OF A CENTER.

DR. TAYLOR: WITH RESPECT TO FRAMING OF THE GOAL, IF THE GOAL IS TO MAKE THINGS GENERALLY AVAILABLE, PEOPLE MIGHT FRAME THAT ISSUE DIFFERENTLY IN TERMS OF WHETHER YOU NEED TO GO BEYOND SCIENTIFIC REVIEW TO INCLUDE, FOR EXAMPLE, THE KIND OF CONSIDERATION THAT PROFESSOR ROBERTS TALKED ABOUT.

SECONDLY, WHEN IT COMES TO THE METHODS, METHODS OF EXCLUSIVE LICENSES VERSUS OTHERWISE, I THINK THERE CAN BE SOME ISSUES AROUND WHAT FRAMEWORK IS GENERATED, DIFFERENT ETHICAL CONSEQUENCES.

DR. COUTURE: RIGHT. SO WHAT I HAVEN'T TOUCHED ON AT ALL AND I THINK IS GOING TO COME UP LATER, AND MAYBE OTHERS CAN COMMENT ON THIS AS WELL, ARE THE LICENSING ISSUES BEHIND THESE CELL LINES. THAT'S NOT A BLACK-AND-WHITE ISSUE, AND IT'S NOT ENTIRELY CLEAR HOW THAT WILL WORK. THAT WILL BE TRUE FOR REGARDLESS OF WHERE THE CELLS COME FROM. THEY COME INTO THE FACILITY. IF THEY'RE FUNDED BY CIRM OR BY THE NIH, THERE ARE LICENSING ISSUES.

NOW, OUR JOB IS SIMPLY TO CREATE THE CELL

BANK. TRANSFERRING THOSE CELLS TO ANY INVESTIGATOR, INCLUDING A CIRM-FUNDED INVESTIGATOR, WOULD HAVE TO, AND THIS IS TRUE FOR ALL THE REAGENTS WE PRODUCE, HAS TO ADDRESS INTELLECTUAL PROPERTY ISSUES AS WELL, AND THAT'S SOMETHING THAT HAS TO BE SORTED OUT.

DR. TAYLOR: TO MAKE SURE I UNDERSTAND. THE KEY POINT YOU'RE MAKING IS THAT WE'LL HAVE TO MOVE BEYOND A MODEL UNDER WHICH WE'RE FUNDING INDIVIDUAL PROJECTS WHICH END UP BEING IN A SENSE PROPRIETARY AND, INSTEAD, CREATE A RESOURCE WHICH IS MULTIPLY AVAILABLE. IN TERMS OF MEETING THE GOAL AND THE METHODS, THERE OBVIOUSLY ARE ISSUES TO CONSIDER BOTH BASED ON EXPERIENCE AND ON --

DR. COUTURE: THE ETHICAL ISSUES AND THE IP ISSUES REALLY DON'T CHANGE BECAUSE IT REALLY JUST REDEFINES -- ONE COULD ARGUE IT JUST REDEFINES WHO THE PI IS FOR THE CREATION OF THE BANK, WHETHER IT'S THE CENTER OR IT'S THE PI. EVERYTHING ELSE STAYS THE SAME.

DR. TAYLOR: THANKS.

DR. TROUNSON: BERNIE, CAN I JUST ASK ONE QUESTION JUST QUICKLY? IF YOU ARE GOING TO HAVE A COMMON STOCK IN A MASTER BANK, I THINK THERE ARE SOME CONCERNS, SAY, FROM A COMPANY'S POINT OF VIEW IS IF THERE'S A FINDING SOMEWHERE ELSE, AN ADVERSE

FINDING SOMEWHERE ELSE, THAT WILL REFLECT UPON THEM. AND THEY WILL HAVE TO DO SOMETHING ABOUT IT. WHEREAS, SO IT MAY HAVE NOTHING TO DO WITH THE WAY THEY'VE TREATED THE CELLS, BUT SOMEBODY ELSE. IS THERE SOME WAY OF MANAGING THIS CONCERN?

DR. COUTURE: YES. I THINK THERE IS. THE FIRST IS, AGAIN, TO GO BACK TO WHAT I SAID IS THIS ISN'T THE PRODUCT. SO THIS IS NOTHING MORE THAN A RAW MATERIAL. SO IF IT TURNS OUT THERE'S A GENETIC ABNORMALITY IN THE CELL, THAT NOT ONLY WILL, IT SHOULD REFLECT ON ALL OTHER TRIALS USING THE CELL WHETHER IT'S FROM THE SAME BANK OR NOT. SO IF IT TURNS OUT H9S HAVE SOME GENETIC DEFECT THAT MAKES THEM VERY UNTENABLE AS A CLINICAL PRODUCT, ANYBODY WORKING WITH H9S IS GOING TO GET A LETTER FROM THE FDA. THAT'S JUST THE WAY IT'S GOING TO BE.

IN THIS PARTICULAR CASE, I PURPOSELY EXCLUDED THE ISSUE OF THE BANKING OF CELL PRODUCTS. I COULD HAVE TAKEN THIS FURTHER AND SAID WE COULD MAKE LARGE LOTS OF CARDIOMYOCYTES EVERYBODY CAN USE, AND THAT'S WHY I DIDN'T RAISE THAT PARTICULAR ISSUE BECAUSE NOW YOU'RE TALKING A CLINICAL PRODUCT THAT GOES IN. AND YOU'RE ABSOLUTELY RIGHT. DIFFERENT COMPANIES, DIFFERENT PARTIES MAY HAVE DIFFERENT DIFFERENTIATION PROCESSES AND MAY HAVE SLIGHT TWISTS

ON HOW THEY MAKE THAT PRODUCT. AND EVEN IF THEY MIGHT BE WILLING, WHICH IS THE CASE IN THE PACT PROGRAM, BY THE WAY, WE'RE PROBABLY GOING TO DO THAT, BUT IT'S ON A VERY SMALL SCALE FOR VERY TRUE, PURE ACADEMIC INVESTIGATORS WITHOUT ANY REALLY CORPORATE INVOLVEMENT.

SO THE ANSWER TO THE QUESTION HERE IS I DON'T THINK THAT REALLY BECOMES A PROBLEM AT THE MASTER CELL BANK STAGE WHEN THE MASTER CELL BANK ISN'T YOUR TYPICAL MASTER CELL BANK. IT'S ACTUALLY ONLY A RAW MATERIAL. SO SOMETHING HAS TO BE DERIVED FROM IT.

DR. ROBERTS: JUST PICKING UP ON THAT, I WONDERED IN THAT PROCESS FROM THE RAW MATERIAL TO THE SUCCESSFUL PRODUCT, WHERE DOES PATENTING COME IN? WHO GETS --

DR. COUTURE: AT EVERY STEP OF THE WAY.

DR. ROBERTS: AT EVERY STEP OF THE WAY.

DR. COUTURE: SO THERE ARE PATENTS THAT SOME HERE MIGHT BE ABLE TO SPEAK TO THAT ARE HELD THAT COVER EMBRYONIC STEM CELLS. THERE ARE ALMOST CERTAINLY GOING TO BE PATENTS ON DIFFERENTIATION PROCESSES, AND THERE ARE VERY LIKELY GOING TO BE PATENTS ON THE USE OF CERTAIN DIFFERENTIATED DERIVED CELL PRODUCTS IN VERY SPECIFIC APPLICATIONS.

DR. ROBERTS: SOME OF IT IS ALREADY PATENTED. WE DON'T KNOW YET EXACTLY WHAT THE PATENT LANDSCAPE WILL LOOK LIKE FOR THE FINISHED PRODUCT BECAUSE I WOULD ASSUME THE EARLY PATENTS WILL HAVE SOME IMPACT ON WHAT CAN BE PATENTED AT THE END.

DR. COUTURE: THAT'S CORRECT. NO. NO. NO. EARLY PATENTS REALLY ONLY HAVE -- THE ONLY IMPACT EARLY PATENTS HAVE IS YOU CAN'T REPATENT SOMETHING THAT'S ALREADY PATENTED. BUT YOU CAN PATENT SOMETHING THAT WOULD BE SUBORDINATE TO AN EXISTING PATENT.

DR. ROBERTS: I GUESS I'M THINKING OF THE WHOLE MYRIAD LAWSUIT GOING ON NOW THAT DOES INVOLVE THE IMPACT OF MYRIAD PATENTING THE BRCA 1 AND 2 GENES ON WHO COULD PATENT OTHER PRODUCTS IN THE FUTURE. AS YOU KNOW, IT'S A BIG CONTROVERSY NOW.

DR. COUTURE: AND I CAN TELL YOU THAT THERE'S CHALLENGES TO THE EXISTING PATENTS OUT THERE AS WELL, AND WE'LL HAVE TO WAIT AND SEE HOW THAT PLAYS OUT OVER TIME. THAT BECOMES MORE OF A MATTER OF NEGOTIATING WITH THE CURRENT PATENT HOLDERS ON HOW LICENSES ARE GOING TO BE DEALT WITH AND RIGHTS TO TRANSFER. I CAN TELL YOU IT'S PROBABLY PUBLIC KNOWLEDGE THAT WE GET THESE CELLS FROM A COMMON SOURCE AS EVERYBODY DOES, AND THOSE TRANSFERS

PRECLUDE THE TRANSFER TO A THIRD PARTY WITHOUT PERMISSION, ETC., ETC.

SO THAT'S FAIR AND REASONABLE. THE OWNER OF A MATERIAL HAS THE RIGHT TO LIMIT AND RESTRICT THOSE. WHAT STANDS TO BE NEGOTIATED COMPLETELY IS JUST HOW SUPPORTIVE THOSE PARTIES WILL BE IN LETTING THESE MASTER CELL BANKS BE USED BY MULTIPLE PARTIES.

DR. ROBERTS: EVEN THOUGH YOU COULD SAY THIS IS A LEGAL IP ISSUE, IT RELATES TO THE ETHICAL ISSUE THAT WAS JUST RAISED ABOUT THE POSSIBILITY FOR ACCESS AND THAT SORT OF THING. I DON'T KNOW HOW MUCH WE'RE GOING TO GET INTO THAT.

DR. COUTURE: WHAT I'M PROPOSING HERE JUST ADDS THE SLIGHTEST LITTLE TWIST TO THE INTELLECTUAL PROPERTY ISSUES IS ALL THE INVESTIGATORS USING THE CELLS INITIALLY FOR THEIR PRECLINICAL WORK LONG BEFORE THEY CAME TO CIRM OR PACT FOR FUNDING HAD TO HAVE RECEIVED THOSE CELL LINES. SO ALL WE'RE REALLY AT THE POINT OF, AND I CAN TELL YOU THAT THE ORGANIZATION THAT CONTROLS THESE IS BEING VERY COOPERATIVE IN WORKING WITH US, AND WE'RE SORTING OUT SOME OF THESE ISSUES, NOT ON A NATIONAL BASIS, BUT ON THE CASE IN POINT FOR US TO BE ABLE TO TRANSFER CELLS THAT WE MAKE ON BEHALF OF SOMEONE, WE HAVE PERMISSION TO HAVE THE CELLS, THEY HAVE THE

PERMISSION TO HAVE THE CELLS. WE'RE JUST REALLY ASKING TO SWAP FROM ONE LAB TO ANOTHER.

I DON'T FORESEE A REAL PROBLEM THERE. THAT DOESN'T ADDRESS LICENSING ISSUES DOWN THE ROAD, PARTICULARLY IF THESE START TO LOOK INTERESTING. AND THAT'S SOMETHING -- BUT THAT'S NOT UNIQUE TO EMBRYONIC STEM CELLS. THAT'S TRUE FOR EVERY FIELD THAT WE WORK WITH FROM ANTIBODIES TO VIRAL VECTORS TO GENES THAT ARE PUT INTO VECTORS, ETC., ETC. IT'S JUST SOMETHING EVERYBODY IN THE FIELD HAS TO DEAL WITH, AND I'M NOT A LAWYER.

DR. ROBERTS: I BASICALLY WANT TO KNOW THE BACKGROUND BECAUSE I THINK IT'S RELEVANT.

DR. COUTURE: I WILL SAY JUST THAT I THINK THE INTELLECTUAL PROPERTY ISSUES FOR OUR PURPOSES KIND OF TO SOME DEGREE OUTWEIGH THE ETHICAL ISSUES OF USING THESE CELLS BECAUSE THAT'S BEEN SOMEWHAT VETTED FOR THESE LINES. AS YOU KNOW, SOME OF THESE VERY LINES ARE ALREADY WORKING THEIR WAY INTO THE CLINIC, SO IT'S WHETHER THERE'S SOCIAL ISSUES THAT NEED TO BE ADDRESSED. OUR JOB IS TO DEAL WITH, MAKE SURE THAT WE'RE ABOVEBOARD IN TERMS OF INFORMED CONSENTS AND REGULATORY AND INTELLECTUAL PROPERTY, AND THE FDA BUYS OFF ON ALL OF THAT.

WE HAVE PRODUCTS THAT ARE APPROACHING THE

CLINIC AS WELL, FETAL-DERIVED TISSUE WHICH HAS THE SAME ISSUES. AND WE WERE JUST TAKEN OFF OF A CLINICAL HOLD THIS WEEK, AS A MATTER OF FACT, FOR OUR CLINICAL TRIAL WITH A FETAL-DERIVED NSC PRODUCT. WE KNOW THAT THE AGENCY CAN WORK WITH LINES THAT HAVE BEEN AROUND FOR A WHILE, DERIVED UNDER SOMEWHAT RESEARCH CONDITIONS, ETC., ETC.

WE KNOW GERON IS GOING INTO THE CLINIC WITH ONE OF THEIR CELL LINES, ONE OF THESE NIH CELL LINES THAT WE'RE TALKING ABOUT, NIH REGISTRY LINES. SO WE KNOW THAT ALL THOSE ISSUES CAN BE ADDRESSED TO GET THESE LINES INTO THE CLINIC. WE DON'T HAVE ANY REAL CONCERNS ABOUT GETTING THESE INTO THE CLINIC AND SUPPORTING THE DISEASE TEAMS THAT HAVE BEEN FUNDED.

CHAIRMAN LO: LET ME JUST SAY SOMETHING. AFTER LUNCH WE'RE GOING TO HAVE A PRESENTATION TO FOLLOW UP ON THE PATENTING IP ACCESS ISSUE, AND IT WILL BE A DIFFERENT MODEL. IT WILL BE A MODEL OF SORT OF MAKING INTELLECTUAL PROPERTY AVAILABLE FOR WIDESPREAD USE AT REASONABLE COST. SO LET'S HOLD OFF ON THE IP DISCUSSION. WE'VE HEARD ABOUT THIS ALTERNATIVE MODEL THAT REALLY COMES OUT OF AGRICULTURAL INNOVATION.

DR. KIESSLING: I HAVE A QUESTION FOR

LARRY. THANK YOU VERY MUCH FOR THAT. I'M NOT FAMILIAR WITH THE NATIONAL HEART, LUNG, BLOOD INSTITUTE PROGRAM YOU'RE TALKING ABOUT. WHAT HAVE THEY ASKED YOU TO DO?

DR. COUTURE: SO THIS IS NATIONAL HEART, LUNG, AND BLOOD INSTITUTE IS CALLED THE PROGRAM FOR ASSISTANCE IN CELLULAR THERAPIES OR PACT, P-A-C-T. IT JUST WENT INTO ITS SECOND VERSION, PACT II. THERE ARE FIVE-YEAR CONTRACTS. IT'S LIKE OTHER GOVERNMENT NIH-FUNDED PROGRAMS, I THROW OUT ACRONYMS, NGBL AND GTRP, VARIOUS PROGRAM WHERE THE NIH THROUGH VARIOUS CENTERS, NHLBI IN THIS CASE, HAS A PROGRAM THAT BASICALLY THEY FUND MANUFACTURING FACILITIES THAT WILL PROVIDE MATERIALS FOR INVESTIGATORS WHO ARE MOVING TECHNOLOGIES FROM THE BENCH INTO THE CLINIC.

DR. KIESSLING: HOW MANY OF THESE HAVE THEY FUNDED, DO YOU KNOW?

DR. COUTURE: THERE ARE FIVE PACT CENTERS NOW. ONLY TWO OF US ARE DOING EMBRYONIC STEM CELL-RELATED STUFF. THERE ARE CELL THERAPIES IN OTHER AREAS. THERE'S A LOT OF T-CELL PRODUCTS, A LOT OF MESENCHYMAL CELL PRODUCTS, A LOT OF PATIENT-SPECIFIC CELLULAR THERAPIES. IT'S ONLY RECENTLY WITH OUR CONTRACT AND WITH WISCONSIN'S

WHERE THEY'VE ACTUALLY MOVED INTO THIS EMBRYONIC STEM CELL FIELD. AND WE'RE ONLY A BIT UNIQUE IN THIS PACT PROGRAM IN THAT THE ONLY THING WE'RE DOING UNDER THE PACT CONTRACT IS EMBRYONIC STEM CELL THERAPIES. WE'RE NOT PRODUCING THE OTHER KINDS OF CELL PRODUCTS.

DR. KIESSLING: SO THERE ARE FIVE EXISTING CELL BANKS?

DR. COUTURE: NO. NO. NO. THESE ARE CENTERS, GMP PRODUCTION FACILITIES, THAT EXIST IN ACADEMIC CENTERS. THERE'S NO BANKS IN THOSE PROGRAMS. MOST OF THE PRODUCTS THAT ARE MADE IN THE OTHER CENTERS, VIRTUALLY ALL OF THE PRODUCTS MADE IN THE OTHER CENTERS ARE PATIENT-SPECIFIC CELLULAR PRODUCTS, AGAIN, LIKE A MESENCHYMAL DERIVED FROM A PATIENT, ENGINEERED OR NOT, AND THEN DELIVERED BACK TO THE PATIENT. SO THERE REALLY ARE NO OTHER BANKS. SO THIS WHOLE NOTION OF BANKING AND SHARING AND FUNDING A CENTER TO PRODUCE THE BANK IS ACTUALLY NEW THIS TIME AROUND.

DR. KIESSLING: THANK YOU.

DR. COUTURE: JUST THE ONLY CAVEAT IS THE PACT CENTER, LIKE CIRM, IS ACTUALLY FUNDING THIS TIME AROUND ALSO, NOT JUST CLINICAL MANUFACTURING, BUT MANUFACTURING TO SUPPORT PRECLINICAL

DEVELOPMENT, WHICH IS WHY WE'RE PRODUCING BANKS RIGHT NOW FOR PRECLINICAL WORK WITH THE ANTICIPATION DOWN THE ROAD OF CLINICAL TRIALS, SIMILAR, ON A SMALLER SCALE, BUT SIMILAR TO WHAT CIRM IS DOING WITH THEIR DISEASE TEAM PROGRAMS.

DR. KIESSLING: IS THE NHLBI THE ONLY NIH INSTITUTE THAT HAS THIS?

DR. COUTURE: CURRENTLY, TO THE BEST OF MY KNOWLEDGE, YEAH, THAT'S THE CASE.

CHAIRMAN LO: OKAY. I'D LIKE TO CALL ON DR. RAYMOND CYPRESS, WHO'S THE CHAIRMAN, PRESIDENT, AND CEO OF AMERICAN TYPE CULTURE COLLECTION AND ALSO THE INTERNATIONAL BIORESOURCES GROUP. HE'S HAD EXTENSIVE EXPERIENCE SORT OF MANAGING AND RUNNING CORPORATE STRUCTURES THAT REALLY PROVIDE A RESOURCE. HE'S ALSO WORKED WITHIN ACADEMIA AS WELL.

SO, DR. CYPRESS, AGAIN, IT WOULD HELP US A LOT TO HEAR FROM YOUR PERSPECTIVE AND EXPERIENCE WHAT ARE THE ETHICAL ISSUES WE SHOULD BE KEEPING IN MIND AS WE THINK ABOUT A CIRM SUPPORTED ISC BANK AS ALAN PROPOSED.

DR. CYPRESS: WELL, THANK YOU VERY MUCH FOR THE INVITATION. THIS IS A FIELD, OF COURSE, THAT THE ATCC HAS BEEN INVOLVED WITH FOR OVER 90 YEARS. AND I THINK I WOULD CAUTION YOU IN THE

BEGINNING DON'T REINVENT THE WHEEL. A LOT OF THESE THINGS HAVE BEEN WORKED OUT SUCCESSFULLY, INCLUDING PARTNERSHIPS WITH LARGE NIH AGENCIES, FOR MANAGEMENT OF LARGE REPOSITORIES, RECENTLY THE BIODEFENSE EMERGING INFECTION REPOSITORY, A $120 MILLION CONTRACT CONSORTIUM WITH ACADEMIA AND INDUSTRY TO MANAGE BIOMATERIAL DISTRIBUTION AND STORAGE.

I WANT TO ALSO SAY THAT HAVING SOME PEOPLE SAY WASHINGTON IS THE EPICENTER OF THE WORLD, IT'S NOT. FAR FROM IT. IT HAS ITS OWN SET OF CUSTOMS AND MORAYS, BUT THERE ARE TWO VERY IMPORTANT TRENDS EMERGING OUT OF THE AGENCIES IN WASHINGTON THAT I THINK YOU SHOULD BE AWARE OF BEFORE I GET INTO THE STORY ABOUT NEEDS AND SOLUTIONS.

THERE ARE TWO HOT TOPICS NOW COMING OUT OF THE AGENCIES. ONE IS BIOMATERIAL SCIENCES, WHICH ACTUALLY STARTED AS BIOSPECIMEN SCIENCES BEING PUSHED BY NCI. ATCC WAS THE CO-INVENTOR OF THE TERM AND WAS PUSHING BIOMATERIAL. BIOSPECIMIN IS A SUBCATEGORY OF BIOMATERIALS SCIENCES. WHAT EXACTLY IS BIOMATERIAL SCIENCES BECAUSE THAT'S WE'RE TALKING ABOUT TODAY? I'LL GIVE YOU THREE EXAMPLES OF AREAS OF INTEREST THAT FALL UNDER THAT.

ONE IS CRYOPRESERVATION, WHICH WE'RE ALL GOING TO HAVE TO ENGAGE WITH IF WE'RE GOING TO DEAL

WITH THIS, A FIELD THAT SCIENCE IS BASED ON 1930 WORK THAT WAS DONE IN THE SEMEN AND BLOOD AND FOOD INDUSTRIES. NOT VERY MUCH PROGRESS HAS BEEN MADE IN CRYOPRESERVATION. IF YOU THINK ABOUT THE FACT THAT WE'RE GOING TO HAVE TO STORE THIS MATERIAL AND SHIP IT, YOU CAN SEE HOW IMPORTANT IT IS.

ANOTHER IS CELL CULTURING, ANOTHER FIELD THAT SORT OF LOST ITS MOMENTUM A LONG TIME AGO IS NOW COMING BACK INTO VOGUE BECAUSE OF THE RENAISSANCE OF CELL BIOLOGY, OF COURSE.

AND THEN, OF COURSE, IS THE WHOLE AREA OF DISTRIBUTION, SUCCESSFUL DISTRIBUTION. YOU DON'T HAVE TO PUT EVERYTHING FROZEN AND SHIP OVER THE WORLD. YOU CAN TAKE DNA AND PUT IT ON A PIECE OF PAPER. SO THERE'S A LOT OF ENGINEERING IN BIOLOGY THAT NEEDS TO COME TOGETHER IN THIS FIELD. AND ANOTHER FIELD THAT'S COMING UP AND YOU'RE HEARING IT OVER AND OVER. WE JUST MET WITH THE FDA AND THEY BROUGHT UP THE TOPIC OF REGULATORY SCIENCES. THIS IS AN INTERESTING TERM. I ASKED THE HIGH LEVEL FDA PERSON WHAT DOES THAT MEAN. HE SAID ANY SCIENCE THAT CONTRIBUTES TO A REGULATOR MAKING A DECISION, REGULATORY SCIENCES. SO YOU HAVE A WHOLE GAMUT OF SCIENCES INVOLVED WITH THAT, BUT YOU ARE GOING TO HEAR A LOT MORE ABOUT IT BECAUSE THE FDA

COMMISSIONER IS VERY, VERY INTERESTED IN STANDARDS, AS WE REVEALED IN A MEETING WE HAD WITH THEM TWO WEEKS AGO WHEN THE ALLIANCE MET WITH DR. HAMBURG.

ANYWAY, I'M GOING TO TALK ABOUT NEEDS AND SOLUTIONS, DEVELOPMENT AND MANAGEMENT OF TOOLS FOR THE FIELD OF REGENERATIVE MEDICINE. I STAND HERE NOT JUST AS A BUSINESS PERSON NOW, BUT AS A FORMER VICE PROVOST FOR RESEARCH AND DEAN OF A GRADUATE SCHOOL AT THE HEALTH CENTER, AND, OF COURSE, A VETERINARIAN, WHICH, AS YOU ALL KNOW, IS THE KINDER, MORE GENTLER HEALTH PROFESSIONAL. ANY PEDIATRICIANS IN THE ROOM? SO I GOT YOU AWAKE.

NEEDS OF THE FIELD, I'M NOT GOING READ IT TO YOU, BUT I THINK I'M GOING TO HIGHLIGHT SOME IMPORTANT THINGS. WE CALL THE BIOMATERIAL PROCESS, WE PUT THIS INTO SOME ENGINEERING DIAGRAM APPROACH. BUT AUTHENTICATION IS THE CENTRAL POINT IN THE FIELD, VALIDATION OF SUCCESSFUL BIOLOGICAL TOOLS DEVELOPED BY EXPERTS IN THE FIELD, A CENTRALIZED RESOURCE -- AND THERE'S THE KEYWORD -- EQUITABLE, CONVENIENT, AND COST-EFFECTIVE AVAILABILITY. EQUAL ACCESS IS THE KEY POINT IN THIS WHOLE SYSTEM. OF COURSE, THAT'S WHAT ATCC HAS BEEN ALL ABOUT.

A BROAD RANGE OF QUALITY BIOLOGICAL TOOLS AND REAGENTS FOR THE LIFE SCIENCE COMMUNITY,

DEVELOPMENT OF WRITTEN CONSENSUS STANDARDS AND AUTHENTICATION METHODS TO PROMOTE BEST PRACTICES IN THE FIELD. I GAVE YOU AN ACCOMPANYING ARTICLE THAT JUST CAME OUT A WEEK AGO IN *NATURE* WHICH TELLS YOU WHAT'S GOING ON IN THE FIELD OF STANDARDIZATION. WE DON'T HAVE ANYTHING IN BIOLOGY LIKE USP. THE USP IS, OF COURSE, THE AGENCY GIVEN THIS AREA IN 1928 IN THE COSMETICS ACT. WE DON'T HAVE ANYTHING -- CLOSEST THING WE HAVE IN THIS IS NIST, AND NIST HAS NOT PUT A LOT OF EMPHASIS ON BIOLOGICAL MATERIAL STANDARDS, ALTHOUGH WE'RE NOW WORKING CLOSELY WITH THEM.

ATCC THREE AND A HALF YEARS AGO BEGAN ITS REAL MOVEMENT INTO THIS FIELD. IT RECEIVED ISO CERTIFICATION 9001:34 AND THEN BECAME AN SDO. SO ATCC IN THE LAST YEAR AND A HALF HAS GONE FROM DE FACTO BUREAU OF STANDARDS OF LIFE SCIENCES TO DU JOUR BUREAU OF STANDARDS OF LIFE SCIENCES. AND THAT'S WHAT THIS ARTICLE IS ALL ABOUT. AND NOW WE HAVE CONSENSUS COMMITTEE GROUPS WORKING ON IT. IF YOU LOOK AT THE GROUP THAT WAS IN THE PUBLICATION, THREE MEMBERS OF THE GROUP COME FROM THE STATE OF CALIFORNIA FROM ALL STRATA OF THE STATE'S ACTIVITIES IN LIFE SCIENCE, INDUSTRY, OKAY, ACADEMIA, AND GOVERNMENT. AND IT'S ALSO INTERESTING THAT THE

FATHER OF THE STANDARDIZATION MOVEMENT PROBABLY IN BIOLOGY WAS A BERKELEY SCIENTIST WHO PASSED AWAY IN 2009. CALIFORNIA HAS HAD A LOT OF INVOLVEMENT AND I HOPE CONTINUES TO HAVE INVOLVEMENT.

DEVELOPMENT OF WRITTEN CONSENSUS STANDARDS AND AUTHENTICATION METHODS TO PROMOTE BEST PRACTICES IN THE FIELD. THE ISSUE OF NOMENCLATURE CAME UP, AND THAT'S PART OF WHAT THESE COMMITTEES WILL BE INVOLVED WITH. REMEMBER WE CAME OUT OF THE FIELD OF MICROBIOLOGY. NOMENCLATURE REALLY STARTED IN THE FIELD OF MICROBIOLOGY WITH THE LINNAEAN SYSTEM OF CLASSIFICATION OF GENUS AND SPECIES. NOW WE'RE FACED WITH A DIFFERENT KIND OF A CLASSIFICATION PROBLEM. WE'RE DEALING WITH CELL BIOLOGY. AND I LIKE TO USE THE FDA APPROACH TO CLASSIFICATION AND NOMENCLATURE. IT IS WHAT IT IS. IT'S NOT CONTAMINATED, AND IT DOES WHAT IT'S SUPPOSED TO DO. OKAY. I SIMPLIFIED IT.

IN MANY, MANY, MANY WAYS THOSE ARE THE THREE CRITERIA FOR SUCCESS GOING FORWARD. NOW, IT IS WHAT IT IS IS A REAL CHALLENGE TO THIS FIELD, AND THIS IS WHERE YOU ARE GOING TO NEED YOUR EXPERTS TO COME IN AND BE ABLE TO AGREE UPON WHAT A CHARACTERISTIC VALIDATED AND AUTHENTICATION CELL LINE IS ALL ABOUT.

AND THEN FINALLY, A PLATFORM OF BIOLOGICAL MATERIALS AND PROCESSES STANDARDS TO UNDERPIN THE REGULATORY PROCESS. OF COURSE, YOU'RE NOT GOING TO GO ANYWHERE IN COMMERCIALIZATION TILL YOU MEET THE STANDARDS OF THE REGULATORY AGENCIES.

IMPORTANCE OF AUTHENTICATION AND BIOLOGICAL TOOL STANDARDIZATION. I JUST HEARD MY BROOKLYN ACCENT CAME THROUGH. IMPORTANCE OF AUTHENTICATION IN BIOLOGICAL TOOL STANDARDIZATION UNDERPINNING OF THE SCIENTIFIC METHOD, REPLICABILITY. I THINK WE FAIL TO REALIZE HOW IMPORTANT REPLICABILITY IS. IT HAS BEEN CENTRAL TO THE SCIENTIFIC METHOD. IT'S THE AREA THAT HAS BEEN UNDER ASSAULT BY THE FACT THAT WE'RE USING MATERIALS THAT ARE INVALID, CONTAMINATED, AND DON'T DO WHAT THEY'RE SUPPOSED TO BE DOING. WE ESTIMATE AS MUCH AS 20, CONSERVATIVELY 30 PERCENT OF MATERIALS USED IN RESEARCH TODAY ARE INVALID. OKAY. THE HELA CELL STORY IS JUST THE TIP OF THE ICEBERG.

IDENTITY, CHARACTERIZATION, VALIDITY OF MATERIALS, VERIFIED CONTAMINATION FREE, VERIFIED FUNCTIONALITY. THOSE ARE THE THREE FDA CRITERIA.

COMPLIANCE WITH APPLICABLE CLINICAL AND REGULATORY GUIDELINES. VALUE AND PREDICTABILITY OF MARKETS FOR DRUG DISCOVERY DEVELOPMENT AND

DIAGNOSTICS.

SO WHAT'S THE BENEFITS OF GOOD BIOLOGICAL MATERIALS MANAGEMENT? I ADDED THIS SLIDE AS MUCH AS ANYTHING TO GIVE YOU THE RATIONALE AND THE JUSTIFICATION FOR THE INVESTMENT IN THIS AREA OF THE PROCESS. FIRST, YOU GET CENTRALIZATION, YOU GET THE ABILITY FOR COMMERCIALIZATION, ACCESSIBILITY TO ALL PARTS THAT NEED TO BE INVOLVED IN THIS, ACCOUNTABILITY, IP MANAGEMENT. AND, AGAIN, I THINK ATCC HAS SET PRETTY MUCH THE SYSTEM IN PLACE FOR THAT. WE HAVE A BLANKET AGREEMENT WITH THE UNIVERSITY OF CALIFORNIA SYSTEM. ATCC TOOK ABOUT THREE YEARS FOR US TO GET THAT DONE. WE ALSO HAVE AN AGREEMENT WITH GERON CORPORATION. THAT TOOK A LITTLE LONGER.

ECONOMIES OF SCALE. LAURIE PRESENTED SOME IMPORTANT INFORMATION ON COSTING. THE WHOLE AREA OF COSTING OF BIOLOGICAL MATERIAL MANAGEMENT IS UNDERDEVELOPED. WE DON'T KNOW WHAT ANYTHING COSTS IN ALL WE'RE DOING IN BIOLOGICAL SCIENCES. WE ATTACKED THAT AREA OURSELVES. IT'S INTERESTING. OUR COSTS COME VERY CLOSE TO WHAT LAURIE PRESENTED THIS MORNING.

BIOMATERIAL INTEGRITY, COMPLIANCE, PRESERVATION, SECURITY, AND DEDICATION. WHAT'S THE

BENEFIT OF STANDARDIZATION? ENSURES USE OF QUALITY BIOMATERIALS IN R&D ACTIVITIES. WE TALKED ABOUT THE PROBLEM OF INVALID MATERIALS.

FOURTH IS EXPERIMENTAL VALIDITY AND REPRODUCIBILITY, WHICH IS CRITICAL TO THE SCIENTIFIC METHOD. ENSURES INTERORGANIZATIONAL PROCESS CONSISTENCY WITHIN THE DISCIPLINE. AND I THINK THE WHOLE WAY OF GOING FORWARD IS GOING TO BE THE CONSORTIUM APPROACH, WHICH IS WHAT YOU'VE DONE HERE WITH CIRM. AND INCREASED ROI ON RESEARCH FUNDING DUE TO THE VALIDITY OF EXPERIMENTAL RESULTS. ACCELERATED R&D PRODUCTIVITY IMPROVES EFFICIENCY IN THE REGULATORY PROCESS. YOU ARE GOING TO HAVE TO PROVE TO FDA THAT IT IS WHAT IT IS, IT'S NOT CONTAMINATED, AND DOES WHAT IT DOES.

THE CONCLUSION: A NATIONAL INFRASTRUCTURE PROVIDING STANDARDIZED TOOLS AND REAGENTS WILL BE REQUIRED TO OPTIMIZE THE GROWTH OF THE FIELD OF REGENERATIVE MEDICINE. I BELIEVE AND I HAVE PROPOSED A STRUCTURE TO DO THAT. THERE ARE INTERESTS IN NIH TO FUND THIS CONSORTIUM CONCEPT THAT I HAVE PROPOSED. AND I WOULD LOOK EAGERLY TO THE PARTICIPATION OF CIRM IN THESE ACTIVITIES IN ORDER TO ENSURE THE SUCCESS AND TO BRING THE BENEFITS THAT YOU HAVE PUT TOGETHER TO THIS POINT TO

THIS PROGRAM. THANK YOU.

CHAIRMAN LO: QUESTIONS FOR DR. CYPRESS? DR. KIESSLING.

DR. KIESSLING: THANK YOU VERY MUCH. DOES THIS MEAN THAT THE ATCC IS NOW WILLING TO ACCEPT EMBRYONIC STEM CELL LINES?

DR. CYPRESS: THE ATCC IS WILLING TO PARTICIPATE IN A PROGRAM WHICH IS A HUB-AND-SPOKE APPROACH TO THIS CONSORTIUM, WHICH WE WILL ACCEPT LINES FOR THE PURPOSE OF STORAGE AND DISTRIBUTION.

DR. KIESSLING: BECAUSE FOR A WHILE THAT WASN'T THE SITUATION, CORRECT?

DR. CYPRESS: YES. SO LET ME EXPLAIN WHY. IT WAS A CHALLENGE. WE WERE LOCATED -- WE ARE LOCATED IN THE STATE OF VIRGINIA, AND STEM CELLS ARE A NO-NO IN THE STATE OF VIRGINIA, PARTICULARLY A NO-NO IN PRINCE WILLIAM COUNTY. ATCC HAS RECENTLY ESTABLISHED A SATELLITE FACILITY IN THE STATE OF MARYLAND HEADED BY SHERRY CHALLBERG, THE FORMER CEO OF MARLIGEN, AND DIRECTED BY WILL RUST, FORMER NOVARTIS LANZA CELL DIRECTOR, WHO IS NOW RAMPING UP OUR STEM CELL AND IPS PROGRAM.

DR. KIESSLING: OKAY. GREAT. THANK YOU.

CHAIRMAN LO: I WANT TO SORT OF SWITCH GEARS HERE AND SORT OF ASK MEMBERS OF THE SWG TO

SORT OF START THINKING ABOUT OUR CHARGE, WHICH IS TO IDENTIFY AND START TO THINK THROUGH ETHICAL ISSUES WITH REGARD TO THE STEM CELL BANK AND ITS SEVERAL DIFFERENT SORT OF MANIFESTATIONS OR PROPOSALS. SO ANYBODY WANT TO START US OFF ON EITHER ISSUES WE HAVEN'T YET IDENTIFIED OR SORT OF PUSHING IT A LITTLE FURTHER ON ISSUES THAT HAVE BEEN MENTIONED, BUT OBVIOUSLY NOT SETTLED IN DETAIL?

DR. KIESSLING: I HAVE ONE COMMENT ABOUT THAT. WHEN YOU'RE THINKING ABOUT CREATING BANKS NOW OF IPS CELLS, THE CONSENT CONSIDERATIONS ARE GOING TO BE VERY SIMILAR TO USING EMBRYOS FOR RESEARCH, RIGHT. AND I THINK THAT THE ANONYMITY ISSUES ARE -- I DON'T KNOW THAT WE'RE -- I THINK NOW THAT WE CAN PROBABLY SEQUENCE EVERYBODY'S GENOMES, I THINK ANONYMIZING CELLS IS GOING TO BE VERY DIFFICULT. I THINK CREATING ANY KIND OF BIOLOGIC THAT YOU'RE NOT GOING TO BE ABLE TO TRACE BACK TO THE PERSON WHO DONATED IT AT SOME TIME IS GOING TO BE REALLY PROBLEMATIC.

SO IT SEEMS TO ME, AS I LISTEN TO THIS, THAT WE HAVEN'T CHANGED THE CONSENTING ISSUES BY GOING FROM HES CELLS TO IPS CELLS.

CHAIRMAN LO: THAT'S A REALLY IMPORTANT ISSUE. GEOFF IS HOPEFULLY HEADING TO THE PODIUM

RATHER THAN OUT FOR A BREAK. I WANT HIM TO REMIND US OF OUR CURRENT STANDARDS WITH REGARD TO DONATING MATERIALS FROM WHICH WE THEN DERIVE PLURIPOTENT LINES BECAUSE OUR REGULATIONS ACTUALLY HAVE CARRIED OVER THE DONATION OF SOMATIC CELLS FOR IPS DERIVATION SIMILAR TO HOW WE -- BUT I THINK ANN'S POINT THAT GIVEN -- I THINK WE HEARD THIS MORNING THE SCIENTIFIC IMPORTANCE OF BEING ABLE TO DO WHOLE GENOME SEQUENCING BOTH ON THE FIBROBLASTS BEFORE YOU DERIVE THE IPS CELLS AND AFTER WE GET THE MASTER IPS LINE, AGAIN, TO MAKE SURE YOU'VE INTRODUCED NO GENETIC ABNORMALITIES.

SO WITH THOSE WHOLE GENOME SEQUENCING RESULTS, IT WILL BE INCREASINGLY POSSIBLE TO GO BACK AND REIDENTIFY FROM OTHER SORT OF DATABASES THAT MATCH NAME TO EITHER WHOLE GENOME SEQUENCING OR SNP'S OR FOR THAT MATTER IF YOU COULD BREAK INTO THE DEPARTMENT OF JUSTICE DATABASE AND LOOK AT THEIR 13 STR'S. THAT IS AN ISSUE. I THINK ALONG WITH THAT, THE CONSENT THAT'S TYPICALLY GIVEN FOR A LOT OF THESE IS FOR RESEARCH OR EVEN STEM CELL RESEARCH AND MAY NOT EXPLICITLY MENTION WHOLE GENOME SEQUENCING. THERE'S A LOT OF ISSUES HERE.

GEOFF, WHY DON'T YOU AT LEAST ANCHOR US IN WHAT OUR CURRENT REGS ARE.

DR. LOMAX: I APOLOGIZE FOR NOT HAVING THE IDEAL SLIDE FOR THIS, BUT HOPEFULLY I CAN TALK YOU THROUGH THIS AND IT WILL BE CLEAR BECAUSE IT REALLY REFLECTS WORK THAT YOU ALL HAVE DONE OVER THE PAST COUPLE OF YEARS. SO LET ME SAY FIRST AND FOREMOST IF A CIRM GRANTEE IS COLLECTING ANY EMBRYO, GAMETE, OR SOMATIC CELL FOR CIRM-FUNDED RESEARCH AND THE PROTOCOL IS DESIGNED TO DEVELOP A PLURIPOTENT PRODUCT, AND PLURIPOTENCY IS AN IMPORTANT POINT BECAUSE IT HINGES ON OUR DEFINITIONS OF A COVERED STEM CELL LINE, IF OUR GRANTEE IS DOING THE PROCUREMENT, THAT'S THE CRITICAL CONDITION, SO THEY'RE USING OUR DIME TO GO OUT AND GET THOSE MATERIALS, THEN OUR EXTENSIVE CONSENT REQUIREMENTS APPLY TO ANY PROCUREMENT.

SO WE DON'T DIFFERENTIATE ON THE SOURCE MATERIAL. WHAT WE LOOK AT IS IF YOU ARE INTENDING TO DERIVE A PLURIPOTENT LINE, OUR CONSENT REQUIREMENTS KICK IN BECAUSE OUR CONSENT REQUIREMENTS WERE DEVELOPED WITH AN EYE TOWARDS THESE ARE THE IMPORTANT THINGS YOU NEED TO TELL SOMEONE WHEN YOU'RE MOVING THAT MATERIAL INTO A PLURIPOTENT STATE.

MS. LANSING: THAT'S WHAT I THOUGHT. JUST TO CLARIFY, WHEN WE STARTED ORIGINALLY, WE HAVE A

STANDARDIZED CONSENT THAT APPLIES TO IPS, EMBRYONIC, TO EVERYTHING, RIGHT?

DR. LOMAX: FOR MATERIALS THAT OUR GRANTEES ARE COLLECTING.

MS. LANSING: THAT'S CORRECT.

DR. LOMAX: WE HAVE THE ABILITY TO IMPOSE THAT CONDITION AS THE FUNDER.

MS. LANSING: IT'S DIFFERENT FOR THINGS THAT WE'RE NOT COLLECTING. SO WE COVERED THIS. AND WE SAW THE FUTURE.

DR. LOMAX: HATS OFF TO YOU ALL.

MS. LANSING: NO. NOT TO ME, BUT TO ALL OF YOU.

DR. LOMAX: WITH THAT SAID, I THINK IT'S IMPORTANT TO UNDERSTAND, AND I THINK, BERNIE, THIS RELATES, BECAUSE ALAN RAISED THIS POINT AND IT'S AN IMPORTANT POINT, THAT THERE ARE MATERIALS THAT CAN COME INTO THE RESEARCH STREAM AND CIRM GRANTEES CAN USE THEM WHERE THE CONSENT MAY NOT MAP ONTO OUR STANDARDS EXACTLY OR THE CONSENT MAY BE NONEXISTENT.

SO LET ME JUST REMIND YOU REALLY WHAT THE FEDERAL -- THIS IS SORT OF A GENERIC VIEW OF FEDERAL POLICY. AND I KNOW THERE'S A NUMBER OF WORKING GROUP MEMBERS WHO ARE VERY WELL VERSED IN THIS, SO FEEL FREE TO INTERRUPT IF MY COMMENTS NEED TO BE

CLARIFIED.

SO UNDER FEDERAL LAW YOU LOOK AT FOR WHAT REASON THIS TISSUE IS BEING OBTAINED. IF IT'S FOR RESEARCH PURPOSES, WHICH IS THE LEFT SIDE OF THAT, THEN IT'S AN INTERVENTION FOR RESEARCH, YOU DO INFORMED CONSENT, AND TYPICALLY THAT GOES PRETTY WELL, ALTHOUGH THERE'S AN UNUSUAL STEP IN HERE WHERE AFTER COLLECTING MATERIALS FOR RESEARCH, IF IT BECOMES DEIDENTIFIED AND THEN GOES -- IT CAN THEN GO INTO RESEARCH. AND THIS DEIDENTIFICATION STEP UNDER FEDERAL LAW, WHAT IT ALLOWS, IT ALLOWS MATERIALS -- THIS IS SORT OF WHAT HARVARD RAN INTO WITH THE HUMAN EMBRYONIC STEM CELL LINES AND THE NIH REGISTRY, IF I'M CORRECT. THOSE STEM CELL LINES WERE DERIVED UNDER A SPECIFIC CONSENT. THEY WERE IDENTIFIABLE FOR THE PERIOD OF TIME IN THE RESEARCH. THE RESEARCH WAS CONCLUDED. THEY WERE THEN DEIDENTIFIED WITH THE IDEA OF MAKING THEM AVAILABLE FOR GENERAL RESEARCH, BUT THEN NIH CAME BACK LATER IN THE REGISTRY AND DECIDED TO REIMPOSE RESTRICTIONS BASED ON THE ORIGINAL CONSENT. I THINK I'M CHARACTERIZING THAT CORRECT.

SO THERE'S THIS DEIDENTIFICATION STAGE UNDER FEDERAL RULES WHICH OFTEN IS USED AND THE MATERIALS COME INTO THE RESEARCH STREAM, BUT THERE

HAVE BEEN QUESTIONS ABOUT SORT OF, I GUESS, THE APPROPRIATENESS OF THAT PHASE FOR STEM CELL RESEARCH.

ON THE OTHER SIDE OF THE SPECTRUM, AND THIS IS, I THINK, THE MORE MAINSTREAM ISSUE WE RUN INTO WITH OUR GRANTEES, YOU CAN HAVE MATERIALS COLLECTED FOR CLINICAL CARE. AND THE FIRST QUESTION BECOMES IS THE TISSUE IDENTIFIABLE. IF IT'S NOT IDENTIFIABLE, IT'S TYPICALLY CHARACTERIZED AS MEDICAL WASTE. MEDICAL WASTE CAN ACTUALLY GO DIRECTLY INTO THE RESEARCH STREAM WITHOUT ANY CONSENT. AND THERE ARE CELL LINES, I SUSPECT SOME OF OUR PANELISTS KNOW THIS BETTER THAN I DO, THERE ARE CELL LINES THAT ARE BANKED THAT CAME THROUGH THIS MEDICAL WASTE PATHWAY WITHOUT CONSENT. AND OUR REGULATIONS DO ALLOW THOSE MATERIALS TO BE USED FOR BASIC RESEARCH. THAT WAS A SET OF THINGS WE DISCUSSED ABOUT TWO YEARS AGO. IT WAS DEIDENTIFIED SOMATIC CELLS THAT COMPLY WITH FEDERAL STANDARDS.

SO WE ALLOW THAT FOR USE IN BASIC RESEARCH. WHERE YOU ALL DREW THE LINE IS THERE'S A PROVISION IN OUR REGULATIONS THAT SAY IF YOU ARE DEVELOPING A CLINICAL PRODUCT WITH THE INTENT TO TRANSPLANT IT TO HUMANS, THERE HAS TO BE CONSENT. SO BY DEFAULT THAT PROVISION SORT OF WOULD

DISQUALIFY MATERIALS PROCURED THROUGH THAT PATHWAY FROM BEING USED BY A CIRM GRANTEE. AND I DON'T SUSPECT THERE ARE GRANTEES TRYING TO USE THIS PATHWAY TO DEVELOP CLINICAL PRODUCTS. CERTAINLY IN THE COMMENTS WE GOT, THAT SEEMED LIKE A REASONABLE PROVISION.

SO YOU ALL HAVE KIND OF DRAWN THE LINE THAT SAID IN BASIC RESEARCH, MATERIALS THAT MEET FEDERAL STANDARDS ARE FINE. FOR CLINICAL RESEARCH YOU NEED TO DO BETTER.

THEN, AGAIN, ON THE FEDERAL SIDE, YOU CAN SEE IF THE MATERIAL IS IDENTIFIABLE, YOU DO NEED TO GET CONSENT. THAT'S SORT OF STANDARD HUMAN SUBJECTS RESEARCH. IF THE DONOR CAN BE IDENTIFIED, THEY NEED TO CONSENT FOR THE USE OF THEIR MATERIAL IN RESEARCH. BUT, AGAIN, IF IT BECOMES DEIDENTIFIED OR YOU DON'T HAVE -- WHAT THERE IS -- EXCUSE ME. THAT "NO" UNDER INFORMED CONSENT, THERE ARE ACTUALLY PROVISIONS UNDER FEDERAL LAW WHICH ACTUALLY I DON'T UNDERSTAND TOO WELL WHERE YOU CAN HAVE EXEMPTIONS FROM INFORMED CONSENT EVEN FOR IDENTIFIABLE MATERIALS. AND, AGAIN, THERE MAY BE PARTICIPANTS ON THE PANEL OR IN THE WORKING GROUP THAT UNDERSTAND THOSE PROVISIONS BETTER THAN I DO.

AND SO JUST TO LET YOU KNOW THAT KIND OF

UNDER THE FEDERAL RULES, IT SORT OF CUTS BOTH WAYS WITH REGARD EVEN TO IDENTIFIABLE MATERIALS THAT ARE OBTAINED IN A CLINICAL CONTEXT.

MS. LANSING: I'M PARTICULARLY INTERESTED. WHEN WE STARTED THIS, WE WERE ALONE, SO TO SPEAK. CALIFORNIA WAS THE ONLY ONE THAT WAS ABLE TO DO THIS RESEARCH BECAUSE OF THE PROPOSITION. AND WE ALL SAID WE ARE GOING TO ERR VERY, VERY, VERY MUCH ON THE SIDE OF CAUTION. AND I STILL THINK THAT'S THE RIGHT PHILOSOPHY TO HAVE. COULD YOU JUST SIMPLY EXPLAIN TO ME WHERE THE FEDERAL LAWS, WHICH NOW HAVE CAUGHT UP, SO TO SPEAK, WHERE THEY'RE STRICTER THAN WE ARE AND WHERE WE'RE STRICTER THAN THEM? I DON'T BELIEVE THEY'RE EVER STRICTER THAN WE ARE.

DR. LOMAX: SPECIFICALLY WITH REGARD TO HUMAN EMBRYONIC STEM CELL LINES? WE'VE POURED OVER THAT PRETTY CAREFULLY, AND I'D SAY AT THIS STAGE THAT THEY'RE SUBSTANTIALLY EQUIVALENT TO KIND OF USE A LAWYERLY TERM BECAUSE, IF YOU LOOK, THE NIH GUIDELINES PRESCRIBE A SET OF CONDITIONS ON THE CONSENT SIDE FOR THOSE EMBRYOS, WHEN THOSE EMBRYOS ARE DONATED TO RESEARCH. THAT CONSENT LANGUAGE MAPS ALMOST IDENTICALLY TO OUR CONSENT REQUIREMENT. SO I THINK IN THE HUMAN EMBRYONIC STEM CELL-SPECIFIC CONTEXT, I WOULD CHARACTERIZE IT AS WE'RE ALL

OPERATING OFF AN EQUIVALENT STANDARD.

MS. LANSING: IPS. IS THERE ANY DIFFERENCE IN ANYTHING ELSE?

DR. LOMAX: AGAIN, THE DIFFERENCE WOULD BE ON THE IPS SIDE WITH SOMATIC CELLS, THAT IF WE'RE FUNDING THE COLLECTION OF THE CELLS AND THE CELLS ARE BEING COLLECTED TO MAKE THEM PLURIPOTENT, THEN WE HAVE A DETAILED SET OF CONSENT STANDARDS. THOSE SAME STANDARDS, THERE ISN'T A FEDERAL EQUIVALENT FOR THOSE.

NOW, IT'S STILL HUMAN SUBJECTS RESEARCH AND THERE WOULD STILL BE INFORMED CONSENT IF SOMEBODY IS GETTING NIH FUNDING AND COLLECTING THOSE CELLS TOMORROW. SO THAT DIFFERENCE MAY NOT BE TERRIBLY IMPORTANT. THEY'RE STILL GOING TO HAVE TO GET INFORMED CONSENT.

WHERE THINGS GET A LITTLE BIT DIFFERENT IS WHEN YOU START DEALING WITH DEIDENTIFIED MATERIALS THAT COME THROUGH THIS SORT OF MEDICAL WASTE AND THOSE SORT OF PROVISIONS.

MS. LANSING: THANK YOU.

CHAIRMAN LO: LET ME ELABORATE A LITTLE BIT. WITH REGARD TO THE CIRM REQUIREMENTS FOR INFORMED CONSENT TO TAKE MATERIALS, TO PROCURE MATERIALS AND THEN TURN THEM INTO PLURIPOTENT STEM

CELLS, OUR REQUIREMENTS FOR CONSENT ARE MORE RIGOROUS AND MORE COMPREHENSIVE THAN THE FEDERAL GUIDELINES. THAT'S SOMETHING WE DID EARLY ON AND, IN FACT, IT WAS PRESENT EVEN IN THE LEGISLATION PRECEDING CIRM. SO CALIFORNIA HAS HAD MORE RIGOROUS CRITERIA FOR WHAT CONSTITUTES INFORMED CONSENT IN THE CONTEXT OF DERIVING PLURIPOTENT MATERIALS.

MS. LANSING: SO THIS IS SOMETHING I WOULD LIKE TO LOOK AT BECAUSE, AS CAUTIOUS AS I HAVE BEEN, I DON'T THINK THAT WE SHOULD -- WE CAN'T DO ANYTHING ABOUT WHAT'S IN THE BILL. WE CAN'T CHANGE THAT. I'M NOT SUGGESTING WE WOULD WANT TO. BUT IF THERE ARE SPECIFIC -- AND I DON'T HAVE THE SOPHISTICATION TO KNOW THAT. BUT IF THERE ARE SPECIFIC AREAS WHERE WE ARE TOUGHER AND, THEREFORE, THE SCIENTISTS ARE BEING HURT, AND THAT'S THE REAL QUESTION, BY OUR RULES BECAUSE WE WERE THERE FIRST, THEN PERHAPS WE SHOULD HAVE THE SAME RULES AS THE FEDERAL GOVERNMENT.

DR. TAYLOR: I THINK ONE OF THE MAJOR CONTRIBUTIONS OF CALIFORNIA, WHICH IS THE LEADER TO THIS AREA, WAS IN TAKING FAIRLY BROAD FEDERAL STANDARDS AND TRANSLATING THEM INTO SOME SPECIFICS, WHICH HELPED GIVE SOME ASSURANCE TO SCIENTISTS ABOUT WHAT A MEANINGFUL AND EFFECTIVE INFORMED CONSENT

WOULD BE IN PRACTICE. AT THAT TIME I THINK THAT LEVEL OF CERTAINTY WAS CRITICAL.

I THINK THIS IS A GREAT DIAGRAM BECAUSE IT SHOWS HOW TIDY WORLDS BREAK DOWN OVER TIME. SO REFERRING BACK TO THE POINT, THE FACT THAT YOU CAN, AT LEAST WITH THE USE OF CROSS-REFERENCE TO PUBLIC DATABASES, HYPOTHETICALLY IDENTIFY ANYBODY FROM DNA, SHOWS THAT THE FIRST -- THERE'S A DISTINCTION BETWEEN IDENTIFIABLE AND DEIDENTIFIABLE, WHICH HAS BEEN SO CRITICAL IN THIS AREA. IT'S STARTING TO BREAK DOWN.

THE GREAT EXAMPLE OF THAT IS WHAT THE NIH ITSELF DID WITH GWAS STUDIES BECAUSE IN THE CONTEXT WHERE THEY HAD FREELY PROVED PREVIOUSLY RESEARCH WITH WAIVED CONSENTS IN DEIDENTIFIED CONTEXTS, THEY SAID YOU'VE GOT TO HAVE FULL CONSENT, WHATEVER THAT MEANS, AND YOU'VE GOT TO HAVE IRB CERTIFICATION, CERTIFICATION, THAT THIS IS ADEQUATE FROM A HUMAN SUBJECT PERSPECTIVE AND IT'S GOT TO BE DEIDENTIFIED AND IT'S GOT TO HAVE ALL THESE EXTRA STEPS TO PROTECT PRIVACY. IN SHORT, WE WANT NOT ONLY THE GILDED LILY, BUT WE'D LIKE PLATINUM, SILVER, AND SO ON TOO. YOU CAN UNDERSTAND THAT IN THE CONTEXT OF THE FEARS AND ALSO THE POTENTIAL OF GWAS STUDIES.

SO THAT PARADIGM IS NOW BREAKING DOWN

BECAUSE OF THE POINT THAT WAS MADE EARLIER. WHAT DO YOU DO WITH THAT PARADIGM? WELL, SOME PEOPLE'S REACTION TO THAT IS TO SAY WE BETTER MAKE SURE THE CONSENT IS REALLY, REALLY, REALLY SPECIFIC. SO I GAVE A TALK NOT SO LONG AGO AT THE AMERICAN SOCIETY FOR HUMAN GENETICS. THERE WERE ACTUALLY 500 GENETICISTS THERE, WHICH IS AMAZING FOR AN ETHICS TALK, I GUESS, AND THEY ALL WERE THERE PRETTY MUCH TALKING ABOUT THE IDEAL COMPLETE CONCEPT.

SO IT WAS INTERESTING TO ASK THEM BY A SHOW OF HANDS, COOL. YOU'VE GOT ALL THESE POINTS IN THE CONTEXT OF GENETICS. HOW MANY OF YOU HAVE READ THE PAPERS ON WHAT STEM CELL ETHICISTS ARE SAYING IS IMPORTANT FOR IN A SENSE APPLIED GENETICS WHEN YOU GO TO TAKE THESE BANKS AND USE SOME OF THESE CELLS TO CREATE IPS CELLS? SO REFERRING TO SOME OF DR. LO'S WORK, FOR EXAMPLE, HOW MANY OF YOU HAVE INCLUDED THE POTENTIAL FOR THESE CELLS TO BE USED TO CREATE GAMETES? GUESS HOW MANY HANDS THERE WERE. NONE.

SO IT WAS VERY CLEAR TO ME THAT THERE WAS A DISCIPLINARY BARRIER BETWEEN PEOPLE WITHIN GENETICS WHO ARE TRYING TO ESTABLISH THE IDEAL PERFECT CONSENT AND THOSE WHO WERE WORKING IN A SENSE IN APPLIED GENETICS AT THE CUTTING EDGE OF

THEIR OWN SET OF STANDARDS. AND SO SHOULD BIOBANKING GENETIC CONSENTS START TO INCLUDE THE KINDS OF THINGS THAT MIGHT WELL INCLUDE FOR APPLIED GENETICS, INCLUDING THE POTENTIAL, THAT PEOPLE SEE IN EMBRYONIC STEM CELLS OR IPS CELLS.

TO ME ONE OF THE FUNDAMENTAL QUESTIONS TO DEAL WITH IS IS THE ETHICAL -- HOW DO YOU RESOLVE THE ETHICAL BALANCE. YOU REFERRED TO THE NEEDS OF SCIENTISTS AND SORT OF ANALYSIS. OBVIOUSLY THAT'S A CRITICAL POINT, BUT I THINK THAT ONE REASON I LIKED DR. TROUNSON'S TALK SO MUCH IS IT POINTS US TO THE FACT THAT THE CUTTING EDGE IS NEARER THAN WE THINK WITH RESPECT TO HOW MULTIPLE CONFLICTING ISSUES ARE GOING TO BE ADDRESSED. THE REALITY IS THERE NEVER WILL BE 100 PERCENT CONSENT. THERE NEVER WILL BE 100 PERCENT CONSENT, ALAS, IN COMMUNITIES THAT ARE USED TO AND HAVE REASONS TO DISTRUST POTENTIAL RESEARCH USES.

SO WHAT DOES THAT MEAN FOR THE JUSTICE OF APPLICATIONS? IS THERE A REBALANCING AROUND CONSENT? IS GETTING THE PERFECT MULTIPAGE, 90-PAGE CONSENT GOING TO GET US THERE? WHAT DOES RIGOROUS MEAN IN THIS CONTEXT? THAT'S THE MOST BIG ETHICAL ISSUE IS HOW PEOPLE THINK THROUGH HOW THESE DEVELOPING ETHICAL APPLICATIONS MAY COMPETE WITH

EACH OTHER AND HARM EACH OTHER.

DR. ISASI: YOU COVER A LOT OF THE TOPICS I WAS GOING TO RAISE, BUT I JUST WANTED TO HIGHLIGHT THE NEED TO REDEFINE OR HAVE A NEW PARADIGM OF HOW WE DEFINE ANONYMIZATION AND IDENTIFIABILITY GIVEN THE POSSIBILITY OF DONOR IDENTIFICATION WITH THE STEM CELL LINES, NOT ONLY WITH THE PUBLIC REGISTRIES AVAILABLE WITH A NUMBER OF GENOTYPIC AND PHENOTYPIC INFORMATION IS AVAILABLE. BUT THIS IS IN THE CONTEXT OF EMBRYONIC STEM CELLS. THERE'S STILL A REMOTE POSSIBILITY OF IDENTIFICATION. IMAGINE THE PROBLEM WITH IPS RESEARCH. AND I KNOW NEXT SESSION WE WILL TALK MORE IN DETAILS ABOUT THAT, AND I WILL LIKE TO TALK ABOUT THE INTERNATIONAL STEM CELL CHARACTERIZATION INITIATIVE WHO IS ABOUT TO PUBLISH A STATEMENT ON DONOR IDENTIFIABILITY AND THE NEED TO REAPPRAISE THE INFORMED CONSENT IS SOMETHING THAT WE SHOULD KEEP IN MIND AND BRING TO THE NEXT SESSION.

CHAIRMAN LO: AND, AGAIN, TO GO BACK TO SHERRY'S ORIGINAL POINT, THIS IS AN ISSUE THAT HAS BEEN DISCUSSED IN THE ETHICS LITERATURE FOR A NUMBER OF YEARS NOW, BUT WHAT'S LACKING ARE GUIDELINES THAT ARE ACTIONABLE AND SPECIFIC SO THAT RESEARCHERS CAN SAY -- SO THE RESEARCHERS CAN SAY THIS IS THE STATE OF THE ART AT THAT TIME. THAT'S A POTENTIAL PLACE

FOR US TO SORT OF GET INVOLVED.

NUMBER OF QUESTIONS OVER HERE.

DR. CYPRESS: I WANT TO GET BACK TO THIS IS CRITICAL. IF WE'RE GOING TO HAVE A CONSORTIUM AND YOU'RE GOING TO HAVE TO HAVE PARTNERS INVOLVED, I'VE RECENTLY BEEN APPROACHED BY TWO MAJOR ORGANIZATIONS WITH HIGH VISIBILITY AND CAPABILITY IN STEM CELLS AND IPS. IN BOTH CASES WE WOULD NOT AGREE TO PARTNER WITH THEM UNLESS THEY INDEMNIFIED US FOR THE PROPER SOURCING OF MATERIALS AND PROPER OWNERSHIP. SO WE'RE GOING TO HAVE TO COME TO GRIPS WITH THIS IN THAT WE'RE GOING TO HAVE TO HAVE A STANDARD TOOL -- I TALK A LOT ABOUT STANDARD TOOLS. WE'RE GOING TO HAVE TO HAVE STANDARD TOOLS THAT DEAL WITH OWNERSHIP AND IDENTIFICATION IF YOU ARE GOING TO HAVE ANY KIND OF APPROACH, DOMESTIC AND INTERNATIONAL. AND THOSE ARE THE TWO 800-POUND ELEPHANTS IN THE ROOM WHEN WE'RE DEALING WITH THIS IS THE ISSUE OF OWNERSHIP AND THE ISSUE OF INDEMNIFICATION.

SO I THINK THIS IS A VERY IMPORTANT CHALLENGE TO THIS ORGANIZATION.

DR. ROBERTS: I JUST WANTED TO REVISIT AGAIN THE ETHICAL ISSUES SURROUNDING DIVERSITY THAT CAME UP EARLIER AND TO MAKE SURE THAT WE MAKE A

DISTINCTION BETWEEN WANTING TO RECRUIT A DIVERSE POOL OF PEOPLE AS DONORS FOR THE SCIENTIFIC AND SOCIAL REASONS. I THINK THEY'RE INTERSECTING. I DON'T BELIEVE THAT IT'S TWO DISCRETE KINDS OF CONCERNS. BUT TO HAVE A DIVERSE POOL TO ENSURE THAT PEOPLE ARE REPRESENTED, BUT THAT DOESN'T ANSWER THE QUESTION OF CATEGORIZATION OF MATERIALS THROUGHOUT THE PROCESS. I THINK THERE IS A DANGER IN CATEGORIZING MATERIALS BY RACE THAT WE HAVE TO BE AWARE OF.

SO WE COULD -- I'LL JUST EXPRESS MY OPINION IS THAT IT'S GOOD TO HAVE DIVERSE RECRUITMENT OF DONORS. I THINK THAT THERE ARE TERRIBLE DANGERS IN CATEGORIZING MATERIALS AND PATIENTS AND PRODUCTS BY RACE, AND WE SHOULD BE CAREFUL OF THAT AS WE MOVE ALONG.

ALSO, THIS ISSUE OF DIVERSITY IS INTERSECTED WITH THE INFORMED CONSENT ISSUE AND I THINK MAKES INFORMED CONSENT EVEN MORE IMPORTANT BECAUSE OF A HISTORY OF EXPLOITATION AND ABUSE OF GROUPS, ESPECIALLY PEOPLE OF COLOR, IN THIS COUNTRY. BUT WE SHOULD ALSO MAKE SURE THAT INFORMED CONSENT ISN'T SEEN AS A SOLUTION TO THE ETHICAL ISSUES BECAUSE YOU DON'T WANT TO APPROACH IT AS, WELL, WE CAN CONTINUE TO DO THINGS AS WE HAVE AS LONG AS WE

GET PEOPLE'S CONSENT. THE CONSENT DOESN'T -- IN OTHER WORDS, THE CONSENT SHOULDN'T BE A WAY OF GETTING AGREEMENT TO A PROCESS THAT MAY BE UNETHICAL IN OTHER WAYS. IT DOESN'T ANSWER ALL THE QUESTIONS.

MS. LANSING: SO I KNOW WHY OBVIOUSLY YOU'RE CONCERNED WITH THIS. I REALLY RESPECT IT. AND I WOULD BE VERY CONCERNED EXCEPT FOR THE FACT THAT -- I'M A LAYPERSON, SO I'M GOING TO ASK THE QUESTION. AS A CANCER ADVOCATE, THE BRCA GENE IS SAVING LIVES IN A PREVENTIVE WAY IF YOU CHOOSE TO BE DIAGNOSED FOR IT AND WHATEVER. SO MY QUESTION IS WOULD THAT -- I UNDERSTAND. WOULD THAT RESEARCH HAVE HAPPENED IF IT WASN'T, AND I DON'T KNOW THE ANSWER TO THIS, THAT'S WHY I'M ASKING THE PANEL, WOULD THAT RESEARCH HAVE HAPPENED IF IT WASN'T SEGMENTED TO ASHKENAZI JEWS? AND SO YOU ARE SAYING, NO, IT WOULD NOT.

SO AS A JEWISH PERSON, I COULD SAY, WELL, THAT'S RACIAL PROFILING. THEY TOOK A DISEASE. THEY MADE IT ASHKENAZI JEWS. I HAPPEN TO BE FROM AN ASHKENAZI JEWISH FAMILY, AND I AM SO GRATEFUL FOR THAT RESEARCH. AND SO I KNOW MANY, I CAN'T SAY MILLIONS BECAUSE I DON'T KNOW MILLIONS OF PEOPLE, BUT I KNOW PROBABLY HUNDREDS OF WOMEN THAT ARE BENEFITING FROM THIS TESTING. AND IT'S NO DOUBT

SAVED LIVES.

ACTUALLY I JUST WOULD LIKE TO -- THAT'S THE ONLY EXAMPLE I CAN GIVE BECAUSE AS A CANCER ADVOCATE, THAT'S ALL I KNOW ABOUT, BUT I SEE IN THE FUTURE OTHER POTENTIALS. AND TO THINK -- SEE, I DON'T KNOW -- I KNOW THE CONCERNS, SO I DON'T WANT THIS TO BE ABUSED. SO I'M JUST SPEAKING JEWISH, ASHKENAZI JEW, THAT I'M GRATEFUL THAT HAPPENED. SO HOW DID IT HAPPEN?

DR. LORING: IT HAPPENED BECAUSE PEOPLE HAD LIMITED RESOURCES, AND SO THEY FOCUSED DOWN ON SURROGATES FOR PEOPLE WITH DISEASE. SO THE OBSERVATION WAS THAT ASHKENAZI JEWS HAD BREAST CANCER IN AN APPARENT INHERITED WAY MORE OFTEN THAN OTHER GROUPS, WHATEVER GROUP IT IS. AND SO WITH LIMITED RESOURCES, YOU FOCUS ON THE NARROW RANGE OF PEOPLE THAT YOU KNOW YOU CAN GET AN ANSWER FROM.

SO I WANTED TO ADDRESS YOUR QUESTION THOUGH. BECAUSE RACE IS NOT REALLY THE BASIS OF THIS, AND SKIN COLOR IS NOT THE BASIS OF THIS. ETHNIC DIVERSITY IS REALLY A SURROGATE FOR GENOMIC DIVERSITY. AND WHAT WE'RE REALLY CONCERNED WITH IS WHETHER CELLS FROM YOU CAN BE TRANSPLANTED TO ME. AND THAT HAS TO DO, EVERYTHING TO DO WITH THE ACTUAL MOLECULES ON THE SURFACE OF CELLS WHICH ARE

PREDICTABLE BASED ON ETHNICITY. SO IT WOULD BE NICE FOR YOU TO HAVE SOMEONE WHO WAS ETHNICALLY SIMILAR TO YOU FOR A TRANSPLANT.

SO THE OTHER THING IS, HANG ON, FOR THE DRUG STUDIES, THE THINGS THAT I'M INTERESTED IN, THERE ARE DIFFERENT ENZYMES, DIFFERENT PROTEINS MADE THAT WILL METABOLIZE DRUGS DIFFERENTLY. SO THAT'S WHY SOME DRUGS ARE TOXIC TO CERTAIN PEOPLE. THERE'S HIV DRUGS THAT HAVE A VERY HIGH RATE OF LIVER FAILURE IN PEOPLE OF AFRICAN ANCESTRY. SO IF YOU CAN DETERMINE THE ACTUAL BASIS OF WHATEVER THE PROBLEM IS, IN THIS CASE DRUG ADVERSE EFFECTS, THEN THE RACE REALLY HAS NOTHING TO DO WITH IT. IT ALL COMES DOWN TO YOUR GENETICS AND WHETHER THIS IS APPROPRIATE FOR YOU.

BUT THE TROUBLE IS THAT ON THE SURFACE OUR ANCESTRY IS WHAT DEFINES US. IT'S JUST SORT OF A VISUAL WAY OF KNOWING WHETHER YOUR HISTORY IS LIKELY TO BE LIKE THIS. SO LOTS OF US ARE INCREDIBLY MIXED, AND SO I DON'T KNOW WHETHER I'M EASTERN EUROPEAN OR ENGLISH. THAT MAKES A HUGE DIFFERENCE. SO DO YOU UNDERSTAND WHAT I MEAN?

DR. ROBERTS: YEAH, BUT I DISAGREE WITH A LOT OF IT. I JUST HAVE TO BE HONEST. IN TERMS -- I'LL TELL YOU WHY, BUT I FIRST WANT TO -- I DON'T

MEAN TO BE RUDE AT ALL.

MS. LANSING: IT'S A VERY IMPORTANT ISSUE.

DR. ROBERTS: I THINK IT'S EXTREMELY IMPORTANT. SO IN TERMS OF YOUR POINT, SHERRY, YES, IT'S TRUE THAT ASHKENAZI JEWISH WOMEN HAVE A HIGHER RATE OF THESE BRCA GENES, BUT THEY'RE NOT THE ONLY WOMEN WHO HAVE IT. SO IF WE BELIEVE OR HAVE PRODUCTS OR TESTING OR DIAGNOSES THAT'S BASED ON RACE, YOU ARE GOING TO END UP MISSING THE GENE IN OTHER WOMEN. FOR EXAMPLE, THERE'S STUDIES THAT SHOW THAT BLACK WOMEN WHO HAVE THE BRCA 1 AND 2 GENE ARE NOT DIRECTED TO GENETIC COUNSELING. THEY DON'T GET THE TREATMENT THAT THEY SHOULD GET BECAUSE DOCTORS HAVE A RACIAL CATEGORIZATION IN THEIR MINDS.

SO THAT'S WHY I'M SAYING --

MS. LANSING: THIS IS GREAT. GREAT CONVERSATION BECAUSE -- AND, AGAIN, AS A JEWISH WOMAN, THE IDEA OF SEGMENTING A GROUP OF SOCIETY IS ACTUALLY VERY SCARY AND ABHORRENT TO ME EXCEPT WHEN I HEAR THIS. SO WHAT INTERESTS ME, AGAIN, I NEED TO HEAR FROM THE SCIENTIST, SO THEY DID THIS SUBSET, THEY FOUND A GENE THAT WAS IN THIS SUBSET, WHICH YOU'RE NOW SAYING, AND I AGREE, APPLIES TO A LOT OF THE OTHER PEOPLE. MY QUESTION AND I GUESS THE ANSWER WAS IF THEY HADN'T DONE THIS SUBSET, THEY

WOULDN'T HAVE FOUND THE GENE. NOW EVERYBODY SHOULD GET TESTED FOR IT, AND EVERYBODY SHOULD BE TREATED THE SAME WAY.

DR. ROBERTS: THAT'S WHAT I SAID, THAT WE COULD AT SOME POINT PERHAPS IN TERMS OF RECRUITMENT HAVE THIS DIVERSE GENE POOL OR CELL LINE POOL, YOU WOULD WANT TO TAKE RACE AND ETHNICITY INTO ACCOUNT, BUT IT SHOULD NOT BE TAKEN INTO ACCOUNT THROUGHOUT THE PROCESS. WE DON'T WANT TO CATEGORIZE PEOPLE THROUGHOUT.

MS. LANSING: I AGREE. WE'RE IN AGREEMENT.

DR. ROBERTS: I JUST WANT TO RESPOND TO THE ANCESTRY ISSUE. SO, YES, ANCESTRY -- IT'S TRUE THAT ANCESTRY CAN HELP TO PREDICT WHO HAS A GREATER LIKELIHOOD OF HAVING A CERTAIN GENE VARIANT, BUT IT DOESN'T TELL YOU FOR SURE. AND SO, AGAIN, THAT'S MY POINT IS THAT THE ONLY WAY WE KNOW WHETHER YOU AND I SHOULD GET THE SAME PRODUCT OR NOT IS BY LOOKING AT OUR GENES, WHICH WE SHOULD BE ABLE TO DO NOW. SO IT WOULDN'T MAKE SENSE TO SAY BECAUSE I'M BLACK AND YOU'RE WHITE, WE MAY HAVE EXACTLY THE SAME REACTION, AND SO, AGAIN, THAT'S JUST MY POINT, THAT RACE CAN BE -- IS EXTREMELY AN UNSCIENTIFIC WAY OF MAKING CERTAIN DETERMINATIONS. ACTUALLY LOOKING AT ME, YOU

HAVE NO IDEA WHAT MY ANCESTRY IS.

DR. LORING: YOU MAY BE HALF CHINESE OR THREE-QUARTERS CHINESE.

DR. ROBERTS: EXACTLY. I DON'T WANT TO GO INTO IT, BUT I HAPPEN TO BE MUCH CLOSER IN ANCESTRY TO YOU THAN YOU WOULD THINK.

DR. LORING: THAT'S WHY I DIDN'T WANT TO ELIMINATE THAT AS A POSSIBILITY. I COULD BE A WALKING KIDNEY DONOR FOR YOU.

DR. ROBERTS: THAT'S MY POINT. WHY NOT?

DR. LORING: NO REASON.

DR. ROBERTS: OKAY.

DR. LORING: SO LET ME JUST CLARIFY THIS ONE MORE TIME FOR YOU BECAUSE I AM CONCERNED ABOUT THIS. I HAVE A REALLY DIVERSE GROUP IN MY LAB, INCLUDING PEOPLE WHO ARE AFRICAN AFRICAN-AMERICAN, AND SO THIS IS THE KIND OF THING WE TALK ABOUT ALL THE TIME. AND I THINK THE AFRICAN-AMERICAN PEOPLE ARE JUSTIFIABLY SUSPICIOUS OF THE MEDICAL SYSTEM BECAUSE THEY'VE BEEN TAKEN ADVANTAGE OF OR NOT EDUCATED IN THE PAST.

NOW, WHAT WE'RE SUGGESTING IS TO CHANGE THAT. SO THE DOCTOR YOU GO TO WILL SAY YOU HAVE A HIGHER PROBABILITY OF X, BUT WE'RE GOING TO TEST YOU FOR X, Y, AND Z BECAUSE IT'S A PRETTY HIGH RISK FOR

EVERYBODY. SO THAT BECOMES RACE NEUTRAL. I WANT TO SAY THIS ONE MORE TIME. ETHNICITY IS A SURROGATE FOR GENOMIC DIVERSITY. IT IS NOT ACCURATE, IT'S NOT A ONE-TO-ONE RELATIONSHIP. SO IF I HAVE SOMEONE WHO COMES STRAIGHT FROM NIGERIA, THERE IS A HIGH PROBABILITY THAT I CAN PREDICT WHICH ENZYMES THEY HAVE BECAUSE THAT RUNS VERY CLOSELY WHEN PEOPLE ARE NOT OF MIXED RACE.

YOU'RE RIGHT. WHEN PEOPLE BECOME OF MIXED RACE, AND LOTS OF US WHO LOOK EUROPEAN ARE ACTUALLY VERY, VERY DIVERSE, THEN YOU HAVE TO IGNORE ALL THOSE THINGS. IT'S A SURROGATE. IT'S ALSO A REPLACEMENT FOR FAMILY HISTORY BECAUSE THE ASHKENAZI JEWS, THE REASON WHY PEOPLE KNEW WAS BECAUSE THEY SAID DID YOUR MOTHER GET BREAST CANCER, DID YOUR GRANDMOTHER GET BREAST CANCER, AND THEY FOUND THERE WAS A CERTAIN GROUP OF PEOPLE FOR WHICH THAT WAS TRUE.

THIS IS A SOAPBOX FOR ME. I THINK GENETIC TESTING SHOULD BE INEXPENSIVE, WIDELY AVAILABLE, AND APPLIED IN DOCTOR'S OFFICES. AMEN.

DR. ROBERTS: I AGREE THAT THE GENETIC TEST IS BETTER THAN THE RACIAL SURROGATE, WHICH IS OFTEN WRONG.

DR. ROBSON: JUST TO SORT OF COME AT THIS

ISSUE FROM A SLIGHTLY DIFFERENT DIRECTION, I WAS AT A MEETING RECENTLY AND I WAS SITTING NEXT TO A REPRESENTATIVE FROM A COMPANY THAT DOES GENETIC TESTING AND SCREENING AND TRYING TO DO IT AT LOW COST. THEY'VE GOTTEN INVOLVED WITH SOME PROJECTS WHERE THEY'RE ACTUALLY GETTING GENETIC SAMPLES FROM PATIENTS WHO HAVE PARKINSON'S DISEASE, FOR EXAMPLE, HAD 2,000 PATIENTS, AND THEN THEY CAN DO THE GENETICS. THEN THEY CAN DO THE INFORMATICS AND TRY TO SEE IF THEY CAN FIND GENETIC PROFILES THAT CORRESPOND WITH THE DISEASE.

AND I ASKED HER IF THEY TOOK, WHEN THEY WERE COLLECTING SAMPLES, IF THEY TOOK -- ASKED QUESTIONS ABOUT ETHNIC ORIGIN OR ANYTHING. AND SHE SAID WE DON'T HAVE TO. WE CAN JUST DO THAT POST HOC AFTER WE DO THE GENETIC SCREEN. SO I JUST THOUGHT THAT WAS SORT OF INTERESTING. IT'S COMING AT IT FROM A DIFFERENT PERSPECTIVE, BUT THEY COULD TAKE YOUR GENES AND THEY COULD FIND OUT WHAT YOUR MIX IS, AND THEN THEY COULD TALK TO YOU AND PROBABLY FIND OUT IT'S WHAT YOU WOULD REPORT.

DR. LORING: I'LL JUST FOLLOW UP ON THAT, BUT THAT ETHNICITY STUDY THAT I TOLD YOU ABOUT THAT WE PUBLISHED RECENTLY, WE HAD NO IDEA WHAT THE ORIGIN OF THOSE EMBRYONIC STEM CELLS WAS. WE

DETERMINED IT FROM THEIR GENOTYPE. IT'S VERY EASY TO DO.

DR. PETERS: I LIKE DOROTHY'S WORD CATEGORIZATION. WHERE ARE WE GOING TO START? AND YOUR COMMENT WITH REGARD TO THE GENOME COMES FIRST AND THEN YOU CAN DRAW CORRELATIONS PERHAPS WITH ETHNICITY. SO I LIKE THE WORD "CATEGORIZATION." IF IT COULD BE A GENOMIC CATEGORIZATION, THEN, YEAH, THERE WILL BE HIGHER AND LOWER CORRELATIONS WITH VARIOUS ETHNIC BACKGROUNDS, BUT THAT WON'T BE THE DEFINING CATEGORY.

CHAIRMAN LO: I'VE JUST BEEN PASSED A NOTE SAYING OUR FOOD IS READY. I THINK THIS HAS BEEN A VERY IMPORTANT DISCUSSION. IT'S SOMETHING WE'VE GOT TO ADDRESS BECAUSE CALIFORNIA IS SUCH A WONDERFULLY DIVERSE STATE, AND THIS IS A PUBLIC PROGRAM.

I JUST WANT TO SORT OF ADD A LITTLE BIT OF HISTORICAL CONTEXT TO WHAT SHERRY WAS TALKING ABOUT SO THAT THE STORY OF THE BRCA 1 DISCOVERIES IN THE CONTEXT OF ASHKENAZI JEWISH COMMUNITIES REALLY HAS A HISTORICAL AND CULTURAL CONTEXT. SO IN THE JEWISH COMMUNITY THERE HAD ALREADY BEEN A LOT OF STUDIES WITH REGARD TO TAY-SACHS SCREENING ACTUALLY IN SAN DIEGO WITH MICHAEL KABE (PHONETIC). AND THEY SPENT A LOT OF TIME GOING TO THE COMMUNITY AND SAYING,

LOOK, THIS IS WHAT WE'RE PROPOSING TO DO. THERE ARE SOME REAL CONCERNS WE HAVE ABOUT WILL PEOPLE WHO WE IDENTIFY AS BEING CARRIERS BE UNMARRIAGEABLE, FOR EXAMPLE. AND SO THERE'S LOT OF COMMUNICATION BOTH ON THE COMMUNITY LEVEL AND WITH INDIVIDUAL SCREENING.

WHEN BRCA BECAME POSSIBLE TO DO, AGAIN, RESEARCHERS AT DIFFERENT SITES WENT TO THE COMMUNITY AND THEY WENT TO SYNAGOGUES, IT WAS SPLIT. THERE ARE SOME CITIES WHERE THE SYNAGOGUES SAID, YES, WE WILL HELP YOU DO THIS, WE WILL FACILITATE IT, AND OTHER PLACES WHERE THE DISCUSSION WENT THE OTHER WAY AND SAID, NO, WE DON'T WANT TO GET INVOLVED WITH THIS RESEARCH. WE CAN SEE THE BENEFITS. SO I THINK IT'S THAT NOTION OF IF WE HAVE AN IDEA, WE HAVE TO GO TO THE PEOPLE WE'RE ASKING TO PARTICIPATE IN THIS RESEARCH, REALLY EXPLAIN IT TO THEM IN A WAY THEY CAN UNDERSTAND, AND TRY AND DO IT IN A WAY THAT THEY WANT TO PARTICIPATE BECAUSE WHAT CONCERNS THEY HAD WERE ADDRESSED IN THE WAY IT WAS SET UP. I THINK THAT'S A CHALLENGE THAT WE'RE GOING TO HAVE TO DEAL WITH.

MS. LANSING: CAN I JUST THEN PUT A LITTLE BUTTON ON THAT HAVING BEEN INVOLVED IN THAT AS A PATIENT ADVOCATE? THERE WAS A TREMENDOUS FEAR THAT

THE INSURANCE COMPANIES WOULD STOP YOUR INSURANCE. AND, IN FACT, THEREFORE, THE TESTING WAS DONE IN A HIGHLY CONFIDENTIAL MANNER. AND I THINK ONLY RECENTLY DID WE GET A LAW THAT SAID THAT THEY COULDN'T DISCRIMINATE AGAINST YOU BECAUSE INITIALLY THEY COULD. AND I KNOW THAT THE DOCTORS WERE WONDERFUL. MAYBE I SHOULDN'T SAY THIS PUBLICLY. I THINK THEY WERE WONDERFUL. FEAR OF THE INSURANCE COMPANY, THE TESTINGS WERE DONE ANONYMOUSLY. IT WENT INTO A PRIVACY.

I THINK AT LEAST ONE OF THE STRONGEST ADVOCACY GROUPS IN AMERICAN IS WOMEN WITH BREAST CANCER. AND I THINK MOST OF THEM, I CAN'T SPEAK FOR ALL, BUT ALL OF THE ONES THAT I CAME CONTACT WITH DURING THIS PROCESS TEN YEARS AGO REALLY WANTED THE INFORMATION BECAUSE THEY FELT THAT ANY INFORMATION THAT COULD PREVENT THE DISEASE WAS WORTH ANYTHING. THEY JUST DIDN'T WANT THE PATIENT OR THE PERSON WHO WAS BEING TESTED TO LOSE THEIR INSURANCE.

THEN THERE WAS TREMENDOUS COUNSELING AFTER YOU WERE TESTED. I WAS ONE OF THE PEOPLE THAT WAS TESTED BECAUSE MY MOTHER HAD DIED OF OVARIAN CANCER. AND THERE WERE CENTERS SET UP TO TEST YOU, TO GIVE YOU INFORMATION BEFORE YOU GOT THE TEST, WHAT THE ISSUES YOU MIGHT FACE, TO GIVE YOU INFORMATION AFTER

YOU GOT THE TEST. AND SO MANY OF MY FRIENDS HAVE GONE THROUGH THIS. AS I SAID, IT HAS SAVED LIVES. THERE'S JUST NO DOUBT ABOUT IT. AND THE CHOICE WAS ALWAYS PERSONAL, AND IT WAS ALWAYS PRIVATE UNTIL RECENTLY WHEN THERE WAS NO NEED.

SO I GUESS WHAT I'M SAYING IS I THINK WE'RE IN A HUNDRED PERCENT AGREEMENT. THERE ARE MEN THAT GET BREAST CANCER, AND IT IS THOUGHT OF AS WOMEN'S DISEASE. THERE ARE NON-JEWISH PEOPLE THAT CARRY THE BRCA GENE, AND IT IS THOUGHT OF AS A, QUOTE, JEWISH WOMAN'S DISEASE. WE MUST BREAK DOWN THOSE STEREOTYPES. THAT IS OUR MORAL MISSION. BUT WE MUST ALLOW THE SCIENTISTS TO FIND OUT WHAT CARRIERS THERE ARE TO PREVENT THE DISEASE. I THINK ACTUALLY THIS HAS BEEN A GREAT DISCUSSION, AND I THINK WE'VE ACTUALLY COME, I THINK, TO A CONCLUSION ON THIS.

CHAIRMAN LO: LET'S BREAK FOR LUNCH, WHICH IS OUT THE HALL TO THE LEFT. LET'S COME BACK IN 45 MINUTES BECAUSE WE HAVE A FULL AGENDA.

(A RECESS WAS TAKEN.)

CHAIRMAN LO: WHY DON'T WE GO AHEAD AND GET STARTED. LET'S ASK THE SWG TO RECONVENE. OKAY. WHY DON'T WE GO AHEAD AND RECONVENE. I THOUGHT WE HAD A VERY GOOD DISCUSSION THIS MORNING. WE STILL

HAVE A LOT OF THINGS WE'D LIKE TO ACCOMPLISH. LET ME TRY AND FIRST JUST AS A TIMEKEEPER SAY WHAT I'D LIKE TO TRY AND DO.

WE HAVE TWO GUESTS WHO HAVE A LOT OF EXPERIENCE WITH INTELLECTUAL PROPERTY AND SORT OF SHARING OF MATERIALS WITH OTHER RESEARCHERS. AND I WAS THINKING WE SHOULD TURN TO THAT FIRST SO THE SWG CAN LEARN ABOUT THOSE ISSUES. THEN AT AROUND 2:30 I'D LIKE TO KIND OF SWITCH GEARS. SHERRY ACTUALLY HAS TO LEAVE AROUND THREE. I WANT TO SPEND SOME TIME AS A COMMITTEE THINKING ABOUT WHAT OUR NEXT STEPS ARE IN TERMS OF HOW TO FOLLOW UP ON THIS WORKSHOP WITH PARTICULAR REGARD TO GIVING ADVICE TO ALAN AND TO CIRM IN GENERAL.

AND THEN I THINK THERE'S SOME ISSUES THAT WE SORT OF TOUCHED ON THIS MORNING, WE MENTIONED THIS MORNING AND DIDN'T REALLY HAVE A CHANCE TO DISCUSS IN MORE DEPTH. I THINK WE SHOULD HAVE SOME TIME LATER IN THE AFTERNOON TO SORT OF SEE WHAT ISSUES WE WANT TO DO A LITTLE MORE IN-DEPTH DISCUSSION ON.

BUT I WANT TO START BY CALLING ON DR. GREGORY GRAFF, WHO IS AN ASSISTANT PROFESSOR OF THE ECONOMICS OF INNOVATION AND ENTREPRENEURSHIP AT COLORADO STATE UNIVERSITY. AND HE WAS INVOLVED IN A

VERY INTERESTING PROJECT CALLED THE PUBLIC INTELLECTUAL PROPERTY RESOURCE FOR AGRICULTURE, WHICH WAS AN INTERNATIONAL CONSORTIUM THAT WAS MANAGING INTELLECTUAL PROPERTY WITH REGARD TO GLOBAL AGRICULTURE. SO I'M GOING TO ASK HIM TO SPEAK.

AND THEN DR. ERIK FORSBERG FROM WICELL IS ALSO HERE, AND OBVIOUSLY HE AND HIS GROUP HAS HAD A LOT OF EXPERIENCE WITH IP ISSUES AND CELL BANKING AND DISTRIBUTION OF TISSUE. I'M GOING TO ASK HIM IF HE'D LIKE TO MAKE SOME COMMENTS.

SO I DON'T KNOW IF ANY OF OUR COLLEAGUES ON THE PHONE HAVE REJOINED US AFTER LUNCH. THEY HAD TROUBLE THIS MORNING FIGURING OUT WHO WAS SPEAKING AND CORRELATING SLIDES WITH THE SPEAKER. SO THE FIRST SPEAKER IS GOING TO BE DR. GRAFF, AND I THINK HIS SLIDES WERE ACTUALLY CIRCULATED AS E-MAILS. SO JANET AND ROB ARE HERE, THAT'S OUR FIRST SPEAKER. AND THEN I WILL TRY AND DO A BETTER JOB IN THE OPEN DISCUSSION CALLING ON PEOPLE BY NAME RATHER THAN FIRST NAME OR JUST POINT.

DR. GRAFF, THANKS VERY MUCH. AND, AGAIN, WE LOOK FORWARD TO HEARING FROM YOU KIND OF WHAT ARE THE ETHICAL ISSUES WE SHOULD BE KEEPING IN MIND AS WE SORT OF HEAR ABOUT YOUR WORK IN AGRICULTURE AND TRY TO APPLY IT TO STEM CELLS.

DR. GRAFF: ABSOLUTELY. AND IT'S A REAL HONOR AND PRIVILEGE TO BE HERE. THANK YOU, DR. LO. THANK YOU TO THE CHAIRS AND PARTICULARLY THANK YOU TO GEOFF LOMAX FOR THE INVITATION TO JOIN YOU TODAY.

AND I KNOW WHAT YOU'RE THINKING. INTELLECTUAL PROPERTY IMMEDIATELY FOLLOWING LUNCH SOUNDS LIKE A LICENSE TO NAP. SO MY JOB IS TO PREVENT YOUR NAP. AND BELIEVE ME, I TAKE MY JOB QUITE SERIOUSLY. SO WHAT I WOULD LIKE TO DO HERE IS KIND OF IN THREE PARTS WITH THE EMPHASIS ON THE FIRST, AND WE'LL SEE HOW THINGS UNFOLD TOWARDS THE THIRD. BUT FIRST IS TO BETTER UNDERSTAND, IN FACT, THE GENERAL NATURE OF INTELLECTUAL PROPERTY AND PATENT RISKS ON THE CONDUCT AND COMMERCIALIZATION OF PUBLICLY FUNDED RESEARCH IN GENERAL AND APPLICABLY TO STEM CELL RESEARCH.

SECOND, WHAT I WANT TO DO IS REVIEW THE VARIOUS METHODOLOGIES THAT EXIST AND ARE PRACTICED FOR ASSESSING INTELLECTUAL PROPERTY AND PATENT RISKS IN THE STEM CELL LANDSCAPE, BUT ALSO MORE GENERALLY.

AND THEN FINALLY, IF TIME PERMITS AND AS OUR DIALOGUE UNFOLDS TODAY, MAYBE WE'LL TALK MORE ABOUT THAT LATER, BUT I WANT TO AT LEAST INTRODUCE A PROPOSAL THAT SEVERAL OF US HAVE BEEN FLOATING ABOUT THE MANAGEMENT OF INTELLECTUAL PROPERTY WITHIN WHAT

WE CALL A CONSTRUCTED OR PROTECTED COMMONS. AND THIS IS BASED LARGELY OUT OF THE EXPERIENCE WITH THE AGRICULTURAL LIFE SCIENCES WORK THAT HAS GONE ON PREVIOUSLY.

SO FIRST LET'S TURN TO THE NATURE OF IP RISKS IN RESEARCH AND DEVELOPMENT. MY REAL PURPOSE HERE IS TO TRY TO, FIRST OF ALL, DISABUSE A NUMBER OF COMMON MISCONCEPTIONS ABOUT INTELLECTUAL PROPERTY AND TO GIVE US ALL A COMMON GROUNDING IN INTELLECTUAL PROPERTY BECAUSE I KNOW THIS IS A VERY DIVERSE CROWD. SOME PEOPLE PROBABLY HAVE MORE EXPERTISE THAN I. IF YOU ARE A PATENT ATTORNEY, YOU WILL HAVE TO FORGIVE ME. WHAT I BRING IS A VERY HIGH LEVEL VIEW OF THIS SORT OF QUESTION AS A POLICY ECONOMIST.

AND LET'S START HERE. I THINK MOST OF US WILL AGREE THAT OUR COMMON NOTIONS OF PROPERTY CERTAINLY EXTEND TO CREATIONS OF THE INTELLECT. BUT WE MAY NOT BE FULLY COGNIZANT OF THE WAY THAT WE MAY DIVIDE MODES OF OWNERSHIP OF INTELLECTUAL CONSTRUCTS BETWEEN INFORMAL AND FORMAL TYPES OF INTELLECTUAL PROPERTY. SO WHAT DO I MEAN BY INFORMAL INTELLECTUAL PROPERTY? SIMPLE. SECRECY OR GIVING ATTRIBUTION. MAXWELL'S EQUATION GIVES ATTRIBUTION TO MAXWELL. IT'S A KIND OF OWNERSHIP. STRATEGIC

CONTROL THROUGH HAVING OTHER ASSETS THAT ENABLE YOU TO MAKE USE OF THE INTELLECTUAL PROPERTY IN AN ADVANTAGEOUS WAY.

FORMAL INTELLECTUAL PROPERTY IS WHAT YOU WERE PROBABLY EXPECTING, EVERYTHING FROM TRADE SECRETS TO SIMPLE TERMS OF CONTRACTS. SO IF YOU SIGN A NONDISCLOSURE AGREEMENT FOR A JOB, THAT IS PROTECTING INTELLECTUAL PROPERTY THROUGH A CONTRACTUAL MECHANISM, ALL THE WAY TO THE REGISTERED FORMS OF IP WITH WHICH WE'RE ALL FAMILIAR.

I WANT TO EMPHASIZE THAT ANY PARTICULAR TECHNOLOGY, WHETHER IT'S A STEM CELL LINE OR IT'S A MUSICAL COMPOSITION, WILL BE TYPICALLY OWNED THROUGH A COMBINATION OF DIFFERENT TYPES OF INTELLECTUAL PROPERTY AND MOST OFTEN A COMBINATION OF BOTH INFORMAL AND FORMAL MECHANISMS. SO, FOR EXAMPLE, A NEW TECHNOLOGICAL INVENTION WILL OFTEN START OUT BEING PROTECTED PURELY THROUGH SECRECY OR NONDISCLOSURE UNTIL YOU GET YOUR APPLICATION INTO THE PATENT OFFICE. BUT AT THE SAME TIME, YOU MAY BE WRITING CONTRACTS AROUND DISCLOSURE OF THAT INFORMATION WITH EMPLOYEES OR PARTNERS WHO NEED TO KNOW. AND IT IS ACTUALLY THE INTERPLAY OF THESE DIFFERENT MECHANISMS THAT EFFECTUATE OWNERSHIP.

I ALSO WANT US TO BE REALLY CLEAR THAT NO

FORM OF IP ACTUALLY GRANTS FULL CONTROL. WE DON'T NEED TO BE REALLY SCARED OF PATENTS. FOR INSTANCE, WE HAVE MULTIPLE TYPES OF USES OF A PIECE OF NEW KNOWLEDGE. YOU CAN USE IT FOR PUTTING IT IN A PUBLICATION, EDUCATION, BASIC AND APPLIED RESEARCH, ALL THE WAY THROUGH COMMERCIAL OFFER AND SALE OF PRODUCTS AND SERVICES. PATENTS WILL GENERALLY CONFER OWNERSHIP OVER CERTAIN USES, LIKELY THESE LATTER MORE COMMERCIAL USES, MAYBE EXTENDING INTO SOME OF THESE OTHER USES, BUT SOME OF THOSE EARLIER MORE PUBLIC TYPE USES ARE REALLY ORTHOGONAL TO THIS. PATENTS WILL NOT PRECLUDE YOU FROM ALSO PUBLISHING, OTHER PEOPLE FROM KNOWING ABOUT THE IDEA. THAT ABILITY TO DISSECT BETWEEN USES IS ABSOLUTELY ESSENTIAL TO THEN APPROPRIATELY MANAGING THE INTELLECTUAL PROPERTY AT THE INTERFACE BETWEEN SCIENCE AND THE MARKET.

AND LET'S BE CLEAR. INTELLECTUAL PROPERTY SOMETIMES GETS A BAD WRAP IN MORE ACADEMIC CROWDS, BUT LET'S BE CLEAR ABOUT THE AGREED UPON ADVANTAGES OF THIS SOCIAL INSTRUMENT, THIS LEGAL INSTRUMENT. WE HAVE SOME DEEP-SEATED NOTION OF THE PERSONAL AND ETHICAL RIGHTS OF A LEGITIMATE CREATOR OR INVENTOR OVER THEIR CREATION OR INVENTION, AND INTELLECTUAL PROPERTY HELPS US TO UPHOLD THOSE. IT, OF COURSE,

PROVIDES INCENTIVES FOR INVESTMENT, FACILITATES THE FORMATION OF MARKETS AND THEIR EFFICIENT OPERATION, AND IT ENHANCES, PARTICULARLY IN OUR DISCUSSION HERE, EFFICIENT TECHNOLOGY TRANSFER FROM PUBLICLY FUNDED RESEARCH INTO THE PRIVATE SECTOR.

SOME OF THE CONFLICT THAT ARISES IN DISCUSSIONS ABOUT INTELLECTUAL PROPERTY IN A FORUM LIKE THIS ARISE FROM THE FACT THAT WE REALLY HAVE DISTINCT NORM SYSTEMS THAT WE OPERATE IN OR WE THINK WE HAVE DISTINCT NORM SYSTEMS ANYHOW. THERE IS, OF COURSE, THE OPEN SCIENCE NORM SYSTEM WHERE WE HAVE RAPID FULL DISCLOSURE, SUPPOSEDLY. WE HAVE COMMON OWNERSHIP, OR I PREFER THE SOVIET ADAGE, THAT THAT WHICH BELONGS TO EVERYONE BELONGS TO NO ONE. SO WE MIGHT CONCEIVE OF IT AS NO OWNERSHIP IN THE MERTONIAN WORLD OF SCIENCE AND FREE EXCHANGE OF IDEAS.

IN COMMERCE EVERYONE OPERATES ACCORDING TO A SET OF NORMS OF SECRECY, PROPRIETY. PRIVATE CORPORATE OWNERSHIP IS WIDELY ACCEPTED, AND NEGOTIATED TRANSACTIONS FACILITATE EXCHANGE OF INFORMATION. AND IT OPERATES FAIRLY SEAMLESSLY IN THE CORPORATE WORLD. IT'S WHEN WE TRY TO INTERFACE THE TWO THAT WE START RUNNING INTO SOME ISSUES, SO WE NEED TO BE COGNIZANT THAT WHERE WE ARE OPERATING

TODAY IS AN EMERGING NORM SYSTEM OF ENTREPRENEURIAL SCIENCE. I WOULD IMAGINE MOST OF THE PEOPLE IN THIS ROOM DO INTUITIVELY EMBRACE THIS HYBRID VERSION, THIS THIRD AREA. THIS IS WHERE OUR INTELLECTUAL PROPERTY NEEDS TO BE BLENDED AND BALANCED. OUR RULES FOR DISCLOSURE AND PROPRIETY WHEN WE PUBLISH, WHEN WE PATENT ARE ALWAYS TESTED ON CASE-BY-CASE BASES.

LET ME DEVELOP A COUPLE STYLIZED FACTS ABOUT INTELLECTUAL PROPERTY. FIRST OF ALL, NOT ALL PATENTS OR NOT ALL PIECES OF INTELLECTUAL PROPERTY ARE CREATED THE SAME. IN FACT, EMPIRICAL ANALYSES HAVE SHOWN THAT ACROSS PORTFOLIOS OR ACROSS PARTICULAR FIELDS, THERE'S A VERY HIGHLY SKEWED DISTRIBUTION OF VALUE OR IMPORTANCE OF PATENTS OR INVENTIONS. A STUDY, A SURVEY OF GERMAN CORPORATIONS BASICALLY REVEALED 90 PERCENT OF THE VALUE OF THE CORPORATE PORTFOLIOS IS RESIDING IN 10 PERCENT OF THE INVENTIONS OR PATENTS THAT THEY HELD. SO A 90/10 RULE THERE.

A STUDY THAT I CONDUCTED AT UNIVERSITY OF CALIFORNIA SYSTEMS OFFICE OF TECHNOLOGY TRANSFER ON OUR AGRICULTURAL INVENTIONS AT UC REVEALED 88 PERCENT OF THE VALUE RESIDED IN THE TOP 8 PERCENT OF INVENTIONS THERE. SO THAT KIND OF VERY LONG-TAILED

DISTRIBUTION IS ENDEMIC. IT'S CHARACTERISTIC. IT'S ABSOLUTELY EVERYWHERE IN THE WORLD OF INTELLECTUAL PROPERTY. AND SO WE CANNOT CONCEIVE OF JUST A UNIFORM DISTRIBUTION THAT ALL PATENTS ARE CREATED EQUAL. WE NEED TO UNDERSTAND THIS HEAVY SKEWNESS, THIS HEAVY LOPSIDEDNESS.

IT'S ALSO HELPFUL TO GROUND THE CONVERSATIONS BY LOOKING AT THE NUMBERS ON UNIVERSITY LICENSING AND UNIVERSITY INTELLECTUAL PROPERTY. THIS IS A PARTICULARLY FAVORITE STUDY OF MINE BY A FELLOW WHO WAS MAKING THE ANALYSIS FOR THE COUNTRY OF SOUTH AFRICA AS THEY WERE CONSIDERING NEW POLICIES THERE. AND HE WANTED TO BENCHMARK AGAINST THE EXPERIENCES OF THE U.S., CANADA, THE UK, AUSTRALIA. AND WHAT HE CAME UP WITH WAS, FIRST OF ALL, A 40/20/10 RULE, THAT OUT OF EVERY $100 MILLION OF RESEARCH EXPENDITURES AT UNIVERSITIES, THERE WAS ON AVERAGE ABOUT 40 INVENTION DISCLOSURES. ABOUT HALF OF THOSE WERE ACTUALLY FILED ON, 20, AND ABOUT HALF OF THOSE ACTUALLY RESULTED IN ISSUED PATENTS. SO 40/20/10.

AND THEN LOOKING AT ROYALTY RETURNS, I FOUND, AT LEAST IN THE UNITED STATES, A VERY CONSISTENT 3 PERCENT. SO OUT OF $100 MILLION IN THE RESEARCH BUDGET GOING INTO THE INSTITUTION, THERE

WOULD BE CORRESPONDINGLY ABOUT $3 MILLION OF ROYALTY REVENUES COMING INTO THE INSTITUTION. OF COURSE, THIS IS AFTER THE NECESSARY LAGS WHICH CAN BE UP TO A DECADE TO MATURE THE PATENT PORTFOLIO FOR AN INSTITUTION AND START REALIZING THESE RETURNS. BUT VERY UNUSUAL FOR IT TO GO MUCH HIGHER THAN THAT.

ONE OF THE BIG DISCUSSIONS IN THE INTELLECTUAL PROPERTY WORLD IN RECENT DECADES HAS BEEN REALLY A RESOURCES ISSUE. AND THAT IS A CONCERN THAT OVERSEGMENTATION OF OUR COMMON INTELLECTUAL RESOURCES ARE OCCURRING. THE TERM GIVEN TO THIS BY MICHAEL HELLER IS AN ANTICOMMONS. THE NOTION IS DERIVED FROM GARRETT HARDIN'S PHRASE THAT HE COINED, THE TRAGEDY OF THE COMMONS.

NOW, IN THE TRAGEDY OF THE COMMONS, WE HAVE A LACK OF PROPERTY RIGHTS, A LACK OF STEWARDSHIP, IN ESSENCE, WHICH RESULTS IN OVEREXPLOITATION OF A SCARCE RESOURCE. AND THIS HAPPENS IN DRILLING FOR WATER WELLS TO USE OF PASTURE LANDS, A NUMBER OF RESOURCE-BASED ISSUES IN THE ENVIRONMENT.

THE POSTULATION HERE IS THAT AN ANTICOMMONS MAY BE OCCURRING IN CERTAIN REALMS OF SCIENCE AND TECHNOLOGY WHERE THERE IS, IN FACT, AN OVERESTABLISHMENT OF PROPERTY RIGHTS. AND THAT CAN

RESULT IN AN UNDEREXPLOITATION OF THE SCARCE RESOURCE. AND THIS IS ESSENTIALLY A MARKET FAILURE ISSUE. BY INTRODUCING SO MANY OWNERS, SO MANY CLAIMANTS OVER A COMMON SET OF RESOURCES, WE INTRODUCE HIGH TRANSACTION COSTS, THAT THE RECOMBINATION OF THOSE RESOURCES FROM THOSE WHO OWN TO THOSE WHO ARE GOING TO APPLY THEM ENDS UP BEING SO COSTLY THAT IT DOESN'T END UP HAPPENING. THIS CAN ALSO BE A RESULT OF STRATEGIC BEHAVIOR AS INDIVIDUAL OWNERS REALIZE THAT THEY CAN GAME A SITUATION LIKE THAT. AND I QUOTE HELLER AND EISENBERG. THEY SAID, "MORE INTELLECTUAL PROPERTY RIGHTS MAY, IN FACT, BE LEADING PARADOXICALLY TO FEWER USEFUL PRODUCTS FOR IMPROVING HUMAN HEALTH."

NOW, I THINK ONE OF THE IMPORTANT MISCONCEPTIONS OF THIS ANTICOMMONS THESIS, AND IF YOU HEARD IT BEFORE, I WANT TO ADD A DISTINCTION HERE, AND THAT IS THAT ITS IMPACTS SHOULD BE ANTICIPATED TO BE RATHER DIFFERENT IN THE REALM OF SCIENCE FROM ITS IMPACTS IN THE REALM OF COMMERCE.

SO LET'S DIFFERENTIATE. IN ACADEMIA OR IN SCIENCE, WE SHOULD EXPECT THIS FRAGMENTATION OR THIS EXCESSIVE PROPERTIZATION OF INTELLECTUAL RESOURCES TO RESULT POSSIBLY IN UNREASONABLE COSTS OR TERMS FOR OBTAINING KEY RESEARCH INPUTS FOR ACADEMIC

RESEARCH USE. THIS IS SIMPLY BECAUSE PEOPLE ARE OUT THERE FIGHTING OVER WHO HAS RIGHTS TO WHAT, AND YOU NEED TO GO AND ESSENTIALLY SHOP FOR EVERYTHING EVEN AS AN ACADEMIC. BUT THAT HAS NOT BEEN SUBSTANTIATED IN THE ANALYSES.

I THINK THE SECOND POINT IS FAR MORE PRESCIENT. AND THAT IS THAT IN A VERY DENSE IP ENVIRONMENT, WE ACTUALLY REDUCE OPPORTUNITIES OR RAISE THE HURDLES FOR THE OUTLICENSING OR THE COMMERCIALIZATION OF OUR ACADEMIC RESEARCH RESULTS. IT'S GOING TO BE HARDER FOR YOUR POTENTIAL LICENSEE OR START-UP COMPANY TO PUT TOGETHER THE FULL PACKAGE OF ENABLING TOOLS THAT THEY ARE GOING TO NEED TO HAVE FREEDOM TO OPERATE IN THE MARKETPLACE. WHAT THAT DOES IS IT SHUTS THE DOOR FOR YOUR TECH TRANSFER OFFICE AT YOUR UNIVERSITY TO MAKE THOSE DEALS IN THE FIRST PLACE.

AND THIS IS THE BOOGIE MAN IN THE CLOSET. THERE'S THIS POSSIBLE INCREASED RISK OF LITIGATION TO UNIVERSITIES, AND THIS HAS RAISED A NUMBER OF UNIVERSITY COUNSEL'S FEARS PARTICULARLY FOLLOWING THE 2002 SUPREME COURT CASE OF MADEY VS. DUKE UNIVERSITY. WHETHER OR NOT THAT'S A REAL CONCERN IS STILL VERY MUCH AN OPEN QUESTION, AND I WILL ADDRESS THAT HERE SHORTLY.

LET'S TURN, THOUGH, TO THE COMMERCIAL WORLD WHERE AN OVERFRAGMENTATION OF PROPERTY RIGHTS CERTAINLY RAISES THE REQUIREMENTS FOR INTELLECTUAL PROPERTY DILIGENCE. YOU NEED TO BE GOING OUT AND DOING MORE FREEDOM TO OPERATE, AND IT ALSO RAISES THE NEED FOR MULTIPLE LICENSES TO THE TOOLS, TO THE INPUTS EITHER IN YOUR R&D PROGRAMS, IN YOUR MANUFACTURING, ACROSS THE BOARD POTENTIALLY. AND IT ALSO PUTS THE BUSINESS SECTOR IN SITUATIONS OF POTENTIAL HOLDUP WHERE YOU ARE HAVING TO COORDINATE MULTIPLE DEALS. LET'S SAY YOU FINISHED NINE OUT OF TEN DEALS. YOU NOW GO TO SIT DOWN FOR NEGOTIATION WITH THAT TENTH PROPERTY RIGHTS OWNER. THEY KNOW THAT THEY'VE GOT YOU OVER THEIR KNEE BECAUSE YOU NEED TO CLOSE THAT LAST DEAL OR THE VALUE OF THE PREVIOUS NINE COLLAPSE.

AND, OF COURSE, THERE'S JUST SIMPLY MORE POTENTIALLY UNFORESEEABLE LITIGATION RISK. EVERYTHING FROM SUBMARINE PATENTS, THINGS THAT ARE FLOATING ALONG INSIDE THE PATENT OFFICE AND HAVE NOT PUBLISHED OR ISSUED YET WITH A HIGHER FREQUENCY OF PATENTING OVERALL, TO SIMPLY OPERATORS, RESEARCHERS THAT YOU'RE NOT AWARE OF YET GETTING INTO THE GAME AND FILING SOMETHING THAT MAY END UP BLOCKING YOU IN THE MARKET.

THIS IS A VERY IMPORTANT IMAGE, AND I WANT YOU, IF YOU TAKE ANYTHING FROM WHAT I TALK ABOUT TODAY, IT'S THIS. AND THAT IS THAT OUR NEED FOR INTELLECTUAL PROPERTY ANALYSIS AND DILIGENCE CHANGES, IT'S HETEROGENEOUS, AS YOU MOVE FROM THE WORLD OF PURE ACADEMIC RESEARCH TO THE MARKETPLACE. AND, IN FACT, WE WOULD ALL BE FAMILIAR WITH THIS SORT OF PIPELINE CURVE HERE WHERE THE NUMBER OF CANDIDATE INVENTIONS DROPS OFF QUITE RAPIDLY.

IMAGINE A DRUG DISCOVERY PIPELINE HERE. YOU START WITH A THOUSAND POSSIBLE CANDIDATES, YOU IDENTIFY A HUNDRED TARGETS, YOU FINALLY PICK TEN LEADS OUT OF THAT, AND MAKE SUBMISSIONS TO THE FDA ON JUST ONE OR TWO OF THOSE EVENTUALLY. SO YOU HAVE THIS RAPID DROP-OFF. BUT CONCOMITANTLY YOU HAVE REALLY RATHER LOW RISK OF LITERAL INTELLECTUAL PROPERTY INFRINGEMENT AS YOU ARE DOING EARLY STAGE ACADEMIC RESEARCH. AND THAT'S BECAUSE THE PROBABILITY IS THAT YOU WERE DOING TRULY NOVEL AND NONOBVIOUS WORK. AND IT'S AS YOU GET INTO THE MARKETPLACE AND YOU START DRAWING ON OTHER COMPLEMENTARY INTELLECTUAL ASSETS, YOUR EXPOSURE TO INTELLECTUAL PROPERTY RISK GOES UP AND UP AND UP, BUT IN A STEPWISE FASHION. AND IT'S AS YOU MOVE THROUGH THESE MILESTONES ON THE WAY TO THE

MARKETPLACE THAT YOUR NEED FOR CAUTION INCREASES.

BUT I WOULD ARGUE THAT THE LITERAL INFRINGEMENT RISK AND THE ACTUAL RISK OF LITIGATION DIFFER, AND THEY DIFFER MOST STRONGLY AT THE ACADEMIC RESEARCH END OF THINGS HERE. NOW, THE LITERAL IP INFRINGEMENT RISK HAS BEEN INCREASED BY THAT DECISION IN MADEY V. DUKE EIGHT YEARS AGO. IT ESSENTIALLY NARROWED GREATLY THE RESEARCH EXEMPTION THAT WE THINK WE ALL OPERATE UNDER AT ACADEMIC INSTITUTIONS. BUT I WOULD MAKE AN ECONOMIC ARGUMENT THAT WE STILL HAVE A DE FACTO RESEARCH EXEMPTION AND THAT OUR RISK OF ACTUAL LITIGATION IN THE ACADEMIC LABORATORY REMAINS RELATIVELY QUITE LOW. AND I'VE GOT FOUR REASONS FOR THAT.

AND THESE ARE FUNDAMENTALLY ECONOMIC. FIRST IS THAT THERE'S POTENTIALLY MANY, MANY INFRINGING ACTIVITIES GOING ON WITH THE VAST DIVERSITY OF ACADEMIC RESEARCH GOING ON. AND TRYING TO PURSUE ALL OF THOSE REALLY RAISES COST FOR POTENTIAL LITIGANTS OR ASSERTERS OF IP RIGHTS. BUT AT THE SAME TIME, THE POTENTIAL DAMAGES, THE WINS THAT THEY CAN MAKE IN A COURT OF LAW FOR INFRINGEMENT, ARE RELATIVELY QUITE LOW FROM A UNIVERSITY RESEARCH PROGRAM. SO IT DOESN'T NECESSARILY MAKE A LOT OF ECONOMIC SENSE IN PROSPECT

THEORY FOR THEM TO BE GOING AROUND PLUMBING FOR INFRINGERS.

NO. 3 AND NO. 4 ARE EQUALLY AS IMPORTANT. ENLIGHTENED SELF-INTEREST SAYS THAT THAT COMPANY SHOULD LET THE UNIVERSITY RESEARCHER WORK WITH THEIR INVENTION. IT HELPS VALIDATE THEIR TECHNOLOGY FOR GOOD OR FOR ILL, BUT IT'S NOT ON THEIR DIME. AND IT MAY, IN FACT, LEAD TO POTENTIAL NEW LICENSING OPPORTUNITIES IF PEOPLE ARE USING THEIR WORK. AND, OF COURSE, THERE'S NO. 4, THE POSITIVE-NEGATIVE REPUTATION OR BRAND IMAGE EFFECTS THAT COULD OCCUR WERE A COMPANY TO TURN AROUND AND SUE, SAY, A NONPROFIT CHILDREN'S HOSPITAL OR A WELL-ESTEEMED UNIVERSITY.

THIS BRINGS ME TO THE QUESTION OF WHETHER THIS INTELLECTUAL ANTICOMMONS PROBLEM IS EMERGENT IN STEM CELLS. THERE HAS BEEN CONCERN AND A NUMBER OF PEOPLE HAVE PROPHESIZED THAT AN INTELLECTUAL PATENT THICKET OR AN INTELLECTUAL ANTICOMMONS IS ARISING, MYSELF INCLUDED AND SOME OTHERS I SEE AROUND THE ROOM HERE. I GIVE YOU THIS LIST OF REFERENCES YOU CAN LOOK AT LATER.

BUT THE CONCERNS OF AN INTELLECTUAL ANTICOMMONS AFFECTING PROGRESS IN REGENERATIVE MEDICINE IS BASED ON SEVERAL OBSERVATIONS. FIRST

IS, OF COURSE, THE BROAD SCOPE OF THE FOUNDATIONAL PATENTS. THE THOMSON PATENTS ON HUMAN EMBRYONIC STEM CELLS, THE EMERGING PATENTS IN INDUCED PLURIPOTENT STEM CELLS, AND PATENTS OVER TISSUE-SPECIFIC PROGENITORS, NEURAL CREST STEM CELLS OR HEMATOPOETIC OR WHATNOT. AND THIS RESULTS CLEARLY FROM THE HIERARCHICAL OR DERIVATIONAL STRUCTURE OF THE FIELD. I'LL ELABORATE THAT IN A SECOND.

WE ALSO HAVE A REALLY HIGH DEGREE OF INTERDEPENDENCE BETWEEN THE DIFFERENT MEAN TECHNICAL AREAS IN THIS FIELD, CELL LINES, DERIVATION, GROWTH, CHARACTERIZATION, DIFFERENTIATION, DELIVERY. NOT NECESSARILY ALL OF THESE OPERATE MODULARLY SEPARATE FROM ONE ANOTHER. THERE IS SIGNIFICANT RATES OF PATENTING GOING ON IN ALL OF THESE AREAS, AND THE SITUATION IS COMPLICATED, AS WAS BEING SPOKEN THIS MORNING, WITH OTHER PRIMARY AREAS OF CONCERN, INCLUDING PRACTICAL ACCESS TO TECHNICAL DATA AND CHARACTERIZATIONS OF THESE TECHNOLOGIES AS WELL AS THE REGULATORY AND ETHICAL ISSUES.

THIS IMAGE IS INTENDED TO ILLUSTRATE THE FACT THAT EVERYONE HERE KNOWS THAT THIS IS A TECHNOLOGY THAT HAS ABSOLUTELY EXPLOSIVE COMPLEXITY. SO IF YOU ARE HOLDING RIGHTS TO SOME OF THE THINGS

NEAR IN THE DARKER SHADED AREAS CLOSEST TO THE TOTIPOTENT CELL, YOU, OF COURSE, ARE MAKING CLAIMS OVER POTENTIALLY EACH AND EVERY ONE OF THOSE TERMINAL BRANCHES OF DIFFERENTIATION.

AND JUST A SIDE NOTE. I WAS ACTUALLY UNABLE TO FIND A GOOD IMAGE OF THIS IN ANY OF THE RESEARCH MATERIALS THAT I WAS LOOKING AT FROM THE FIELD. AND SO IT NECESSITATED ME TO GO AND ACTUALLY ASSEMBLE THIS OUT OF PROBABLY A DOZEN DIFFERENT REFERENCES THAT ARE OUT THERE. BUT THAT'S MORE OR LESS WHAT THE SPREAD OF DIFFERENTIATION LOOKS LIKE, AND IT GIVES YOU A SENSE OF THE POTENTIAL POWER OF PATENT CLAIMS VERY EARLY ON, BUT EVEN PATENT CLAIMS, SAY, MESENCHYMAL STEM CELLS OR HEMATOPOIETIC STEM CELLS CAN AFFECT EVERYTHING DOWNSTREAM FROM THEM.

AND THIS LAST POINT, AGAIN, THAT INTELLECTUAL PROPERTY ISSUES ARE COMPLETELY INTERTWINED, INTERWOVEN WITH DATA ACCESS ISSUES, WITH REGULATORY AND ETHICAL ISSUES OF PROVENANCE, CONSENT APPROVALS, AND THE TYPE OF THINGS THAT I KNOW THIS COMMITTEE SPENDS ALL OF ITS TIME WITH.

NOW LET ME TURN TO THE METHODS OF ANALYZING INTELLECTUAL PROPERTY RISKS THAT ARE PRACTICED BOTH IN INDUSTRY AND IN ACADEMIA TODAY. AND I'M GOING TO SEPARATE THESE INTO TWO GENERAL

CATEGORIES. THE FIRST ARE TARGETED LEGAL ANALYSIS, AND THIS ALWAYS FOCUSES ON A PARTICULAR TARGET TECHNOLOGY OF INTEREST. YOU START WITH THAT TECHNOLOGY OF INTEREST AND BASICALLY YOU HIRE A PATENT ATTORNEY OR YOUR TECHNOLOGY OF INTEREST HAS BEEN SUBMITTED TO THE PATENT OFFICE, AND IT IS BEING LOOKED AT SPECIFICALLY FOR HOW IT LANDS WITHIN THE EXISTING INTELLECTUAL PROPERTY LANDSCAPE. THESE INCLUDE FREEDOM TO OPERATE ANALYSES, PRIOR ART SEARCHES, INTERFERENCE SEARCHES, AND THERE ARE MORE, BUT THIS IS GIVES YOU THE GENERAL IDEA.

THEN THERE ARE OTHER HIGHER ORDER WAYS OF STUDYING THE RISK OF INTELLECTUAL PROPERTY, AND THESE INCLUDE SURVEYS OF DOMINANT PATENTS. THESE INCLUDE LANDSCAPE ANALYSES, THESE INCLUDE SURVEYS OF RESEARCHERS AND THE PROBLEMS THAT THEY ARE CONFRONTING IN THEIR LABORATORIES. AND, LASTLY, THERE IS A LITERATURE IN LITIGATION TRENDS. I JUST WANT TO TOUCH BRIEFLY ON EACH OF THESE.

I'VE MORE OR LESS TOLD YOU ALL OF THIS ALREADY, BUT TARGETED LEGAL ANALYSES ARE THE BREAD AND BUTTER OF THE PATENT LEGAL PROFESSION IN MANY REGARDS. AND THE METHODOLOGY THERE IS YOU CHARACTERIZE THE TECHNOLOGY YOU ARE WORKING ON, YOU THEN GO AND SEARCH EXISTING LITERATURE FOR PATENTS

AND PUBLICATIONS THAT POTENTIALLY COVER OR OBVIATE THAT TECHNOLOGY. YOU USUALLY COME UP WITH JUST A HANDFUL, MAYBE A HALF DOZEN OR DOZEN THAT YOU ANALYZE THEN IN DETAIL FOR THE STRUCTURE OF THEIR CLAIMS, HOW THEY WOULD READ OVER THIS TECHNOLOGY. AND AT THE END OF IT, USUALLY THE PRODUCT IS THE RENDERING OF A LEGAL OPINION.

NOW, THAT LEGAL OPINION IS SOMETIMES LITTLE BETTER THAN A WEATHER REPORT IN TERMS OF WHAT YOUR ACTUAL RISK IS GOING TO BE. A 60-PERCENT CHANCE OF RAIN, 60-PERCENT CHANCE OF LITIGATION. AND THAT CAN BE MORE OR LESS COMFORTING DEPENDING ON WHAT THAT NUMBER IS AND HOW MUCH YOU TRUST YOUR ATTORNEY.

THERE ARE A NUMBER OF TOOLS THAT ARE USED IN THIS TYPE OF SEARCH.

CHAIRMAN LO: TIME AND SCHEDULE. I WAS WONDERING IF I COULD ASK YOU TO JUMP TO THE STEM CELL-SPECIFIC ISSUES, AND WE CAN COME BACK TO THE GENERAL ANALYSIS.

DR. GRAFF: WELL, YOU ARE AWARE NOW THAT THERE ARE THESE MULTIPLE KINDS OF ANALYSES THAT ARE GOING ON. SO FOR STEM CELL-SPECIFIC, WHAT I WANT TO SHARE WITH YOU IS A STEM CELL PATENT LANDSCAPE ANALYSIS THAT WE CONDUCTED SEVERAL YEARS AGO WHEN I

WAS AT PIPRA RAISED BY QUESTIONS COMING FROM FOLKS IN GOTHENBURG, SWEDEN, AT THE SAHLGRENSKA MEDICAL HOSPITAL THERE WHERE A NUMBER OF THE ORIGINAL STEM CELLS LINES WERE DERIVED. THE BASIC METHODOLOGY HERE IS TO COMPILE A DATASET, AND IT CAN RANGE FROM HUNDREDS TO TENS OF THOUSANDS OF PATENTS IN A VERY CAREFULLY STRUCTURED METHODOLOGY SUCH THAT YOU ARE CHARACTERIZING THE ENTIRE FIELD, THE ENTIRE INDUSTRY. AND THEN YOU CAN DO VARIOUS ANALYSES OF HOW THE INDUSTRY IS EVOLVING.

SO, FOR INSTANCE, YOU SEE RIGHT HERE THE RATE OF GROWTH IN U.S. PATENT APPLICATIONS AND GRANTED PATENTS THROUGH 2005 IN THE FIELD. WHAT SHOULD CONCERN YOU THERE IS THAT VERY LARGE SPIKE IN APPLICATIONS THAT STARTED COMING ALONG IN ABOUT '01-'02 THAT WOULD THEN LEAD, OF COURSE, TO NEW PATENTS GRANTING.

ANOTHER ANALYSIS WITH THIS TYPE OF 35,000 FOOT LOOK ARE THE STRUCTURE OF OWNERSHIP. AND IN LOOKING AT GRANTED U.S. PATENTS, WE SEE A COUPLE VERY INTERESTING PATTERNS IN STEM CELLS. THE FIRST IS THAT PUBLIC SECTOR INSTITUTIONS OWN 44 PERCENT OF THE INTELLECTUAL PROPERTY IN THIS FIELD. CONTRAST THAT WITH 3 PERCENT ACROSS THE ENTIRE U.S. ECONOMY. SO A VERY HEAVY PUBLIC SECTOR INVESTMENT IN THE

INTELLECTUAL PROPERTY IN THIS SPACE.

THE SECOND CHARACTERISTIC THAT I WANT YOU TO NOTE IS THAT IT'S HIGHLY FRACTURED. THE LARGEST SINGLE PATENT PORTFOLIO OF ANY ORGANIZATION, UNIVERSITY OF CALIFORNIA AND AMGEN ARE TIED AT 3 PERCENT OF THE INTELLECTUAL PROPERTY IN THE FIELD. WE CAN SEE CONCENTRATIONS AS HIGH AS 15, 20, 30 PERCENT OF THE INTELLECTUAL PROPERTY OF A PARTICULAR INDUSTRY IN OTHER FIELDS. SO IT'S STILL HIGHLY FRACTURED ACROSS DIFFERENT ORGANIZATIONS IN STEM CELLS.

THERE ARE ALSO WAYS TO THEN DROP OUT STATISTICALLY FROM A DATASET LIKE THAT THE MOST IMPORTANT PATENTS. AND WE GENERATED A LIST OF WHAT WE CONSIDERED BY INDICATION THE 50 MOST IMPORTANT. OF COURSE, HERE'S ONE THAT IS NOW THE SOURCE OF THE CONFLICT BETWEEN STEM CELL, INC. AND THE CHILDREN'S HOSPITAL OF ORANGE COUNTY. AND WE FIND FROM WISCONSIN ALUMNI RESEARCH FOUNDATION, OF COURSE, THE CONTESTED WARF PATENTS.

TWO OTHER METHODOLOGIES --

CHAIRMAN LO: I'M SORRY. I'M GOING TO ASK YOU REALLY TO JUMP TO, GIVEN OUR TASK OF THINKING ABOUT A POTENTIAL IPS STEM CELL BANK, AS ALAN TROUNSON PRESENTED THIS MORNING, I'M GOING TO ASK

YOU TO SORT OF SKIP YOUR SLIDES AND JUST TELL US BRIEFLY WHAT ARE THE ETHICAL ISSUES REGARDING IP THAT YOU THINK WE NEED TO HAVE OUR ANTENNAE UP FOR, AND WE CAN COME BACK TO YOU LATER FOR DETAILS.

DR. GRAFF: AS AN ECONOMIST, LET ME ASK. I'M NOT USED TO ASKING QUESTIONS ABOUT ETHICAL ISSUES OF IP. SO MAYBE IF YOU COULD ELABORATE YOUR QUESTION FOR ME, AND I CAN RESPOND IN A HELPFUL MANNER.

CHAIRMAN LO: LET'S TRY TO THINK ABOUT IPS STEM CELL BANKS, NOT IP FOR STEM CELLS IN GENERAL. BUT WITH REGARD TO A STEM CELL BANK AND THE THINGS WE TALKED ABOUT THIS MORNING, ARE THERE PARTICULAR ISSUES HAVING TO DO WITH SOMEONE DEPOSITING A LINE FUNDED BY CIRM IN A STEM CELL BANK WITH INTELLECTUAL PROPERTY CONCERNS THAT MIGHT EITHER MAKE IT DIFFICULT FOR OTHER RESEARCHERS TO DO SECONDARY RESEARCH WITH THOSE LINES OR OTHER SUCH ISSUES THAT CIRM AS THE FUNDER OF THE RESEARCH AND THE SPONSOR OF THE BANK REALLY NEEDS TO KNOW ABOUT?

DR. GRAFF: I DON'T SEE CIRM NECESSARILY EXPOSING ITSELF TO RISKS BY MANAGING A BANK OF THAT NATURE. FROM MY PERSPECTIVE THE BIGGEST RISK HERE IS THAT THE CELL LINES GET DEPOSITED AND THEN WE'RE SEEKING TO REDISSEMINATE THEM, BUT WE'RE NOT CLEAR

ABOUT HOW MUCH INTELLECTUAL PROPERTY READS OVER THEM OR WHAT THEY COULD POTENTIALLY BE INFRINGING AS THEY'RE PICKED UP BY VARIOUS USERS IN VARIOUS -- TISSUE TYPES OF VARIOUS DISEASE INDICATIONS BECAUSE OF THE COMPLEXITY OF THE PATENT LITERATURE. FROM MY POINT OF VIEW, IT'S AN EFFICIENCY QUESTION. YOU COULD BE EXPOSING YOUR POTENTIAL USERS TO CERTAIN RISKS OR, IN ESSENCE, THE USEFULNESS OF THE RESOURCE COULD BE OBVIATED BY THE COMPLEXITY OF THE INTELLECTUAL PROPERTY ARENA. BUT GUIDE ME MORE WITH YOUR QUESTIONS.

CHAIRMAN LO: I THINK I WANT TO TABLE THIS FOR ABOUT HALF AN HOUR, IF I MAY. SHERRY NEEDS TO LEAVE AT AROUND THREE, AND I WANTED TO HAVE THE SWG THINK ABOUT NEXT STEPS. WE'LL COME BACK TO IPS. I KNOW SEVERAL OF YOU ON THE PANEL HAVE COMMENTS. I ALSO WANT TO GIVE DR. FORSBERG A CHANCE TO SHARE HIS KNOWLEDGE. BUT I WANT TO TAKE A BREAK HERE AND COME BACK TO THE STANDARDS WORKING GROUP AND REFOCUS US ON WHAT ALAN HAD CHARGED US WITH FOR THIS MEETING, WHICH IS REALLY TO THINK ABOUT WHAT ETHICAL ISSUES CIRM NEEDS TO BE AWARE OF AND THINK ABOUT AS WE POTENTIALLY PLAN THIS STEM CELL BANK. SO WE'RE TALKING NOT ABOUT IP, BUT MORE GENERALLY.

AND AS I WAS TRYING TO THINK ABOUT THIS

MORNING, IT STRUCK ME THAT WE HAD IDENTIFIED A NUMBER OF ISSUES AND STARTED TO DISCUSS A COUPLE IN SOME DETAIL. DOROTHY RAISED THE ISSUE OF DIVERSITY, AND WE GOT INTO, I THOUGHT, A VERY HELPFUL, VERY RICH DISCUSSION. WE STARTED TO TALK ABOUT INFORMED CONSENT FOR THESE IPS LINES GOING IN THE BANK. AND I'M JUST SORT OF TRYING TO THINK AHEAD TO HELP ALAN AND CIRM LEADERSHIP ON HOW THE SWG CAN HELP YOU.

AND IT STRIKES ME THAT THERE ARE A COUPLE SORT OF APPROACHES WE MIGHT WANT TO TAKE, AND I JUST WANT TO SORT OF FLOAT THESE OUT. ONE MIGHT BE JUST TO SORT OF SAY IN THIS LIST OF ISSUES, WE MIGHT WANT TO SUGGEST THAT IN THE RFA'S THAT ARE ASSOCIATED WITH THE STEM CELL BANK, THAT WE ASK APPLICANTS TO SAY HOW ARE YOU GOING TO ADDRESS THE DIVERSITY ISSUE IN BOTH THE UP-FRONT RECRUITMENT AND THE SUBSEQUENT USE, FOR EXAMPLE. ON SOME ISSUES WE MAY JUST SAY TELL US HOW YOU ARE GOING TO ADDRESS THESE ISSUES. THERE MAY BE OTHER ISSUES WHERE WE MIGHT WANT TO GO A STEP FURTHER AND SAY HERE ARE SOME SUGGESTED WAYS YOU MIGHT GO ABOUT ADDRESSING THESE ISSUES. THIS MAY NOT BY THE RIGHT THING FOR THE TYPE OF LINE YOU'RE DERIVING, SO WE'RE NOT GOING TO PRESCRIBE IT, BUT THIS IS ONE APPROACH YOU MIGHT WANT TO TAKE. SO WE MIGHT WANT TO GO BEYOND JUST SAYING TALK ABOUT

THESE ISSUES TO CONSIDER THIS POSSIBLE APPLICATION.

SO THAT'S ONE THING I WANTED TO SORT OF SAY IS THAT THE KIND OF APPROACH THAT MIGHT BE HELPFUL. AND REALLY TO ASK ALAN AND HIS STAFF WHETHER THERE ARE THINGS THAT HE WOULD LIKE TO US KIND OF ADDRESS TODAY THAT WOULD REALLY HELP YOU TAKE THE NEXT STEPS.

THEN I THINK A LITTLE LATER THERE'S SOME OTHER ISSUES WE RAISED THAT WE JUST SORT OF RAISED AND DIDN'T REALLY GET A CHANCE TO DISCUSS. I THINK SOME OF YOU ON THE COMMITTEE MIGHT WANT TO SAY LET'S TALK A LITTLE BIT MORE ABOUT THINGS LIKE, FOR EXAMPLE, IF WE DO GENOMEWIDE ASSOCIATION STUDIES, EVEN WHOLE GENOME SEQUENCING, UNDER WHAT CONDITIONS, IF AT ALL, DO WE WANT TO GO BACK TO THE DONORS AND SAY, HEY, WE FOUND SOMETHING THAT WE THINK HAS SOME REAL CLINICAL SIGNIFICANCE TO YOU. THIS IS AN ISSUE THAT'S COME UP WITH MANY OF THE GENOMEWIDE SEQUENCING STUDIES.

ANOTHER ISSUE THAT WE JUST BARELY TOUCHED ON THIS MORNING WAS THE RIGHT OF A PARTICIPANT TO WITHDRAW FROM A STUDY. SO IF SOMEONE DONATED MATERIALS THAT THEN BECAME IPS CELL LINES, AND FOR SOME REASON LATER ON THEY SAY, YOU KNOW, I CHANGED MY MIND AND I'M NOT SURE, AT WHAT POINT IS IT

IMPOSSIBLE FOR THEM TO WITHDRAW CERTAINLY IF IT'S BEEN ANONYMIZED? THESE ARE JUST OTHER ISSUES THAT WE MAY WANT TO TALK ABOUT. I GUESS I WANTED TO JUST THROW THE BALL BACK TO ALAN AND HIS LEADERSHIP TEAM TO SORT OF ARE THERE SPECIFIC THINGS YOU REALLY WOULD LIKE US TO SORT OF TURN OUR MINDS TO IN THE TIME WE HAVE LEFT?

DR. TROUNSON: I THINK THAT THE LAST MATTER THAT YOU BROUGHT UP, BERNIE, IS REALLY IMPORTANT ABOUT IF YOU ARE GOING TO HAVE A BANK THAT'S GOING TO BE A RESOURCE FOR DECADES OF USE, WHAT SORT OF CONSENT DO YOU TAKE AND WHAT SORT OF BARRIERS DO YOU PROVIDE, IF ANY, FOR INFORMATION TO GO BACK TO THE DONOR OR FOR ENABLING, SAY, COMMERCIALIZATION IN CASE NEW DRUGS WERE FOUND FROM UTILIZATION OF THOSE CELL LINES, OR IS THERE AN ABILITY, SHOULD THERE BE AN ABILITY TO PUT RIDERS ON SOME OF THEM.

FOR EXAMPLE, I THINK IT WAS RAISED EARLIER THAT YOU MIGHT -- THERE MIGHT BE A CASE, BUT I DOUBT IT WOULD BE HAPPENING IN THE CASE OF THESE RESEARCH LINES, BUT THERE MIGHT BE A CASE THOUGHT ABOUT THAT COULD DERIVE SPERM AND EGGS. DO YOU WANT TO CUT -- SHOULD WE CUT THAT OFF SPECIFICALLY, OR WHERE ARE THE PARAMETERS HERE WHERE YOU'VE GOT A LONG-TERM

BANK? AND WHAT SHOULD PATIENTS BE AWARE OF IF THEY'RE PROVIDING IT CLEARLY THROUGH CLINICAL SERVICES THAT ARE ACTUALLY SAMPLING A POPULATION TO TRY AND GET THE HETEROGENEITY OF THAT POPULATION?

CHAIRMAN LO: SHERRY AND THEN MARCY. IS THERE ANYBODY ON THE PHONE, BY THE WAY?

DR. TAYLOR: I'M STILL HERE. ROB TAYLOR.

CHAIRMAN LO: SO FOR ROB'S SAKE, WE'RE GOING TO ASK EVERYBODY TO JUST IDENTIFY THEMSELVES BEFORE THEY SPEAK.

MS. LANSING: SO AT THE RISK OF BEING A LAYPERSON AND REALLY NAIVELY SAYING SOMETHING, I'M JUST GOING TO TELL YOU, AFTER LISTENING AND GOING BACK THROUGH ALL THE MEETINGS THAT WE'VE HAD, TO ME INFORMED CONSENT MEANS THAT YOU HAVE A GREAT DEAL OF TIME SPENT EXPLAINING TO YOU THAT THIS WILL BE USED FOR RESEARCH, PERIOD. DO YOU KNOW? PERIOD. IN OTHER WORDS, RESEARCH IS RESEARCH.

NOW, WE KNOW YOU CAN'T CLONE. WE HAVE THINGS IN OUR LAW, IN OUR BYLAWS THAT SAY WHAT TYPES OF RESEARCH IT CAN BE.

NOW, I THINK IF YOU START TO A DONOR, A LAYPERSON DONOR, START SAYING, WELL, IT COULD BE IPS, IT COULD BE THIS, IT COULD BE THAT, YOU GO CRAZY. I DON'T THINK ANYONE IS GOING TO SIGN

ANYTHING, AND I DON'T THINK WE'RE BEING DISINGENUOUS. I THINK RESEARCH IS RESEARCH. I THINK THAT'S ENOUGH.

NOW, IF WE DECIDE IN CIRM'S, LIKE WE DID WITH CLONING, THEN YOU PUT IN NONE OF OUR RESEARCH CAN INCLUDE CLONING. WE KNOW THAT. AND I THINK THAT'S ENOUGH. DO YOU KNOW? I THINK AS THE WORLD DEVELOPS AND OTHER THINGS HAPPEN THAT I CAN'T EVEN BEGIN TO IMAGINE, CIRM WILL TAKE A STANCE THAT WE DON'T -- OR WE WILL TAKE A STANCE THAT WE DON'T WANT TO DO RESEARCH ON THAT. I ACTUALLY THINK THAT'S ENOUGH, BUT THAT'S A VERY -- MAYBE --

CHAIRMAN LO: I HAVE A NUMBER OF HANDS.

MS. LANSING: SO EVERYONE CAN SAY --

MS. FEIT: I'M GOING TO HAVE TO LEAVE ALSO, BUT I WANTED TO SAY IN THE PAST WE'VE ALWAYS SET A VISION FOR WHAT WE WANTED TO EMBARK ON. THIS IS A WHOLE NEW ARENA FOR CIRM. SO FOR ME ESTABLISHING A VISION FOR THIS PROGRAM WOULD BE IS CIRM GOING TO FUND A BANK? IS CIRM GOING TO OWN A BANK? WHAT DOES CIRM WANT TO DO IS THE FIRST QUESTION I WOULD HAVE. WHAT ROLE -- WE HAVEN'T REALLY DEFINED WHAT ROLE CIRM WANTS TO TAKE.

AFTER THAT, WE'VE DONE EXTENSIVE WORK, AND SHERRY HAS COMMENTED ON SEVERAL TIMES IN TERMS OF

THE PROCUREMENT OF CELLS. I THINK QUESTIONS ARE STILL LEFT AROUND DISTRIBUTION IF WE DO FUND OR RUN OUR OWN BANK OR SUPPORT A BANK OR IDENTIFY WITH A LARGE BANK AND OWN IT AND THEN INDEMNIFICATION. I THINK A REVISIT BACK TO THE CONSENT THAT WE HAD DEVELOPED, WHICH I THOUGHT WAS EXTENSIVE AND VERY WELL DONE WITH A LOT OF CONSIDERATION FOR DONORS, BUT JUST TO MAKE SURE THAT IT STILL WORKS.

SO I THINK STARTING WITH THE VISION THAT WE WANT FOR CIRM IN THIS PROGRAM, WHICH SOUNDS LIKE IT'S THE RIGHT ROAD TO TAKE, WHAT ROLE WILL CIRM PLAY IN THIS? AND THEN BACKING INTO THAT WITH SOME KIND OF WORK PLAN OF HOW WE GO ABOUT ACHIEVING THAT VISION FOR A LARGE INTERNATIONAL CELL BANK.

DR. TROUNSON: IN SOME RESPECTS WE'RE SORT OF LOOKING AT THE ETHICAL ISSUES BEFORE WE ACTUALLY PUT ANY PRIMARY PROPOSAL ANYWHERE. JUST IN A SENSE I THINK IN TALKING WITH GEOFF AND OTHERS, WHAT ARE THE SPECIAL ISSUES HERE PARTICULARLY WHEN THE HELA CELL ISSUES WERE SORT OF BROUGHT UP, HAVE WE BEEN THINKING INTO OUR IPS CELLS PROGRAMS SUFFICIENTLY WELL. I THINK WE HAVE, BUT THEN THIS SORT OF ADDITIONAL ELEMENT THAT MIGHT COME IF IT'S SUPPORTED MORE BROADLY LATER ON BY THE ICOC, THEN WE WOULD NEED TO BE AWARE OF THE KIND OF CONSTRUCT THAT WE

HAVE TO GIVE THE CLINICIANS, AND HOW WE DO YOU WORK TO SAMPLE POPULATIONS AND WHAT KIND OF CONSENTS WOULD YOU NEED TO DRAW FROM THEM.

WE'VE TALKED A LITTLE BIT ABOUT THIS WITH DREW UNIVERSITY, WITH SOME OTHER PEOPLE, THE KIND OF WHAT ARE THE PROBLEMS OF GETTING CONSENT. IN SOME POPULATIONS IT'S MORE DIFFICULT THAN OTHERS. GIVING THEM A LOT OF WRITTEN MATERIAL IS REALLY QUITE DIFFICULT IN SOME CASES. SO THERE ARE ELEMENTS THERE THAT ARE IMPORTANT, SO YOUR THOUGHTS AND YOUR AWARENESS AND ADVICE, I THINK, WOULD BE SOMETHING THAT WE WOULD CERTAINLY TAKE IN ON BOARD WHEN WE WERE TRYING TO FORMAT HOW WE WOULD DO IT.

MS. BAUM: I WANT TO MAKE A QUICK STATEMENT ABOUT THE INFORMED CONSENT JUST BASED ON MY COMMERCIAL EXPERIENCE. AND I WOULD AGREE WITH SHERRY LANSING, THAT I THINK LESS IS MORE. JUST FROM PAST PRACTICES, IT WOULD BE TYPICAL TO SAY THAT YOU GRANT PERMISSION FOR ANY OR ALL RESEARCH. AND WHEN YOU START LISTING ALL THE DIFFERENT TYPES OF RESEARCH, THEN YOU END UP SORT OF COMPROMISING, I THINK, THE BREADTH OF THE CONSENT BECAUSE THERE IS THE CONCERN THAT YOU WILL FORGET TO LIST SOMETHING.

ANOTHER THING THAT'S COMMON IN THOSE CONSENT FORMS IS THAT THERE'S A STATEMENT THAT SAYS

THAT YOU RELEASE AND WAIVE ALL OWNERSHIP OF ANY COMMERCIAL PRODUCT THAT RESULTS FROM THE RESEARCH. SO I JUST WANT TO MAKE SURE PEOPLE UNDERSTAND THAT WOULD BE TYPICALLY DESIRED FROM COMMERCIAL ENTITIES TO BE IN THOSE CONSENTS.

ONE OF THE ETHICAL ISSUES THAT HAS ARISEN IN THE PAST HAS NOT BEEN SO MUCH OF INFORMED CONSENT AND ETHICS IN DOING SO IN THE UNITED STATES, BUT EX-U.S. THERE ARE SOME COUNTRIES WHERE INFORMED CONSENT, SOME SAY ISN'T REALLY INFORMED, THAT IF A DOCTOR IS OVERLOOKING A PATIENT, THAT THE PATIENT WILL DO WHATEVER THE DOCTOR SAYS. AND THAT'S KIND OF WHERE SOME OF THE ETHICS ARISE. IT'S KNOWING SORT OF THE DIFFERENT CULTURAL PRACTICES AND HOW TO DEAL WITH THEM. AND UNFORTUNATELY I HAVEN'T A LOT OF EXPERIENCE IN FOLLOWING THAT ISSUE, BUT I KNOW THAT WHEN I LEFT THE COMMERCIAL FIELD, THEY WERE JUST REALLY TRYING TO STRUGGLE AND DEAL WITH THAT ISSUE, ESPECIALLY INDIA AND CHINA.

MS. LANSING: THAT WAS SOMETHING THAT WE STRUGGLED WITH, THAT IF YOUR DOCTOR -- AND I COULD NOT RECITE BECAUSE WE HAVE SUCH GOOD INFORMED CONSENT, AND I THINK SOMEONE CAN PULL IT UP, BUT THAT WAS SOMETHING WE STRUGGLED WITH WAS THAT IT COULDN'T BE YOUR DOCTOR GETTING YOU TO DONATE. THAT

WAS SOMETHING WE TOOK OUT BECAUSE THAT WOULD BE UNDUE PRESSURE PERHAPS.

DR. CYPRESS: I APOLOGIZE FOR THE SIMPLICITY. I'M GOING TO GIVE YOU THE LIST OF ALL THE THINGS THAT WE HAVE TO DEAL WITH AND ENCOUNTER THAT I THINK YOU WILL ENCOUNTER IN TRYING TO PUT THIS TOGETHER. AND SOME OF THEM HAVE BEEN STATED, AND I'M NOT GIVING YOU SOLUTIONS, BUT I'M TELLING YOU THESE ARE THE THINGS YOU'RE GOING TO HAVE TO MANAGE.

ONE, OF COURSE, IS INFORMED CONSENT, WHICH YOU'VE JUST BEEN TALKING ABOUT. THE SECOND ONE IS RESEARCH VERSUS HUMAN USE. YOU'RE DEALING WITH TWO DIFFERENT COMMUNITIES. THEY HAVE DIFFERENT SETS OF GUIDELINES AND THINGS YOU CAN DO AND YOU CAN'T DO. THE WHOLE QUESTION OF OWNERSHIP, AGAIN, WHICH IS INVOLVED IN INFORMED CONSENT, ATCC GIVES ALL THE OWNERSHIP TO THE INSTITUTION OR THE INDIVIDUAL WHO DONATES THE MATERIAL. THAT'S THE WAY WE OPERATE AND THAT CLEANS UP THE WHOLE SITUATION.

COMMERCIALIZATION RIGHTS, AGAIN, ATCC POLICY IS WE GIVE ALL THE COMMERCIALIZATION RIGHTS TO THE DONOR AND THE INSTITUTION AND WE LET THEM NEGOTIATE THAT. AND IT'S BEEN DONE VERY SUCCESSFULLY.

SOME THINGS YOU PROBABLY HAVEN'T THOUGHT ABOUT IS THE MISUSE OF YOUR NAME, YOUR TRADEMARK, AND YOUR COPYRIGHT IN PEOPLE WHO GET MATERIAL FROM YOU. YOU HAVE TO BE VERY CAREFUL HOW THEY USE THAT IN HOW THEY PROMOTE AND MARKET THEIR POSITION AND THEIR PROGRAMS.

AUTHENTICITY OF MATERIAL, BECAUSE IF IT'S NOT AUTHENTIC, IT CAN LEAD TO ALL KINDS OF PROBLEMS WHETHER CONTAMINATION OR MISIDENTIFICATION. OUTLICENSING, VERY, VERY IMPORTANT. YOU ARE GOING TO BE DOING A LOT OF OUTLICENSING OF THE MATERIAL THAT YOU HAVE, AND HOW IS THAT GOING TO WORK? WHAT IS THE RATE? AND HOW ARE YOU GOING TO MANAGE THAT?

CAME UP A MINUTE AGO. SUBSIDIZATION, ARE YOU GOING TO SUBSIDIZE THE DISTRIBUTION OF THE MATERIALS TO THE RESEARCH COMMUNITY AS NIH IS DOING FOR INFECTIOUS DISEASES? ARE YOU GOING TO PASS ON THE COST OF THE MATERIAL USE TO THE USER, WHICH IS THE POLICY OF NIH IN NONCRITICAL AREAS? SO IS THIS A CRITICAL AREA FOR YOU? IT COULD BE.

AND FINALLY, IT CAME UP A MINUTE AGO, THE WHOLE TERRIBLE ISSUE OF CONFLICTS OF INTEREST WHERE THE PATIENT COMMUNITY IS VERY, VERY SENSITIVE TO WHAT HAPPENS WHEN THE MATERIALS ARE TAKEN FROM THEM AND IN THE HANDS OF PEOPLE WHO OBTAIN THAT MATERIAL

AND THEN COMMERCIALIZE IT AND HAVE A PASS-THROUGH OR A HAND-THROUGH ON THAT MATERIAL.

SO THOSE ARE JUST GENERAL AREAS THAT I LIST. I'M NOT SAYING THAT THESE ARE ONES THAT ARE DEAL BREAKERS. THEY'RE NOT. EVERY ONE OF THESE AREAS CAN BE DEALT WITH AND HAVE BEEN DEALT WITH BY ORGANIZATIONS, BUT THESE ARE THE ONES THAT YOU NEED TO DEAL WITH.

DR. TAYLOR: SO THIS IS SORT OF A NEWCOMER'S QUESTION TO MAKE SURE THAT I'M SCALING THE PROJECT CORRECTLY. I CAN IMAGINE THREE DIFFERENT VERSIONS OF WHAT WOULD BE USEFUL, JUST AMPLIFYING YOUR QUESTION, BERNIE. ONE IS A FAIRLY MINIMALIST ETHICS ANALYSIS OF WHETHER OR NOT AREAS THAT ARE ALREADY SUBJECT TO REGULATIONS ARE ADEQUATE AS THE ETHICIST LITERATURE WOULD FIND THEM. WHAT THAT DOESN'T TAKE INTO ACCOUNT, FOR EXAMPLE, IS WHATEVER THEIR EFFECTS MAY BE ON SCIENTISTS RIGHT NOW, AND IT DOESN'T TAKE INTO ACCOUNT EMERGENT ISSUES PARTICULARLY.

TO GO TO THAT EXTREME, I CAN IMAGINE THE ETHICS LITERATURE IS AS RICH AS ONE MIGHT WANT, AND AN ANALYSIS OF A BANK, SOMETHING I HAVE A LOT OF EXPERIENCE IN, FOR THE FUTURE, UNDER ALL THOSE PARAMETERS, WOULD PRODUCE SOMETHING OF BIBLICAL

PROPORTIONS ALMOST AS LONG AS THAT LIST THAT RAY JUST GAVE OR SOME OF OUR INFORMED CONSENTS. THERE'S SOMETHING IN THE MIDDLE WHICH IS MORE FUNCTIONALLY DEFINED, AND THAT IS TAKING OFF ON YOUR POINT ABOUT REBECCA SKLOOT'S BOOK; THAT IS, TO IDENTIFY THOSE ETHICAL ISSUES THAT HAVE A POTENTIAL OF DISCREDITING IN A SENSE THE EFFORTS IN SOME FAIRLY FUNDAMENTAL WAY BECAUSE THEY PRESENT A PICTURE, SORT OF A MORAL PICTURE OF WHAT'S OCCURRED. THE LACK OF INFORMED CONSENT, THE VAST DISTRIBUTION, LACK OF COMMERCIAL BENEFIT TO A FAMILY THAT MAY DRIVE PEOPLE TOWARDS A PARTICULAR SOLUTION. LET'S GIVE OWNERSHIP RIGHTS TO FAMILIES.

SO LOOKING AT ISSUES THAT ARE EMERGENT AND IN CONFLICT WHICH COULD AFFECT SORT OF FUNCTIONALLY HOW CIRM SETS THIS UP I IMAGINE COULD BE KIND OF A MIDDLE GROUND THAT MIGHT CAUSE FOR RELOOKING AT INFORMED CONSENTS OR IT MIGHT NOT. IS THAT MIDDLE GROUND WHAT YOU HAVE IN MIND? I WANT TO MAKE SURE I DON'T PRODUCE SOMETHING OR CONTRIBUTE IN SOME WAY THAT'S INEFFECTIVE OR UNHELPFUL.

DR. TROUNSON: PATRICK, I JUST HAD TROUBLE FOLLOWING WHAT YOU ARE SAYING. IT'S MY AGE IN HEARING NOW. SO I DON'T KNOW IF ONE OF MY COLLEAGUES HEARD THAT BETTER OR UNDERSTOOD IT

BETTER. BUT MAYBE YOU CAN JUST SORT OF TARGET ON THE QUESTION.

DR. TAYLOR: REALLY THE QUESTION IS WHAT YOU WOULD LIKE, I'M REALLY FOLLOWING UP ON BERNIE'S QUESTION. YOU WANT ETHICS THAT'S USEFUL TO ISSUES THAT MAY ARISE, MAYBE SOME ON THE HORIZON, MAYBE SOME NOT, THAT MIGHT DISCREDIT.

MS. LANSING: I GUESS I CAN EVEN ADD TO THIS. I'M SORRY TO JUMP AHEAD OF THE LINE. WHAT IS IT THAT YOU DON'T FEEL THAT WE'VE COVERED IN THE INFORMED CONSENT AS WE ENTER INTO THIS BANKING AREA BECAUSE HONESTLY, AGAIN, I ALWAYS SPEAK WITH THE KNOWLEDGE WITH A LAYPERSON, SO EXCUSE ME FOR THAT, BUT HONESTLY --

MR. TORRES: THE OLD COUNTRY DOCTOR.

MS. LANSING: WE HAVE SUCH RIGOROUS INFORMED CONSENT. IT CAN'T JUST BE USED FOR ANY OLD RESEARCH. IT HAS TO BE USED FOR RESEARCH FOR THE DISEASE GROUPS. IT GOES DOWN VERY CAREFULLY THE DOCTOR CAN'T GET YOUR LINE. WE WENT THROUGH THIS. WHAT IS IT WHEN YOU'RE -- WE WANT TO BE HELPFUL. AS WE ENTER INTO THIS POSSIBLE NEW WORLD, AS MARCY SAID, WHAT IS IT THAT YOU FEEL THAT WE'RE MISSING IN OUR INFORMED CONSENT, AND MAYBE WE ARE NOT?

DR. WAGNER: BECAUSE ONE THING THAT'S NOT

IN THE INFORMED CONSENT IS THAT IF WE'RE TALKING ABOUT GENETIC DISEASES, AS SOME OF THE THINGS THAT YOU WERE ADDRESSING, SOME OF THOSE DISEASES OCCUR ONLY IN CHILDREN. SO THEN YOU HAVE A PEDIATRIC DONOR WHO CANNOT GIVE CONSENT HIMSELF. IT WOULD NOT HAVE COME UP IN THE PRIOR STEM CELL SOURCES.

CHAIRMAN LO: THERE ARE PARTICULARLY ISSUES OF WHEN THE PEDIATRIC DONOR BECOMES OF AGE AT 18 AND HE/SHE DECIDES THAT, GOSH, I REALLY DON'T AGREE WITH WHAT MOM AND DAD DID. MAY THEY WITHDRAW CONSENT FOR THE STEM CELLS? THERE ARE PARTICULAR ISSUES HAVING TO DO WITH SURROGATE CONSENT FROM PARENTS.

I GUESS, JOHN, TO ADD ON ANOTHER ISSUE IS THERE MAY BE CONSENT -- THERE MAY BE LINES DERIVED FROM PEOPLE WHO CANNOT -- ADULTS WHO CANNOT GIVE CONSENT THEMSELVES BECAUSE THEY HAVE A SEVERE NEUROLOGICAL DISEASE THAT'S ALREADY MANIFEST THEMSELVES. AND SO WHEN YOU GET SURROGATE CONSENT, ARE THERE PARTICULAR -- IT'S AN OPEN QUESTION, I THINK. SHOULD THERE BE ADDITIONAL PRECAUTIONS TAKEN WHEN THE PERSON GIVING THE PERMISSION FOR THE STEM CELL DERIVATION, PROCUREMENT AND DERIVATION, ISN'T THE PERSON FROM WHOM THE CELLS ARE TAKEN?

MS. LANSING: I THINK THAT'S A REALLY

VALID THING.

DR. WAGNER: THAT'S THE ONLY THING I CAN THINK OF THAT WOULD BE IMMEDIATELY DIFFERENT.

MS. LANSING: THAT'S THE ONLY THINK I CAN THINK OF. YOU CAN SAY -- I KNOW WHERE I'D COME OUT ON IT QUICKLY. YOU CAN SAY A CHILD, A PARENT HAS THE RESPONSIBILITY FOR THE CHILD IN ALL WAYS UP TO A CERTAIN AGE WHEN THE CHILD BECOMES FREE, WHICH I GUESS IS EITHER 16 OR 18 DEPENDING ON THE STATE. AND I DON'T THINK THAT YOU SHOULD BE ABLE TO WITHDRAW WHEN YOU'RE 18 YEARS OLD.

DR. WAGNER: SO FOR MOST OF THOSE CIRCUMSTANCES, THE CHILD ONCE BECOMING 18 CAN WITHDRAW CONSENT, AND WE ACTUALLY HAVE TO RECONSENT PATIENTS ONCE THEY HIT THAT AGE. SO IT IS A RISK THAT YOU COULD HAVE DEVELOPED A CELL LINE THAT MAY BE SPECTACULAR AND SOME DISCOVERY THAT THEN NO LONGER IS AVAILABLE TO YOU. AND MANY OF THESE DISEASES, HOWEVER, THE CHILDREN WON'T SURVIVE. SO THAT PROBABLY BECOMES LESS OF AN ISSUE.

I THINK IN THE CIRCUMSTANCE THAT YOU'RE BRINGING UP IN TERMS OF ADULTS WHO HAVE A SURROGATE CONSENTER, THEY'RE PROBABLY IN A CIRCUMSTANCE WHERE THEY'RE NOT GOING TO GET BETTER. SO THAT MAY BE A BIT DIFFERENT. BUT SOME OF THESE CASES OF GENETIC

DISEASES, THEY COULD LIVE UNTIL THEY'RE 18 AND BE FUNCTIONAL. EVEN IF THEIR LIFE IS SHORTENED, IT MAY NOT BE SHORTENED IN EVERY CASE.

DR. TROUNSON: WELL, I THINK WHEN WE THINK BACK TO THE CONSENT THAT YOU GET WITH THE EMBRYOS FOR EMBRYONIC STEM CELLS, THERE'S USUALLY VERY WELL-STRUCTURED PROCESSES THERE BECAUSE THEY'RE VERY USED TO GETTING THAT CONSENT. WHEREAS, MAYBE FROM THE RANGE OF SOURCES THAT WE MIGHT BE GETTING, INCLUDING SOME OF THOSE THAT JOHN JUST RAISED OR VERY SICK PEOPLE, THERE COULD BE A MUCH WIDER RANGE OF BOTH THE CLINICIANS AND THE PATIENTS BEING SAMPLED. AND I THINK WE WOULD LIKE TO STICK TO THE SAME CONSENT PROCEDURES AND ENABLE, EVEN IN POPULATIONS THAT ARE NOT USED TO READING LONG CONSENT FORMS, TO GIVE SOME OTHER PROCESS TO GET THROUGH THEIR CONSENT GIVING.

BUT TO KEEP TO THAT, EVEN I THINK IF IT WAS PROSPECTIVE, OF COURSE, EVEN WITH OUR INTERNATIONAL COLLEAGUES OR INTERSTATE COLLEAGUES TRYING TO GET EXACTLY THE SAME SET OF CONSENT PROVIDED, AND THERE'S NO REASON WHY WE SHOULDN'T BE ABLE TO DO THAT. I THINK UNDER THOSE CIRCUMSTANCES, WE CALL THAT THE SIMPLE THING, I THINK THEN IF THERE ARE VARIATIONS WHICH TURN UP IN DUE COURSE IS

SOMETHING THAT WE CAN THEN RAISE WITH YOU AGAIN IF IT SEEMS TO BE A DIFFICULTY.

SO I GET THE -- I HAVE THE STRONG FEELING THAT THE CONSENT THAT WE WORKED OUT FOR THAT THAT WAS BASED ON THE EMBRYO DONATION PROGRAM WOULD SUIT WITH THE IPS PROGRAM. GOING FORWARD, KEEP IT CONSISTENT, KEEP IT SIMPLE, CONSISTENT, AND IT WILL WORK PRETTY WELL FOR US. I THINK THERE ARE LOTS OF OTHER ISSUES THAT WE HAVEN'T EVEN TRIED TO EXPLORE ABOUT. IF WE ARE STILL IN SOME SORT OF CONTROL, WHAT WE DO WITH THE PROVISION OF THE MATERIALS TO EACH AND EVERYBODY, INCLUDING COMPANIES AND PHARMACEUTICALS AND SO ON, I THINK THEY'RE DIFFERENT QUESTIONS. BUT ON THIS CONSENT, SIMPLE AS IT IS, I THINK THAT THAT'S THE MESSAGE WE ARE GETTING STRONGLY FROM EVERYONE. AND THAT FOR AS LONG AS YOU GET A REASONABLE SAMPLE OF THE POPULATION IF THE CONSENT CAN BE GOT IN ESSENTIALLY THE SAME WAY.

MS. LANSING: SO THE ONLY ISSUE THAT I SEE, I AGREE WITH WHAT YOU SAID, AND I OBVIOUSLY WANT TO KNOW IF ALL OUR COLLEAGUES AGREE WITH THAT. BUT THE ONLY ISSUE IS THE ONE THAT YOU BROUGHT UP, WHICH IS WHAT DO WE DO ABOUT A LINE, AND I DO THINK THAT IS SOMETHING WORTH DISCUSSION, OF A CHILD WHEN THEY TURN 18. AND DO WE HAVE THAT IN OUR -- I DON'T

THINK WE COVERED THAT. WE DID NOT COVER THAT. SO THAT WOULD BE WE HAVE THIS WONDERFUL LINE. DOES THE NOW ADULT HAVE THE RIGHT TO RECLAIM THE LINE, OR ARE THEY BOUND TO THE PROVISIONS THAT THEIR PARENTS MADE?

CHAIRMAN LO: IT SOUNDS LIKE ONE THING WE SHOULD CERTAINLY DO IS SORT OF ASK GEOFF TO REALLY LOOK AFRESH AT OUR CURRENT PROVISIONS FOR CONSENT TO DONATE MATERIALS USED TO DERIVE PLURIPOTENT LINES AND SAY IN THE CONTEXT OF A POTENTIAL STEM CELL BANK THAT CIRM IS INVOLVED IN, ARE THERE ISSUES THAT WARRANT RECONSIDERATION? JOHN RAISED ONE WITH REGARD TO CHILDREN, CHILD DONORS REACHING THE AGE OF MAJORITY. ANOTHER ISSUE MIGHT BE SORT OF WHAT PEOPLE ARE TOLD BEFORE THEY'RE ASKED FOR CONSENT. ONE COULD ARGUE THAT A BROAD CONSENT IS CERTAINLY USEFUL SCIENTIFICALLY. PLEASE TRUST US TO DO OPEN-ENDED -- BROAD, OPEN-ENDED RESEARCH WITHOUT SPECIFYING. BUT THEN YOU COULD ARGUE THAT WHAT THEY'RE TOLD, THE KINDS OF THINGS THAT MIGHT BE DONE INCLUDE, NOW THAT YOU'VE HEARD ALL THAT, THOUGHT ABOUT IT, TALKED ABOUT IT WITH US, DO YOU CONSENT.

SO WE NEED TO SEPARATE SORT OF A BROAD DISCLOSURE FROM ALL KIND OF CONVERSATION TAKES PLACE IN TERMS OF INFORMATION.

DR. ROBERTS: THAT'S EXACTLY THE POINT I WAS THINKING ABOUT, BERNIE, BECAUSE YOU DON'T -- WHAT YOU WANT TO AVOID IS THE SITUATION WHERE YOU TELL SOMEONE YOUR BODY MATERIAL IS GOING TO BE USED FOR -- YOUR LINES -- YOUR CELLS ARE GOING TO BE USED FOR A PARTICULAR TYPE OF RESEARCH AND THEN THE RESEARCHER USES IT FOR SOMETHING ELSE. THAT'S WRONG. THAT'S UNETHICAL. WE JUST HAVE SEEN AN EXAMPLE OF THAT IN THE PRESS WITH THE HAVASUPAI INDIAN TRIBE IN ARIZONA WHO WAS TOLD WE'RE USING YOUR GENETIC MATERIAL FOR DIABETES RESEARCH, AND THEN IT'S USED FOR SCHIZOPHRENIA RESEARCH AND ALCOHOL RESEARCH AND ANCESTRY AND ALL OF THIS, AND IT TURNS INTO A LAWSUIT.

AND IN MY OPINION IT WAS UNETHICAL TO USE THEIR GENETIC MATERIAL FOR SOMETHING THAT THEY WEREN'T TOLD IT WAS GOING TO BE USED FOR. AND SO YOU WANT THE INFORMED CONSENT TO TELL THE DONOR WHAT THEIR MATERIAL WILL BE USED FOR. AND ONE WAY OF AVOIDING THE MISREPRESENTATION IS TO SAY, LOOK, IT'S GOING TO BE USED FOR RESEARCH AND RESEARCH IS RESEARCH. THAT'S ONE. BUT THEN THAT'S ONLY IF THEY KNOW WHAT THAT MEANS, RESEARCH IS RESEARCH.

MS. LANSING: THAT'S WHY -- AGAIN, MAYBE IT WOULD BE HELPFUL ALSO, GEOFF, IF YOU PULL UP ALL

THE STUFF. WE WENT THROUGH REALLY INFORMED CONSENT. IT WASN'T JUST PAPER. IT WAS DIALOGUE, IT WAS CONVERSATION, AND RESEARCH TO HELP IN THE DISEASES. IT'S NOT RESEARCH -- I CAN'T THINK -- TO BUILD A CAR. IT'S LIKE WHATEVER IS TO HELP WITH DISEASE GROUPS. AND ACTUALLY I THINK THERE'S EVEN SOMETHING THAT SAYS, NO, WE CANNOT EVEN EXPLAIN TO YOU WHAT IT'S GOING TO BE BECAUSE THE FIELD IS MOVING SO FAST. IT WAS REALLY IN ITS GENERALITY VERY SPECIFIC, IF YOU KNOW WHAT I'M SAYING.

I THINK, AGAIN, AS A LAYPERSON, I WOULDN'T UNDERSTAND HALF THE STUFF THAT THEY WERE SAYING. AND THEN I WOULD GET TERRIFIED. AND I WOULD GO, OH, MY GOD. DO YOU KNOW? IT SAYS CAN'T CLONE. THAT'S PART OF OUR BYLAWS. BUT I CONSTANTLY HAVE TO REMEMBER WHAT IPS IS. WE'RE JUST NORMAL PEOPLE, AND YOU'RE SAYING I WANT TO DO GOOD. I WANT TO GIVE MY CELLS FOR SCIENTIFIC RESEARCH, OR I WANT TO HELP. AND YOU HAVE THE RIGHT TO SAY IT CAN ONLY BE USED FOR CERTAIN THINGS. YOU ACTUALLY HAVE THAT RIGHT. AND AGAIN, I DON'T WANT TO BELABOR THIS. I THINK IT WOULD BE REALLY HELPFUL TO PULL UP, FOR GEOFF TO PULL UP WHAT WE DID.

AND THE ONE ISSUE I DON'T THINK WE EVER ATTACKED WAS WHEN THE PERSON TURNS 18, YOU KNOW,

PEDIATRIC LINES. BUT I WOULD BE VERY NERVOUS TO BE MORE SPECIFIC THAN RESEARCH FOR THESE DISEASE AREAS.

DR. ROBERTS: THERE IS THAT TENSION BECAUSE IF YOU'RE REAL SPECIFIC, THEN YOU'RE BEING UNETHICAL IF YOU GO BEYOND WHAT YOU SPECIFICALLY TOLD THE PATIENT IT'S GOING TO BE USED FOR. BUT ON THE OTHER HAND, IT IS IMPORTANT TO ENSURE THAT THE PATIENT HAS AN IDEA OF -- SOME IDEA OF WHAT THE POSSIBILITIES ARE. BECAUSE IF A PATIENT -- IF A DONOR, MAY NOT BE A PATIENT, IF A DONOR HAS IN MIND MY TISSUE IS GOING TO BE USED FOR A PARTICULAR KIND OF RESEARCH AND IT ENDS UP CREATING A PRODUCT THAT DOES SOMETHING THAT'S VERY DIFFERENT FROM WHAT THE PATIENT HAD IN MIND, THEN IT WASN'T REALLY INFORMED CONSENT.

MS. LANSING: IF THE PATIENT HAS AN IDEA AND, AGAIN, WE SHOULD LOOK AT THIS, IF A PATIENT SAYS, WELL, YOU KNOW WHAT. I ONLY WANT MINE USED FOR CANCER RESEARCH. THEY CAN WRITE THAT DOWN, AND THEN THAT'S ALL IT CAN BE USED FOR. AND THEY HAVE THE RIGHT TO OPT AND BE VERY SPECIFIC. AND I'M SURE PEOPLE DO DO THAT. BUT THERE WERE SO MANY -- ANN, REMEMBER, WE HAD SO MANY PEOPLE EXPLAINING THINGS OVER AND OVER AGAIN, NOT JUST ONE VISIT, TWO VISITS. I CAN'T REMEMBER ALL OF IT, BUT IT WAS VERY, VERY,

VERY SPECIFIC.

SO I THINK -- AND THEN I'M GOING TO STOP TALKING. BUT THEN I THINK WE SHOULD PULL THIS UP AND LOOK AT IT AGAIN AND SEE WHAT NEW ISSUES. BUT I THINK, ALAN, YOU'RE RIGHT IN WHAT YOU SAID AT LEAST INITIALLY.

DR. TROUNSON: I SUPPOSE, SHERRY, THERE COULD BE SOME CLINICIANS MAY HAVE COLLECTED TISSUES OVER A LONG PERIOD OF TIME FOR PATHOLOGIES. SO THEY MIGHT BE IN THAT CATEGORY, THAT THEY WERE COLLECTED FOR PATHOLOGICAL PURPOSES. THOSE PATIENTS MIGHT HAVE DIED AND SO ON. I DIDN'T ENVISAGE THAT THAT'S WHAT WE'D ACCESS. BUT I SUPPOSE THAT WE WOULDN'T HAVE THOUGHT OF THAT PREVIOUSLY EITHER, THAT THEY MIGHT HAVE COME FROM MATERIALS THAT WERE DERIVED FOR, SAY, PATHOLOGY PURPOSES THAT WERE JUST KEPT BY A CLINICIAN IN A LARGE BANK. BASICALLY THEY'RE INTERESTED IN MAYBE LOOKING AT THE GENOME OR SOMETHING LATER ON.

SO THERE ARE, I SUPPOSE, SOME OTHER CIRCUMSTANCES WHICH MIGHT -- THAT THEMSELVES MIGHT BE VALUABLE FOR THE PURPOSES, BUT IT WOULD BE DIFFICULT TO ENVISAGE THAT ANY KIND OF CONSENT CLEARLY COULD BE GOTTEN REALISTICALLY.

DR. TAYLOR: I FEEL LIKE I DIDN'T DRINK

ENOUGH COFFEE TODAY PROBABLY. I JUST WANT TO MAKE SURE I'M ON THE SAME PAGE. IT SOUNDS LIKE IN THE CONTEXT OF REGULATIONS DEVELOPED FOR NONBANKING PURPOSES, PART OF THE TASK REALLY IS TO IDENTIFY THOSE ISSUES WHICH ARISE BECAUSE OF THE BANKING CONTEXT. IN THAT WAY, IT'S ALMOST AN EASY QUESTION TO ANSWER BECAUSE A LOT OF PEOPLE ARE DOING THIS. SO CERTAIN KINDS OF QUESTIONS ARE NOW WELL GROUNDED IN TERMS OF WHO'S ASKING THEM.

ONE OF THEM, BERNIE, THAT YOU MENTIONED WAS RESEARCH RESULTS. THERE'S A SUBSTANTIAL GROUP OF ARGUERS IN THE CONTEXT OF THESE KINDS OF BANKS, YOU SHOULD -- YOU HAVE AN ETHICAL, LEGAL DUTY, SOME SAY, TO RETURN RESEARCH RESULTS. A SECOND ONE IS PRIVACY, ONE WE REFERRED TO BEFORE. SO GENOMEWISE ASSOCIATION STUDIES BECAUSE OF THE POWER OF THE GENE OR SPECIAL QUESTIONS ABOUT PRIVACY AND DEIDENTIFICATION AND WHAT TO DO ABOUT THAT ISSUE.

THIRD ONE ARISES FROM THEIR LONG-TERM POWER. NOVEL USES, THE QUESTION THAT YOU WERE RAISING, THE QUESTION OF WHEN IS INFORMED CONSENT FULLY INFORMED WHEN IT'S BLANKET? THERE'S A SUBSTANTIAL GROUP OF PEOPLE SAYING A BLANKET CONSENT IS WHERE YOU'VE GOT TO GO, BROAD IN GENERAL. AND UNCERTAINTY IS PART OF WHAT PEOPLE ACCEPT. OTHER

PEOPLE TAKING A VERY SIGNIFICANTLY DIFFERENT VIEW ALL ENHANCED BY THE EXTRAORDINARY POWER THAT PEOPLE SEE IN SUCH BANKS LONG TERM TO CREATE NEW SCIENCE, NEW KNOWLEDGE, NEW DISCOVERIES.

ANOTHER ONE IS THE USE OF EXCESS CLINICAL SAMPLES AND AVAILABLE, WHETHER OR NOT YOU CAN ACTUALLY BANK THINGS, IN EFFECT, WITHOUT ANY INFORMED CONSENT WHATSOEVER BECAUSE IT FOLLOWS THE TRADITIONAL PARADIGM OF EXCESS CLINICAL USES. THERE ARE WHOLE EFFORTS UNDER WAY TO BUILD SUCH SYSTEMS RIGHT NOW WHICH MAY COLLAPSE IF REGULATIONS AND ETHICISTS GO THE OTHER WAY.

LAST ONE IS ALSO THE ROLE OF A BANK IN EXERTING POWER WITH RESPECT TO THINGS LIKE ACCESS, QUALITY, AND COST. SO CERTAINLY IT AROSE TO MY INSTITUTION AND OTHER INSTITUTIONS. WHAT'S THE RESPONSIBILITY? IS IT TO BE SIMPLY A PASS-THROUGH WITH RESPECT TO INTELLECTUAL PROPERTY ISSUES OF THE SORT PROFESSOR GRAFF WAS TALKING ABOUT THAT RAISE QUASI ETHICAL ISSUES? IS THERE SOMETHING MORE? FOR A PUBLICLY FUNDED AGENCY, THERE'S A LITERATURE THAT'S RICHER ABOUT WHETHER THERE IS SOME OBLIGATION TO PROTECT THE PUBLIC'S INTEREST THROUGH THAT KIND OF NONPASSIVE EFFORT.

CHAIRMAN LO: LET ME MAKE ANOTHER

PROPOSAL. I'M SORT OF PUTTING EVERYTHING ON GEOFF HERE. I THINK PATRICK IS ABSOLUTELY RIGHT. IF YOU LOOK AT BIOBANKING, I GUESS, IS THE GENERIC TERM WHERE PEOPLE HAVE AMASSED BIOLOGICAL SPECIMENS OFTEN WITH RICH CLINICAL ANNOTATIONS FOR RESEARCH USE, THEY'VE ADDRESSED THE ISSUES THAT PAT HAS DEALT WITH. AND MAYBE WE CAN ASK GEOFF TO SUMMARIZE FOR US WHAT ARE THOSE SALIENT ISSUES AND HOW THEY'VE BEEN HANDLED. WHAT'S SORT OF THE BEST PRACTICE OR CONSENSUS WITH REGARD TO BIOBANKS AND WHAT LESSONS WE WANT TO TAKE OVER TO THIS PARTICULAR CONTEXT?

MS. LANSING: I HAD TWO THINGS TO SAY. I'M GOING TO LET GEOFF TAKE MOST OF THEM. YOU DON'T HAVE TO CONSENT TO HAVE RESEARCH. THERE'S NO GUN BEING HELD TO YOUR HEAD. THAT'S REALLY IMPORTANT TO KNOW. GEOFF, WHY DON'T YOU JUST READ WHAT WE HAVE A LITTLE BIT THAT YOU SAID BECAUSE IT SAYS AT ONE POINT IT CAN BE USED FOR THINGS THAT WE CAN'T SEE IN THE FUTURE THAT WE CAN'T EVEN TELL YOU ABOUT.

DR. LOMAX: I APOLOGIZE. THIS IS GEOFF LOMAX. THE ONE MEETING WE FORGOT TO INCLUDE A COPY OF THE STANDARDS, OF COURSE, THIS ISSUE COMES UP. IT IS HELPFUL JUST TO TICK THROUGH A COUPLE OF THE REQUIRED STATEMENTS IN THE CONSENT FORM WHERE IT'S DEEMED APPLICABLE. YOU HAVE TO INDICATE TO THE

DONOR WHETHER OR NOT THEIR IDENTITIES WILL BE ABLE TO BE ASCERTAINED, AND THERE'S A LONGER SECTION IN THERE, BUT IT'S ABOUT WHETHER OR NOT ANYONE WILL BE ABLE TO IDENTIFY THE CELL LINE.

HERE ARE THE CRITICAL COUPLE ONES THAT I THINK ARE PERTINENT TO WHAT YOU'VE JUST BEEN DISCUSSING. CELL LINES MAY BE USED IN FUTURE STUDIES WHICH ARE NOT NOW FORESEEABLE. SO THAT WAS THE LANGUAGE TO TRY TO CAPTURE WE DON'T HAVE A CRYSTAL BALL IN SCIENCE. DERIVED CELL PRODUCTS MAY BE USED IN RESEARCH INVOLVING GENETIC MANIPULATION, AND DERIVED CELLS OR CELL PRODUCTS MAY BE TRANSPLANTED INTO ANIMALS AND HUMANS. THEN THERE'S A DISCLOSURE A BIT FURTHER ALONG THAT IF THERE ARE COMMERCIAL PRODUCTS, YOU HAVE NO RIGHTS TO THE FINANCIAL BENEFIT. AND THERE'S A CLEAR DISCLOSURE THAT THE PRODUCTS MAY NOT HAVE ANY BENEFIT TO YOU.

I THINK THAT WAS -- AGAIN, THIS IS VERY MUCH OUT OF THE NATIONAL ACADEMIES. SO I THINK WE BORROWED FROM THE SORT OF CONSENSUS VIEW AT THE TIME. CERTAINLY I WELCOME THE OPPORTUNITY TO GO BACK AND REEVALUATE IT. AND I APPRECIATE ROSIE HAS SORT OF BEEN ON BOARD TO HELP US DO THAT, AND SHE'S GOT THE CONNECTION TO THE BIOBANKING WORLD AND THE GROUP IN MONTREAL. I THINK WE'RE IN EXACTLY THE

POSITION WE WANT TO BE IN TO SORT OF FOLLOW THROUGH ON THESE RECOMMENDATIONS. AND THERE ARE A NUMBER OF POINTS HERE THAT WE CAN TAKE TO HEART AS WE MOVE FORWARD.

DR. ISASI: I THINK THAT IS ESSENTIAL.

CHAIRMAN LO: CAN YOU IDENTIFY YOURSELF FOR PEOPLE ON THE PHONE?

DR. ISASI: ROSE ISASI FROM MCGILL UNIVERSITY AND INTERNATIONAL STEM CELL FORUM. ONE ISSUE THAT WE NEED TO ADDRESS IS LOOKING AT THE GENERAL BIOBANKING PARADIGM WHETHER THERE ARE ISSUES THAT COULD BE EXTRAPOLATED OR NOT BECAUSE WE ARE TAKING THE APPROACH THAT IS A MISTAKE TO SAYING, WELL, THIS WAS SORTED IN THE BIOBANKING FIELD. WE JUST CUT AND COPY AND PASTE AND THE STEM CELL. THERE'S UNIQUE ISSUES ARISING IN THE STEM CELLS EVEN FOR GOING BACK TO PATRICK, THE ISSUE OF PRIVACY AND IDENTIFIABILITY. WE HAVE TO REAPPRAISE THEM IN THE CONTEXT OF STEM CELLS AND DEPENDING ON THE SOURCES OF THE LINES AND THEIR USES IN THE CONTEXT OF INFORMED CONSENT FOR SECONDARY USES.

BUT ANOTHER THING IS SOMETHING THAT I WOULD LIKE TO, THERE'S NO TIME TO DEVELOP, BUT TO RAISE. YOU MENTIONED, PATRICK, THAT THERE IS INDIVIDUAL RETURN OF RESULTS. JUST THE ISSUE OF

INCIDENTAL FINDINGS SO THEIR REACTION IS JUST ANOTHER BULLET POINT TO INCLUDE FOR LATER DEBATE FOR APPRAISAL. AND IN THE STEM CELL FIELD, IT'S WAY MORE COMPLICATED. IF THE JURY IS STILL OUT FOR THE BIOBANKING CONTEXT, IMAGINE FOR STEM CELL RESEARCH. AND THE ISSUE WHERE YOU ARE TALKING ABOUT IPS CELL LINES, WHAT IS EASIER, IN QUOTATIONS, TO GO BACK TO THE ORIGINAL DONOR. WHAT DO YOU CONSIDER A RESULT WHERE MERIT BRINGING BACK AND WHAT YOU CONSIDER IN THE FINDING THAT YOU ARE IN A LEGAL OR MORAL OBLIGATION TO DISCLOSE TO THE DONORS?

THIS IS SOME ISSUES, AND I THINK THAT WILL BE SOMETHING VERY INTERESTING TO LOOK. AND THESE ISSUES HAVE BEEN HIGHLIGHTED AS A MAIN CONCERN FOR BANKERS. THE UK STEM CELL BANK, FOR EXAMPLE, HAVE ASKED US TO LOOK INTO HOW WE DEAL WITH INDIVIDUAL RETURN ON RESEARCH AND INCIDENTAL FINDINGS AND LOOKING AT -- I DID A CURSORY LOOK AT 16 STEM CELL BANKS, HOW THEY DEAL WITH THIS. AND ONLY A COUPLE OF THEM HAVE POLICIES ON THE ISSUE. AND THE NATIONAL ACADEMY OF SCIENCE IS ONE OF THE FEW WITH PROSPECTIVE POLICY ON THAT WE SHOULD NOT FORGET.

DR. WAGNER: I DON'T KNOW THAT I KNOW WHETHER THIS IS DUPLICATIVE OR FROM PRIOR CONVERSATIONS, BUT IS THERE SOMETHING FUNDAMENTALLY

DIFFERENT ABOUT THE CONSENT PROCESS THAT WAS PREVIOUSLY DISCUSSED WITH ES-DERIVED CELLS? EVEN IF IT WAS DISEASED ES-DERIVED CELLS, ES CELLS, FROM A PGD EMBRYO WHERE THE CHILD TO BE DOESN'T EXIST AS COMPARED TO TAKING A PATIENT WITH AN IPS CELL THAT HAS A DISEASE, YOU COULD IMAGINE THAT THE REASON FOR THE DONATION IS GOING TO BE DRIVEN IN A VERY DIFFERENT WAY. OBVIOUSLY HOPING FOR SOME TYPE OF TREATMENT THAT WOULD EVENTUALLY BE USEFUL FOR THAT INDIVIDUAL.

IT JUST FEELS LIKE THE CONSENT PROCESS MIGHT NOT BE QUITE THE SAME AS WHAT WE PREVIOUSLY HAVE DESIGNED.

DR. TAYLOR: TWO THINGS. OF COURSE, SINCE YOU DID THIS WONDERFUL CONSENT GUIDELINES, THE NIH ACTUALLY SPOKE TO THE ISSUE AS WELL. SO I'M WONDERING IF IT WOULD BE USEFUL TO JUST GO BACK AND LOOK AT THEM IN THE LIGHT OF NIH'S TEACHINGS ON THIS ISSUE, WHICH CONCERNED NOT JUST THE SCOPE, BUT ALSO THE MULTIPLE OCCASIONS CONSENTS.

SECONDLY, IN THAT PROCESS, AND DR. LO IS INVOLVED IN THIS, THERE'S ALSO A SORT OF FORGIVENESS SET OF PROVISIONS ACTUALLY RISING FROM SOME OF HIS WORK AND SOME OTHERS, THAT TO THE EXTENT THAT LINES DON'T ACTUALLY MEET ALL THE CRITERIA THAT MIGHT BE

ARTICULATED BECAUSE OF DIFFERENT CUSTOMS, DIFFERENT LOCALE, THAT WAS BERNIE'S PAPER, OR TIME, THERE MIGHT BE SOME ABILITY TO LOOK AT ETHICAL FUNDAMENTALS AND NONETHELESS FUND THEIR USE. SO I THINK THERE'S AT LEAST A QUESTION ABOUT WHETHER OR NOT YOU WANT TO OR DON'T WANT TO ADOPT SUCH A PROCESS.

CHAIRMAN LO: I JUST WANT TO REMIND THE WORKING GROUP THAT WE TOOK THAT GRANDPARENTING APPROACH WITHIN SWG, AND CIRM ADOPTED THAT. WE SAID THAT THERE ARE STANDARDS THAT WERE IN PLACE AT THE TIME THE CELLS WERE DONATED, AND WE DIDN'T WANT TO SORT OF RETROSPECTIVELY GO BACK AND IMPOSE TODAY'S STANDARDS, BUT WE SET A LINE GOING FORWARD WE DID WANT TO HAVE CERTAIN CRITERIA FOR CONSENT SO THAT THAT'S A PRECEDENT WE'VE SET WHICH WE COULD GO BACK TO AGAIN IF WE THOUGHT THAT WAS USEFUL FOR MATERIALS THAT WERE DONATED SOME TIME AGO.

DR. TAYLOR: NIH, FOLLOWING THAT EXAMPLE, TREATED THE ISSUE OF GEOGRAPHIC DIVERSITY THE SAME WAY, SAYING AS OF A GIVEN DATE, WE WILL ACCEPT THINGS TREATED ELSEWHERE UNDER CERTAIN STANDARDS. THE OPEN QUESTION, I THINK, WOULD BE WHETHER OR NOT IF ON AN ONGOING BASIS, THERE CONTINUES TO BE GEOGRAPHIC DIVERSITY, YOU WANT SOME PROCESS FOR

LOOKING AT ETHICAL FUNDAMENTALS AS OPPOSED TO A POINT IN TIME PROCESS BEFORE WE'LL ACCEPT THEM AND AFTER WE WON'T. SO THEY TREATED TIME AND DIVERSITY THE SAME WAY.

CHAIRMAN LO: I HAVE DR. PRIETO AND THEN SENATOR TORRES.

DR. PRIETO: RESPONDING TO JOHN'S POINT, I THINK THERE IS A SIMILARITY BETWEEN WHAT WE CAME UP WITH TALKING ABOUT ES CELLS AND IPS CELLS, THAT ETHICALLY YOU CAN'T MAKE A PROMISE TO SOMEONE THAT YOU DON'T KNOW YOU WILL BE ABLE TO KEEP. AND SO YOU HAVE TO TELL DONORS IN EITHER SITUATION THAT YOU MAY NOT BENEFIT IN ANY WAY DIRECTLY FROM THIS, AND YOU HAVE TO MAKE THIS DONATION KNOWING THAT YOU MAY HAVE NO DIRECT BENEFIT. I THINK THAT'S THE SAME IN EITHER CASE.

DR. WAGNER: IF I MAY RESPOND TO THAT, THE QUESTION REALLY IS -- I AGREE WITH THAT ENTIRELY, BUT MY CONCERN IS REALLY THE FEELING OF URGENCY FROM THE INTERNAL CONFLICT OF GIVING CONSENT ALMOST IN A COMPULSORY WAY BECAUSE OF THE POTENTIAL BENEFIT EVEN THOUGH THEY KNOW THERE MAY NOT BE BENEFIT. MY ONLY POINT IS REALLY, I DON'T KNOW THE ANSWER, BUT MAYBE THIS IS NOT WORTH TOO MUCH DISCUSSION RIGHT NOW, BUT THIS REALLY HAS MORE TO DO WITH THE CONSENT PROCESS

ITSELF THAN IT DOES THE CONSENT FORM.

DR. PRIETO: I THINK THAT SPEAKS TO THE DONOR'S MOTIVATION. I THINK YOU HAVE TO REMOVE YOURSELF FROM -- YOU CAN NEVER COMPLETELY KNOW A PERSON'S INNERMOST MOTIVATION.

DR. WAGNER: EXCEPT REMEMBER, THOUGH, THAT IT IS IN A WAY, I THINK, UNPRECEDENTED TO DEVELOP CELL LINES THAT MIGHT POTENTIALLY HAVE BENEFIT TO YOURSELF.

MR. TORRES: I THINK IT'S APPROPRIATE FOR AT LEAST NEW BOARD MEMBERS, AT LEAST FOR A YEAR AND A HALF NOW, BUT OTHERS AS WELL, THAT WE HAVE IN FRONT OF US CASE LAW THAT WE CAN REFER TO BECAUSE I KNOW THERE HAVE BEEN SOME CASES IN THIS AREA. NO. 2, JUST WHAT THE NIH HAS ADOPTED, WHAT OTHER STATES HAVE ADOPTED, AND, QUITE FRANKLY, WHAT OTHER INTERNATIONAL ORGANIZATIONS HAVE ADOPTED BECAUSE I BELIEVE, DR. WAGNER, THAT IT'S BOTH FORM AND PROCESS, THAT THE FORM, AS I INDICATED EARLIER, THE CONCERNS OF DREW UNIVERSITY DOCTORS WERE WITH 48 PERCENT OF PEOPLE BEING FUNCTIONALLY ILLITERATE, WHAT IS NATURE OF THE FORM GOING TO TAKE SO THAT IT'S CLEAR IN TERMS OF ITS UNDERSTANDING. NO. 2, THE PROCESS BY WHICH WE GET TO THAT POINT, AND HOW DO WE AVOID CAREFULLY -- THE ONLY CASE THAT I CAN

RECALL IS THE INTERFERON CASE WHERE WE KNOW WHAT THE PROBLEMS WERE THERE. I THINK WE'VE CORRECTED MUCH OF THAT. BUT I THINK IF WE'RE GOING TO PRESENT THIS AREA TO THE BOARD, MAYBE GENERAL COUNSEL FROM THE PRESIDENT'S OFFICE THAT CAN PUT TOGETHER A MEMORANDUM TO US AND, THEREFORE, WE CAN MAKE A MORE COHERENT DECISION SO THAT THE BOARD CAN DISCUSS IT WITH EVERYTHING IN FRONT OF THEM, IF THAT'S ACCEPTABLE TO THE PRESIDENT AND GENERAL COUNSEL. THAT WAS MY ONLY CONCERN.

CHAIRMAN LO: IT SOUNDS LIKE THERE'S A COMMON THEME RUNNING THROUGH HERE THAT OTHER PEOPLE HAVE THOUGHT ABOUT THIS, EITHER IN ETHICS LITERATURE IN RUNNING A BANK, OR AS SENATOR TORRES POINTED OUT, IN ACTUAL CASE LAW OR REGULATION. AND WE SHOULD MAKE SURE WE UNDERSTAND ALL THAT AS BACKGROUND INFORMATION WHEN WE GO BACK TO RELOOK AT WHAT WE'VE DONE, OUR COMMITTEE.

MS. LANSING: OUR COMMITTEE NEEDS TO MAKE SURE THAT WE'RE COMFORTABLE FOR RECOMMENDING CERTAIN AREAS TO CHANGE.

CHAIRMAN LO: AGAIN, I THINK THIS IS A WORK IN PROGRESS. IT MAY WELL BE THAT WE SAY HERE'S AN ISSUE THAT WE THINK HAS A YELLOW OR RED FLAG ATTACHED TO IT, AND WE STILL MAY WANT TO PROCEED,

BUT WE NEED TO MAKE SURE THAT AS WE ARE DEVELOPING THE INFRASTRUCTURE AND PROCESS, WE NEED TO KEEP ADDRESSING THIS ISSUE.

DR. TROUNSON: BERNIE, I DON'T THINK THERE IS A LOT OF INTERNATIONAL LAW AT THIS TIME OVER IPS CELLS. YOU MIGHT BE ABLE TO REFLECT IT BACK ON TISSUE SAMPLING, MAYBE YOU CAN REFLECT IT BACK ON GENOMICS BECAUSE THERE WOULD BE SOME IN THOSE CASES. AND PERHAPS THAT THERE LEADS TO WHERE YOU ARE GOING.

I AGREE WITH JOHN, THAT IN THE CASE OF EMBRYONIC STEM CELLS, THE EMBRYO ISN'T GOING TO BE -- IS DESTROYED IN THE PROCESS OF MAKING THE EMBRYONIC STEM CELLS OR USUALLY. SO THAT CAN'T BE A BENEFICIARY SPECIFICALLY, AND THE PARENTS ARE QUITE DISTANT THEN IN SOME RESPECTS FROM THAT BENEFIT. BUT PEOPLE WHO ARE GOING TO DONATE TISSUES WILL BE -- I THINK THEY'LL BE VERY SENSITIVE. THEY MAY HAVE A CANCER, THEY MAY HAVE A CONDITION, THEY MAY BE VERY CLOSE TO PEOPLE WHO HAVE AND BE MUCH MORE SENSITIZED. SO I THINK IT IS DIFFERENT, BUT I THINK ESSENTIALLY WE'RE SAYING WE WENT A LONG WAY WHEN WE MADE THE CONSENT RULES FOR CIRM.

AND I THINK IN THE BEST SITUATION, THAT WOULD BE THE WAY TO FOLLOW IT PROSPECTIVELY. I THINK THE ONLY TIMES, AS YOU SAID, WE PULLED OUT

SOME ODD SITUATIONS WHERE IT MAY BE FROM VERY YOUNG PEOPLE OR INFANTS AND PERHAPS FROM MATERIAL BANKS THAT ALREADY EXIST HAVE TISSUE IN THEM THAT CAN'T BE GOTTEN ANY OTHER WAY. PERHAPS THAT'S A DIFFERENT SITUATION, AND THAT TISSUE MIGHT EXIST FROM PATIENTS WHO HAVE HAD SEVERE DISEASE AND BE ACCESSIBLE, BUT THE CONSENT PROCESSES WOULDN'T BE EXACTLY WHAT WE REQUIRED.

CHAIRMAN LO: OTHER COMMENTS ON THIS ISSUE? WELL, I --

DR. WAGNER: DID WE STATE THAT WE WOULD NEVER MAKE GAMETES IN THE CONSENT FORM?

CHAIRMAN LO: NO. IT'S CERTAINLY A CURRENT ISSUE THAT WE ARE CURRENTLY REVIEWING.

DR. WAGNER: SO THE ONLY THING WE DID SO FAR WAS WE JUST STATED NO CLONING. WAS THAT THE ONLY STATEMENT OF WE WON'T DO?

CHAIRMAN LO: AGAIN, I THINK THE MORE GENERAL QUESTION, I THINK, JOHN IS RAISING IS ARE THERE -- SO WE'RE SAYING THAT WE'D LIKE PEOPLE TO BE TOLD A FAIR AMOUNT, IF THEY WANT TO HEAR IT, ABOUT WHAT THE RESEARCH MIGHT INVOLVE AND THEN CONSENT VERY BROADLY TO RESEARCH WITHOUT FURTHER SPECIFICATION WITH THE UNDERSTANDING THAT CERTAIN TYPES OF RESEARCH ARE OFF THE TABLE. WE SAID

CLONING, BUT I GUESS JOHN IS RAISING, I THINK, A QUESTION ARE THERE OTHER TYPES OF RESEARCH WE SAY WE'RE NOT GOING PERMIT WITH YOUR CELLS.

DR. WAGNER: BUT ALSO I WOULD ARGUE THAT THERE MIGHT BE CERTAIN CIRCUMSTANCES, HOWEVER, THAT, FOR EXAMPLE, YOU MIGHT WANT TO MAKE GAMETES. NOT SO MUCH TO MAKE GAMETES FOR REPRODUCTIVE PURPOSES, BUT TO MAKE GAMETES BECAUSE THEY HAVE A GENETIC DISEASE FOR WHICH THEY CAN'T MAKE GAMETES.

DR. TROUNSON: THAT'S EXACTLY RIGHT. THAT'S WHAT WE CURRENTLY DO, OF COURSE, WITH EMBRYONIC STEM CELLS. WE HAVE GRANTS IN THAT AREA. AND I THINK THERE'S AT LEAST ONE PAPER I'VE READ, JOHN, WHERE IT WOULD BE ARGUED STRONGLY THAT THE MAKING OF IPS FROM A POPULATION OF INFERTILE MEN OR WOMEN MAY BE VERY INFORMATIVE ABOUT THE CAUSE OF THE INFERTILITY. SO I DON'T THINK WE'D WANT TO CUT IT OFF, BUT IT MAY BE AN ISSUE THAT MIGHT BE OF CONCERN TO SOMEBODY WHO HAD SOME TOTALLY OTHER CONDITION, I SUPPOSE, THAT WOULD NOT WANT IT MADE INTO GAMETES.

DR. WAGNER: THE ONLY THING I COULD COMMENT IS THAT YOU PROBABLY KNOW THAT INFORMATION ALREADY FOR THAT SPECIFIC INDIVIDUAL WHETHER OR NOT THIS IS AN IMPORTANT AREA OF RESEARCH. SO YOU COULD HAVE SORT OF A CHECK-OFF BOX, SO TO SPEAK, SAYING

THEY WOULD REFUSE THAT BECAUSE THAT'S GOING TO BE, I THINK, A HOT AREA IN PARTICULAR. BUT IN CERTAIN CIRCUMSTANCES, BECAUSE YOU KNOW THE DISEASE WHERE INFERTILITY ALREADY EXISTS, YOU MIGHT WANT TO TARGET THAT AREA OF RESEARCH AND HIGHLIGHT IT.

MR. TORRES: I WOULD JUST CAUTION ABOUT CHECK BOXES. VERY, VERY DANGEROUS.

DR. WAGNER: YOU KNOW WHAT THE INTENT IS. I UNDERSTAND.

MR. TORRES: FOR TRANSCRIPT PURPOSES.

CHAIRMAN LO: I THINK WE ARE GETTING AT A FUNDAMENTAL ETHICAL CONUNDRUM, WHICH IS THAT ON THE ONE HAND WE'D LIKE BROAD CONSENT BECAUSE WE DON'T WANT TO TIE THE HANDS OF RESEARCHERS DOWNSTREAM WHO HAVE SOMETHING THAT WE COULDN'T HAVE CONTEMPLATED AT THE TIME WE GOT THE ORIGINAL DONATION. SO WE WANT BROAD CONSENT TO SORT OF FURTHER THE SCIENTIFIC ENTERPRISE, ASSUMING, OF COURSE, THE PERSON DONATING THE MATERIALS KNEW THAT A LOT OF STUFF COULD HAPPEN. BUT IF THERE'S A PARTICULAR TYPE OF RESEARCH THAT WE'RE CONTEMPLATING WITH SOMEONE'S CELLS THAT IS SENSITIVE, THAT WE MAY WANT TO SPECIFICALLY ASK FOR CONSENT TO DERIVE GAMETES FROM SOMEONE WHO HAS A DISEASE WHERE INFERTILITY IS PART OF THE MANIFESTATION RATHER THAN SAY, WELL, YOU SAID ALL

RESEARCH, AND SO NOTHING IN THAT PRECLUDES US FROM DOING RESEARCH ON GAMETOGENESIS AND FERTILIZATION.

WHAT WE DON'T WANT TO DO IS OPEN OURSELVES TO THE CONCERN COMING BACK, WELL, YOU TOLD ME BROAD RESEARCH. IT NEVER OCCURRED TO ME THAT YOU WERE THINKING OF DOING THAT.

MS. LANSING: THAT'S WHY IT SAYS IT. I THINK YOU'RE OPENING JUST AN UNBELIEVABLE CAN OF WORMS. I REALLY DO. BECAUSE THAT'S WHY IT SAYS THAT SENTENCE, IT COULD BE USED IN WAYS THAT ARE UNFORESEEABLE, WHATEVER. SO, AGAIN, NO ONE IS BEING FORCED TO DO IT. THEY'RE BROUGHT BACK MANY TIMES BEFORE THEY SIGN THE PIECE OF PAPER, IF THEY CHOOSE TO SIGN THE PIECE OF PAPER. AND I JUST THINK OTHER THAN WHAT WE KNOW WE CAN'T DO, BECAUSE IT'S IN OUR BYLAWS AND WE MAY HAVE OTHER THINGS THAT WE DECIDE WE CAN'T DO THAT ARE IN OUR BYLAWS, I THINK WHAT'S SENSITIVE TO ONE PERSON, SOMEBODY ELSE IS GOING TO SAY BUT YOU DIDN'T TELL ME ABOUT THIS AND YOU DIDN'T TELL ME ABOUT THIS. I DON'T KNOW WHAT IT IS. THAT'S WHY IT HAS TO BE THERE, AND THAT'S WHY A LOT OF PEOPLE WON'T SIGN IT.

DR. WAGNER: IF I MIGHT JUST SAY ONE WORD TO THAT. THAT IS, YOU KNOW THERE'S CERTAIN HOT-BUTTON ITEMS. YES, I MIGHT NOT KNOW THAT YOU

MIGHT DISCOVER A TEST THAT WE DIDN'T CONSIDER, OR WE MIGHT HAVE A NEW USE THAT WE DIDN'T CONSIDER THAT THESE CELLS DO SOMETHING OR GO DOWN THE AREA OF RESEARCH. BUT YOU ALREADY KNOW THAT CLONING, YOU ALREADY KNOW THAT GAMETES ARE GOING TO BE A HOT-BUTTON ISSUE. AND BY NOT TELLING THEM -- I THINK THAT IF I WERE A FAMILY WITH FANCONI ANEMIA WHERE THEY HAVE INFERTILITY AS WELL AS BONE MARROW FAILURE, THEY DIE OF BONE MARROW FAILURE. THEY MAY NOT EVEN THINK ABOUT THE INFERTILITY AND HOW THAT MIGHT BE SOMETHING IMPORTANT FOR US GENERALLY TO UNDERSTAND.

AND SO NOT TELLING HIM, JUST BECAUSE HE DIDN'T THINK OF IT, MIGHT BE IMPORTANT FOR THEM TO KNOW. BECAUSE THAT MIGHT BE DISCONCERTING TO KNOW THAT YOU ARE MAKING MALE AND FEMALE GAMETES THAT COULD RESULT IN -- THEY NEED TO BE JUST REASSURED, I THINK, THAT IS THIS OKAY BECAUSE YOU ALREADY UP FRONT THAT THIS IS GOING TO BE AN ISSUE. OF COURSE, I THINK -- AND I AGREE WITH YOU ENTIRELY. I DON'T WANT TO BE RESTRICTIVE. I WANT TO BE AS UNRESTRICTIVE AS POSSIBLE, BUT THIS ONE SEEMS TO BE A BIT CLEARLY GOING TO BE SOMETHING THAT I THINK BOTHERS SOME PEOPLE MORE AND WE ALREADY KNOW IT.

CHAIRMAN LO: I THINK THIS IS A REALLY

IMPORTANT TOPIC, AND I JUST WANT TO SORT OF SUGGEST THAT, AGAIN, IN RESEARCH ON INFERTILITY THERE'S DIFFERENT STAGES. SO JUST TO DERIVE A GAMETE IS PROBABLY LESS SENSITIVE THAN FERTILIZING THAT GAMETE IN VITRO AS PROOF OF CONCEPT THAT THEY ACTUALLY MIGHT BE AN APPROACH FOR THERAPY. SO I THINK ONCE YOU START TO CREATE EMBRYOS, I THINK THEN YOU HAVE EVEN A MORE HEIGHTENED SENSITIVITY. AND WE MAY -- AGAIN, THE QUESTION IS DO WE WANT TO INCLUDE THAT UNDER BLANKET CONSENT OR ASK FOR SPECIFIC CONSENT FROM A PERSON WHERE IT IS FORESEEABLE BECAUSE INFERTILITY IS PART OF THE CLINICAL MANIFESTATION OF THE SYNDROME OR DISEASE.

MS. LANSING: I HAVE TO GO. I'M AN HOUR LATE. THIS IS FASCINATING. IT'S MUCH MORE FUN THAN WHERE I'M GOING. AT ANY RATE, I'M VERY NERVOUS ABOUT THIS IS TODAY'S HOT-BUTTON ISSUE. THERE'LL BE SOMETHING ELSE TOMORROW, AND WE'RE GOING TO HAVE A LIST THAT JUST GOES ON AND ON AND ON. WE HAVE BEST PRACTICES ALSO. WE HAVE A SIDE OF BEST PRACTICES. I GUESS YOU CAN SAY IN THE ISSUE OF GAMETES WHERE THERE'S INFERTILITY, BEST PRACTICES WOULD BE TO ADVISE. THERE'S THINGS TO DO. BUT I'M REAL NERVOUS ABOUT -- NOT CHECKLIST. I KNOW THAT'S NOT WHAT YOU MEANT. I'M JUST REAL NERVOUS BECAUSE I'M NOT SURE

THAT MOST PEOPLE WHO CHECK THAT BOX WILL EVER -- IT'S NOT THAT YOU DON'T CARE. YOU DO CARE. BUT YOU KNOW IT'S GOING TO THE BETTERMENT OF MANKIND TO CURE DISEASES. THAT'S REALLY WHERE YOU COME OUT.

MR. SHEEHY: I ACTUALLY TEND TO AGREE WITH JOHN ON THIS ONE. I THINK GAMETES -- I THINK GAMETES REALLY DO REPRESENT A UNIQUE CIRCUMSTANCE. THAT'S WHY WE'RE HERE, RIGHT, FOR EMBRYONIC RESEARCH. YOU START TALKING ABOUT THE POTENTIAL TO MAKE A NEW HUMAN BEING, EVEN THOUGH YOU'RE ONLY USING THOSE MATERIALS FOR RESEARCH PURPOSES, ALL SORTS OF OTHER BAGGAGE GETS BROUGHT INTO THE EQUATION. AND I DON'T THINK THAT THIS IS NECESSARILY -- I UNDERSTAND YOUR FEAR, SHERRY, THAT THIS IS CRACKING THE DOOR OPEN AND THEN WE'RE GOING TO END UP WITH A LAUNDRY LIST. BUT IN THIS PARTICULAR INSTANCE, I THINK IT NEED NOT BE A WHOLE LAUNDRY LIST, BUT THIS MIGHT BE ONE THAT WE MIGHT NECESSARILY NEED TO INCLUDE BECAUSE WE ALREADY KNOW. IT'S AN EXISTENTIAL ISSUE FOR US. WE'RE HERE BECAUSE THIS IS WHEN WE START TALKING ABOUT THE POTENTIAL TO CREATE A NEW HUMAN BEING OUT OF THESE MATERIALS, WHICH IS WHAT A GAMETE IS. IT CONTAINS PEOPLE'S GENETIC MATERIAL. YOU CAN POTENTIALLY DERIVE A GAMETE AND PRODUCE TWO DIFFERENT GAMETES.

YOU CAN MAKE AN EGG BANK FOR PEOPLE WHO ARE INFERTILE.

AND SO I JUST THINK IT'S JUST A BOX TO ASK PEOPLE HOW THEY FEEL ABOUT IT BECAUSE WE CAN END UP DOWN THE ROAD IN THE SAME WAY THAT WE'RE SEEING WITH EMBRYONIC STEM CELL RESEARCH, THAT PEOPLE ARE SAYING, WELL, H9 IS NOT A GREAT LINE BECAUSE WE DIDN'T GET DONOR CONSENT, AND WE CAN BE IN THAT SAME CIRCUMSTANCE IN THAT WE DIDN'T -- WE KNOW THAT THIS IS A SENSITIVE AREA. I DON'T THINK THAT'S GOING TO CHANGE.

MR. TORRES: JUST A QUICK NOTE ON SHERRY'S POINT, AND TO GIVE IT THE CONSTITUTIONAL GRAVITAS THAT IT REQUIRES. THE ANTICLONING PROVISION IS IN PROPOSITION 71. THAT'S IN THERE. THAT IS IN THE CONSTITUTION OF THE STATE OF CALIFORNIA. QUESTION BECOMES WHERE DO WE GO OUTSIDE OF THAT. THERE ARE OTHER CONSTITUTIONAL LEGAL ISSUES THAT WE HAVE TO DISCUSS.

DR. WAGNER: CLONING WE'VE ALREADY DEALT WITH. IT'S JUST THAT THIS IS REPRODUCTION USING A SPERM OR AN EGG THAT SOMEHOW GETS INSEMINATED OR WHATEVER THE RIGHT --

MR. TORRES: I UNDERSTAND THAT.

MR. SHEEHY: THIS IS DIFFERENT FROM

CLONING. I'M INFERTILE. THEY'RE ABLE TO TAKE AN IPS CELL AND TURN THAT INTO SPERM. IS THAT CLONING? IT'S NO DIFFERENT FROM WHAT I MIGHT PRODUCE NATURALLY. AND THEN LET'S SAY THAT GOES INTO AN ANONYMOUS SPERM BANK WITHOUT MY CONSENT. THAT'S THE TYPE OF SITUATION YOU'RE TALKING ABOUT. WE'RE NOT THAT PARTICULAR ABOUT WHERE PEOPLE'S SPERM GOES. WE ARE VERY SENSITIVE ABOUT EGGS. WE TALKED ABOUT THAT BEFORE. THAT HAS HAD A LESSER DEGREE OF SENSITIVITY, BUT THAT'S A REAL EASY SLIPPERY SLOPE YOU CAN SEE GOING DOWN. AND SUDDENLY SOMEBODY IS SAYING, YOU KNOW, I DIDN'T INTEND TO HAVE OFFSPRING IN THIS MANNER AND I DIDN'T CONSENT TO THAT.

MS. LANSING: WHAT WE'VE WRITTEN, THEY WOULDN'T HAVE A LEGAL LEG TO STAND ON.

DR. TAYLOR: LET'S TALK ABOUT LEGAL LEGS.

MR. SHEEHY: WE'RE TALKING ABOUT ETHICS, NOT LAW.

MS. LANSING: WHAT I'M SAYING IS I THINK ETHICS IS RESEARCH, AND ON ANY UNFORESEEABLE MATTER YOU WOULD SAY CAN YOU DO THAT.

DR. TAYLOR: LET'S TALK ABOUT LEGAL LEGS AND LEGAL GAMETES AND ARMS AND SO ON. SO WHAT'S THE HISTORY HERE? ONE PIECE OF HISTORY IS WHEN DID WE START WORRYING ABOUT THE GAMETES ISSUES? WAS IT

FIVE YEARS AGO? NO. IT WAS BECAUSE WHEN A FEW PEOPLE CAME OUT WITH PAPERS THAT SUGGESTED THAT CREATION OF GAMETES FROM IPS CELLS WAS GOING TO BE POSSIBLE. MARK THAT POINT.

SECOND THING IS WHAT'S HAPPENED HISTORICALLY WITH AUTOPSIES? SO WITH AUTOPSIES, YOU HAD TONS OF HOSPITALS COLLECTING MATERIALS UNDER GENERAL CONSENTS OR NO CONSENT. AND THEN 20 YEARS LATER IN LONDON PEOPLE CONDEMNING CHILDREN'S HOSPITAL FOR HAVING GRAPHICALLY DESCRIBED KEGS OF CHILDREN'S HEARTS AND BRAINS.

SO WHAT WE'VE DONE IS HISTORICALLY, WHAT SOCIETY HAS DONE, IS LOOKED AT SITUATIONS THAT WERE TACITLY OR EXPRESSLY APPROVED AT THE TIME AND SAID THIS IS REALLY BOTHERING OUR CURRENT SENSE OF HOW THESE THINGS OUGHT TO BE DONE, AND IT'S APPLIED STANDARDS RETROACTIVELY. I DON'T MEAN TO IMPLY THAT THAT'S ALWAYS GOING TO OCCUR AND THAT OUR DIRECTION SHOULD, THEREFORE, BE ONE OF GREAT RISK AVERSION BECAUSE MAYBE IT'S PART OF A PENDULUM SWINGING UNDER WHICH WE'RE GOING OPPOSITE DIRECTIONS. BUT CHECK THE BOX IS THE RULE FOR AUTOPSIES NOW, INCLUDING FOR ALL SAMPLES GOING FORWARD AND TONS OF THINGS THAT WERE COLLECTED, AND PART OF PATHOLOGY MUSEUMS AND SO ON WERE DESTROYED BECAUSE OF THE RETROACTIVE

APPLICATION OF STANDARDS.

WHERE I'M GOING IS ACTUALLY I THINK THAT CIRM COULD DO SOMETHING REALLY UNUSUAL HERE AND AVOID THE SLIPPERY SLOPES YOU'RE CONCERNED ABOUT IF IT ACTUALLY IDENTIFIED A STANDARD UNDER WHICH INFORMED CONSENTS WOULD BE MODIFIED IN THE FUTURE. WHAT IS THE STANDARD OF ADEQUACY? SO I KNOW BERNIE HAS ARTICULATED A MODEL UNDER WHICH YOU ARTICULATE AND, IT'S REFLECTED IN SOME COMMENTS HERE, YOU ACTUALLY AMEND THE CONSENT, YOU INCLUDE A PROVISION WHEN IT IS SO SURPRISING, SO COUNTERINTUITIVE, SO FRANKENSTEINISH, SOME WOULD SAY, TO THE POPULATION AT LARGE, THAT UNLESS YOU TELL SOMEONE THEY'RE NOT GOING TO LIKE IT, THEY'RE NOT GOING TO KNOW ABOUT IT, AND PEOPLE WILL THINK IT'S WEIRD. HE SAYS THE STANDARD MUCH BETTER THAN THAT.

BUT THERE'S SOME ARGUMENT TO PROVIDING PROTECTION TO SCIENTISTS AND THE COMMUNITY BY IDENTIFYING THOSE NOVEL AREAS THAT ARE NONSPECULATIVE WHERE THE SCIENCE IS GOING THAT ARE SO UNUSUAL, THAT YOU WOULD FEED THE ENERGY OF YOUR SIGNIFICANT OPPONENTS IF YOU DON'T PROVIDE FOR SOME DIRECT INTERACTION WITH PEOPLE ABOUT THEM.

SO YOU CAN HAVE SOME INFORMED CONSENT WHICH IS PRETTY CLEAR, BUT ALSO CALL YOURSELVES TO

KEEP YOUR MIND WHERE THE SCIENCE IS GOING. AND IF IT'S SO SURPRISING AND NOVEL THAT IT WILL BE CHARACTERIZED IN WAYS THAT NOT ONLY ARE BAD FOR SOCIETY OR BAD FOR THE SOCIETY WE'RE CONSTRUCTING, BUT VIOLATE INDIVIDUAL RIGHTS.

DR. TROUNSON: JUST BEFORE SHERRY GOES, I THINK THE PROBLEM IS THAT WE MIGHT HAVE TO REVISIT THE EMBRYONIC STEM CELLS BECAUSE, YOU KNOW, YOU'RE TALKING ABOUT THAT IN RESPECT TO TRANSPLANTATION, WHICH I THINK IS MORE RELEVANT. IF YOU'RE USING IT AS A SCREENING TOOL, I HONESTLY DON'T THINK IT WOULD EVER HAPPEN BECAUSE YOU'RE USING IT AS A SCREEN FOR SOMETHING TO HAPPEN. WHEN YOU'RE COLLECTING THE CELLS FOR TRANSPLANTATION, PARTICULARLY ALLOGENEIC TRANSPLANTATION AS YOU WOULD DO AN EMBRYONIC STEM CELL, IN THEORY THEY'RE NOT THAT VERY DIFFERENT, TO BE HONEST.

AND SO I THINK SHERRY IS RIGHT. IN THE SENSE OF IT, IF WE DO DO THAT, AND THERE MAY BE A CASE FOR THAT, WE MIGHT NEED TO REVISIT THE EMBRYONIC STEM CELL ONE BECAUSE I CAN'T ACTUALLY SEE IT BEING THAT DIFFERENT.

MS. BAUM: AND THEN TO FOLLOW UP ON THE SCREENING CONCEPT, BECAUSE I THINK THAT THE SCOPE OF THE INFORMED CONSENT SHOULD BE DIFFERENT, FOR THE

SCREENING CONCEPT, IT WILL BE VERY DIFFICULT FOR US, I THINK, TO IMPLEMENT THIS CELL BANK IF WE HAVE THE ABILITY TO SCRATCH IN OR HAVE AMENDMENTS TO DIFFERENT CONSENTS BECAUSE WE'RE SORT OF COUNTING ON A VERY BROAD CONSENT. WE WILL NOT BE ABLE TO PRACTICALLY ASCERTAIN WHAT THE DIFFERENT -- WHEN WE OUTLICENSE, WHAT THE DIFFERENT PROJECTS ARE OR IT WILL PUT A LOT OF BURDEN ON US. AND IF WE MISS IT, THEN WE COULD BE LIABLE. SO I'M CONCERNED FROM A LEGAL PERSPECTIVE OF HAVING LIMITATIONS ON INFORMED CONSENTS HERE AND THERE.

CHAIRMAN LO: THESE ARE TOUGH ISSUES, AND WE HAVE COMPETING GOALS FOR TRYING TO ACCOMPLISH. AND BY SORT OF PUSHING IN ONE WAY, WE MAKE IT MORE DIFFICULT IN OTHERS. WE HAVE TO SORT OF FIND THE RIGHT SET OF TRADE-OFFS. I'M GOING TO GIVE ANN THE LAST WORD, AND THEN I'M GOING TO REWARD US WITH A BREAK BECAUSE WE'VE BEEN WORKING HARD, I THINK.

DR. KIESSLING: MAYBE WE SHOULD WAIT TILL AFTER THE BREAK THEN BECAUSE I WANTED TO REALLY ASK DR. CYPRESS A QUESTION OF HOW DOES THIS KIND OF CONSENTING RELATE TO STEM CELL BANKING. IF YOU HAD LINES THAT WERE COMING INTO YOUR BANK AND THEY HAD REAL RESTRICTIONS ON THEM, WHAT KIND OF A LOGISTICS PROBLEM DOES THAT CREATE? I THINK WE SHOULD WAIT

FOR THE ANSWER TILL AFTER THE BREAK.

CHAIRMAN LO: WE'LL LET DR. CYPRESS THINK ABOUT THAT. LET'S GIVE OURSELVES A 15-MINUTE BREAK.

(A RECESS WAS TAKEN.)`

CHAIRMAN LO: OKAY. WHY DON'T WE RECONVENE. I'M GOING TO START BY ASKING GEOFF LOMAX TO CLARIFY SOMETHING. WE HAVE BEEN TOSSING AROUND THE TERM "CLONING," AND CIRM FORBIDS CLONING. I WANT GEOFF TO BE VERY PRECISE FOR THE RECORD SAYING WHAT EXACTLY CIRM DOES NOT PERMIT BECAUSE IT'S REALLY A VERY PRECISE THING THAT'S BANNED.

DR. LOMAX: THANK YOU, BERNIE. I THINK IN SOME OF THE DISCUSSIONS, WE'VE FALLEN INTO A LITTLE BIT OF SHORTHAND, BUT I DID WANT TO EMPHASIZE FOR THE RECORD WHEN WE'RE REFERRING TO CLONING, THE SPECIFIC PROHIBITION, AND IT'S ACTUALLY AN ACTIVITY THAT'S NOT ELIGIBLE FOR CIRM FUNDING, AND THIS IS, AS SENATOR TORRES POINTED OUT, REFLECTED IN PROPOSITION 71 AND IS ACTUALLY PART OF THE CALIFORNIA CONSTITUTION COVERING FUNDS BY CIRM.

OUR GRANTEES ARE EXPRESSLY PROHIBITED FROM PERFORMING HUMAN REPRODUCTIVE CLONING WHICH INVOLVES USING SOMATIC CELL NUCLEAR TRANSFER TECHNIQUES TO ACTUALLY PRODUCE AN OFFSPRING. WHEN THE TERM -- SO WHEN THE PEOPLE INDICATE THAT WE PROHIBIT CLONING,

IT'S THAT SPECIFIC METHOD OF ATTEMPTING TO REPRODUCE THAT IS PROHIBITED UNDER PROPOSITION 71.

CHAIRMAN LO: THANKS FOR THAT VERY IMPORTANT CLARIFICATION. NOW WE'RE GOING TO SORT OF GO BACK AND HAVE ANN KIESSLING ASK HER QUESTION WHICH SHE DIRECTED AT DR. CYPRESS WHO HAS REAL-LIFE EXPERIENCE DEALING WITH SOME OF THE ISSUES WE'VE BEEN TALKING ABOUT.

DR. KIESSLING: MY QUESTION RELATES TO THE ISSUES OF INFORMED CONSENT AND HOW MANY RESTRICTIONS AND EXACTLY HOW TO GO ABOUT THIS FOR SOME OF THE THINGS THAT WE'VE RAISED, THAT JOHN WAGNER IS CONCERNED ABOUT.

SO HOW DOES THIS RELATE TO ANY KIND OF REALISTIC STEM CELL BANKING, THE KIND THAT ALAN TROUNSON IS TRYING TO GET ORGANIZED? WHAT KINDS OF CONSENT FORM RESTRICTIONS ARE PRACTICAL?

DR. CYPRESS: THANK YOU, ANN. WELL, FIRST OF ALL, I THINK TO DEAL WITH THIS, YOU HAVE TO DEAL WITH A NUMBER OF APPROACHES THAT YOU INTEGRATE TOGETHER. AS I SAID, OUR PRACTICE, WHICH SOLVES A LOT OF THE PROBLEMS, IS THAT THE DONOR, WHETHER IT'S THE DONOR AND THE DONOR INSTITUTION, OWNS THE MATERIAL. AND THEY RETAIN ALL THE COMMERCIAL RIGHTS. OKAY. AND IT'S ONLY FOR RESEARCH PURPOSES.

IN ORDER TO DEAL WITH THE QUESTION OF THE PROPER ACQUISITION OF THE MATERIAL BY THE BANK, WE HAVE DEVELOPED A MATERIAL ACQUISITION AGREEMENT WHICH WE USE ALONGSIDE AN MTA, MATERIAL TRANSFER AGREEMENT. I WOULD RECOMMEND VERY HIGHLY TO CIRM IN SOME OF THE TOOLS THAT YOU NEED TO PUT TOGETHER TO OPERATE THAT YOU DEVELOP THIS MATERIAL ACQUISITION AGREEMENT. AND IN THAT THERE WILL BE SEVERAL BOXES THAT YOU CHECK OFF, WHICH SAYS THAT YOU HAVE COLLECTED THIS MATERIAL ACCORDING TO THE PROPER INFORMED CONSENT WHICH IS ON FILE, ETC., ETC., ETC. AND WE'RE GOING TO ONLY ASK YOU FOR ONE THING. WE'RE GOING TO SAY TO YOU YOU ARE GOING TO INDEMNIFY US, AND I MENTIONED THAT BEFORE, THAT YOU'VE DONE ALL THESE THINGS IN THE PROPER WAY AND YOU ARE GOING TO PROTECT US FROM ANY LAWSUITS RELATED TO THAT. THAT'S THE WAY WE DEAL WITH THAT, ANN.

BUT I THINK THE MATERIAL ACQUISITION AGREEMENT, AND I WAS SAYING TO PAT AFTERWARDS, IF HARVARD AND CALIFORNIA AND NORTH CAROLINA AND HOPKINS AND ALL THE REST OF THE PLAYERS WOULD GET TOGETHER AND COME UP WITH A COMMON MATERIAL ACQUISITION AGREEMENT, THIS IS GOING TO MAKE LIFE SO MUCH EASIER BECAUSE YOU ARE GOING TO GET CONSISTENCY. AND YOU NEED TO PUT THE THOUGHT INTO

GETTING THE PROPER FORM TOGETHER, BUT IT'S NOT THAT BIG A DEAL BECAUSE WE'VE DONE IT BEFORE.

NOW, WHEN WE'RE DEALING WITH MICROBES, AND IT'S SIMPLER THAN WHEN YOU'RE DEALING WITH HUMAN SPECIMENS OBVIOUSLY. ALTHOUGH NOW ATCC IS MANAGING THE HUMAN MICROBIOME PROJECT. AND I WAS JUST LAUGHING BACK THERE. IT ALL STARTED YEARS AGO WITH KATHY KU AT STANFORD UNIVERSITY AND ATCC WORKING OUT AN AGREEMENT TO START THAT PROJECT. NOW THE HUMAN MICROBIOME PROJECT IS COLLECTING MICROBES FROM THE HUMAN SURFACES, AND THAT BROUGHT INTO US SOME INTERESTING DIFFERENT IDEAS ABOUT THAT MATERIAL AND HOW YOU ARE GOING TO DEAL WITH THAT.

BUT MY ANSWER TO ANN IS A MATERIAL ACQUISITION AGREEMENT ALONGSIDE SOME OF THOSE OTHER TOOLS THAT WE TALKED ABOUT TOGETHER, THAT WILL GIVE YOU THE PROCESS YOU NEED TO SIMPLIFY AND TO MAKE IT EFFICIENT.

DR. KIESSLING: SO YOU ACTUALLY DON'T CARE ABOUT THE INFORMED CONSENT?

DR. CYPRESS: YOU'RE GOING TO CHECK OFF THAT YOU HAVE THE PROPER INFORMED CONSENT, THEN YOU'RE GOING TO INDEMNIFY FOR US. NOW, WHEN IT COMES TO A MATERIAL, WE PREFER -- AND, AGAIN, THIS IS DIFFERENT. WE PREFER TO HAVE YOU SUBMIT A

PUBLICATION WITH THE MATERIAL THAT YOU SUBMIT. THE PUBLICATION BECOMES THE REFERENCE POINT TO THE CHARACTERIZATION AND THE DOCUMENTATION. OF COURSE, WHEN YOU'RE DEALING WITH MATERIAL FROM PATIENTS, YOU DON'T HAVE ANY PUBLICATIONS YET. AND, THEREFORE, YOU HAVE TO HAVE THE PROPER DESCRIPTORS AS RELATE TO HOW YOU GOT THE MATERIAL, THE PROCUREMENT PROCESS.

THERE'S A BIFURCATION WHEN YOU'RE DEALING WITH THE TYPE OF MATERIALS YOU'RE GETTING. WHEN YOU'RE DEALING WITH INERT MATERIALS -- AND BY THE WAY, AGAIN, THERE'S BEEN SOME ISSUE RIGHT NOW WHO OWNS MICROBES. WE HAD A VERY BAD INCIDENT WITH THE SWINE FLU. WE WERE THE REFERENCE COORDINATING CENTER FOR THE SWINE FLU DIAGNOSTIC PROGRAM. THERE WERE CERTAIN COUNTRIES THAT WOULD NOT MAKE THE VIRUS AVAILABLE OVER SOMETHING THEY CALL SOVEREIGN MICROBIOLOGY. THIS IS A NEW ONE. SOVEREIGN, YES.

ANYWAY, BUT WHEN YOU'RE DEALING NOW WITH MICROBES, THERE'S BEEN A LITTLE CHANGE OF PRACTICE WHERE PEOPLE ARE SAYING THEY WANT TO OWN THE RIGHTS TO THE MICROBES. I'M NOT GOING TO EVEN TRY TO ANSWER THAT ONE. I'LL TURN TO THE LAWYERS AND THE EXPERTS ON THAT ONE.

DR. KIESSLING: BUT IF YOU WERE TO GET -- SO SAY YOU'RE NOW GOING TO GET 5,000 CELL LINES FROM

CALIFORNIA IF CALIFORNIA DECIDES NOT TO DO ITS OWN STEM CELL BANKING. AND 1,000 OF THOSE HAVE CONSENT FORM A AND YOU CAN'T USE THOSE LINES FOR X AND X AND X. HOW WOULD ATCC DEAL WITH THAT?

DR. CYPRESS: IT WOULD PUT IN ITS MTA AGREEMENT THAT YOU'RE NOT ALLOWED TO USE THESE LINES FOR X, X, AND X.

DR. KIESSLING: OKAY. SO EACH CELL LINE CAN HAVE ITS OWN MTA AGREEMENT, AND THAT DOESN'T CAUSE ANY KIND OF UNDUE BURDEN?

DR. CYPRESS: NO. YOU'RE GOING TO HAVE A GENERIC MTA AGREEMENT, AND IT'S LIKE THE ANTIBODY --

DR. KIESSLING: BOXES TO CHECK.

DR. CYPRESS: THAT'S HOW YOU WOULD DO IT. AGAIN, IF THEY'RE SAYING TO US WE WANT TO GIVE YOU 5,000, WE WOULD SAY TO THEM THE CONDITIONS ARE THE FOLLOWING. YOU OWN IT, YOU TAKE THE COMMERCIAL RIGHTS, YOU NEGOTIATE THE COMMERCIAL THINGS, YOU ARE GOING TO INDEMNIFY US. YOU ARE GOING GIVE US ALL THE CRITICAL INFORMATION ON THE SOP'S YOU USED TO GET THAT MATERIAL, THE PROCESS TO AUTHENTICATE IT, AND THEN WE'LL TAKE IT FROM THERE.

CHAIRMAN LO: OKAY. I'M GOING TO SWITCH GEARS A LITTLE BIT, BUT CONTINUE THIS LINE OF DISCUSSION AND ASK DR. ERIK FORSBERG, WHO IS THE

EXECUTIVE DIRECTOR OF WICELL, WHICH NOW HAS A WISCONSIN INTERNATIONAL STEM CELL BANK. I DON'T KNOW HOW YOU PRONOUNCE THE ACRONYM WISC OR SOMETHING. SO HE'S ACTUALLY IN THE BUSINESS OF BEING A STEM CELL BANK, AND HIS BANK INCLUDES SOME IPS LINES THAT JAMIE THOMSON DERIVED AS WELL AS HESC LINES. SO, DR. FORSBERG, FIRST OF ALL, THANK YOU FOR COMING AND BEING PATIENT THROUGH THIS LONG MEETING.

BUT JUST TO LET US KNOW YOUR THOUGHTS ON WHAT WE MIGHT LEARN FROM YOUR EXPERIENCE AT WICELL, PARTICULARLY WITH REGARD TO ARE THERE ETHICAL ISSUES THAT YOU'VE FACED IN RUNNING THE BANKS YOU'VE RUN.

DR. FORSBERG: THANKS A LOT. I APPRECIATE THE INVITATION FROM GEOFF TO GIVE SOME PRACTICAL ASPECTS OF WHAT MAKING AND BANKING CELLS IS, INCLUDING THINGS LIKE CONSENTS AND MTA'S AND THAT SORT OF THING. I'D LIKE TO AGREE WITH RAY, THAT WE HAVE THE SAME TYPE OF POLICY REGARDING RESTRICTIONS. WE JUST PUT IT IN THE MTA. SO THAT REALLY JUST FOLLOWS THROUGH. IN TERMS OF OWNERSHIP, THE OWNERSHIP OF THE CELL LINES BELONG TO THE ORIGINAL PROVIDER. IN OUR CASE IT'S A LITTLE BIT DIFFERENT THOUGH BECAUSE THE INTELLECTUAL PROPERTY, IT WAS ORIGINALLY PATENTED BY WARF. AND TYPICALLY THE, IN

OUR CASE AT LEAST FOR THE EMBRYONIC STEM CELLS, THE OWNERS DON'T OWN THE IP. SO WE HAVE SOME LIMITATIONS ON LICENSING.

HOWEVER, I'D LIKE TO POINT OUT THAT FOR RESEARCH USE, THERE'S NO RESTRICTIONS FOR RESEARCH FOR ANY USER USING THE EMBRYONIC STEM CELL LINES, AND THAT'S BEEN VERIFIED ALSO BY THE OTHER PROVIDERS THAT WE HAVE CURRENTLY IN PLACE.

IN TERMS OF COMMERCIAL USE, TO USE IT FOR COMMERCIAL OR CLINICAL PURPOSES, OUR MTA, WHICH WE CALL AN MOU, DOES ASK THAT YOU HAVE TO GET ANOTHER LICENSE. HOWEVER, I'D LIKE TO POINT OUT THAT WARF HAS NEGOTIATED 40 COMMERCIAL LICENSES WITH GROUPS AROUND THE WORLD, INCLUDING BIG PHARMA, BIOTECHS, A LOT OF SMALL COMPANIES. SO IT'S BEEN A VERY SUCCESSFUL PROGRAM AT GETTING LICENSES OUT TO THE COMMUNITY.

AND IN TERMS OF THE NUMBER OF CELL LINES, NUMBER OF USERS, THIS IS JUST A SUMMARY OF THE NATIONAL STEM CELL BANK CONTRACT, WHICH HAS ENDED, BUT JUST LIKE TO POINT OUT THE BOTTOM NUMBER. ABOUT 1287 ORDERS COMPLETED, ABOUT TWO VIALS PER ORDER, SOMETHING LIKE 2500 OR SO VIALS SHIPPED, IN MANY CASES IN TWO DIFFERENT SHIPMENTS, BUT EACH OF THE USERS IN THOSE CASES SIGNED AN MTA THAT ALLOWS THEM

TO USE THEM WITH UNRESTRICTED USE FOR RESEARCH PURPOSES.

I'D ALSO LIKE TO POINT OUT THAT THERE ARE, OF COURSE -- THE SWITCH, OF COURSE, FROM THE NATIONAL STEM CELL BANK TO WHAT WE CALL THE WISC, THE WISCONSIN INTERNATIONAL STEM CELL BANK, ALL THE CELL LINES ARE STILL AVAILABLE FROM THAT SOURCE, AND IT'S THE SAME TYPE OF ORDERING PROCEDURE. WE HAVE THE SAME TYPES OF INFORMATION, CERTIFICATES OF ANALYSIS, THE SOP'S FOR THE DERIVATION AND TESTING OF ALL THE CELL LINES. AND ALTHOUGH WE DO CHARGE FOR EACH SHIPMENT, WE DO HAVE A NUMBER OF CORE LABS AROUND THE COUNTRY WHERE WITHIN AN INSTITUTION AND IN SOME CASES BETWEEN INSTITUTIONS WE ALLOW THE REDISTRIBUTION OF THESE CELL LINES WITHOUT CHARGE. THERE'S NO PARTICULAR BENEFIT TO WICELL ALTHOUGH WE DO ALL THE PAPERWORK REGARDING THE MOU.

SO IT'S SOMETHING THAT WE'VE PUT IN PLACE TO AID THE RESEARCH COMMUNITY IN USING THESE CELLS FOR PRODUCTIVE PURPOSES.

I'M JUST GOING TO GO THROUGH THESE SLIDES QUICKLY. WE, OF COURSE, LIKE I MENTIONED, WE GIVE OWNERSHIP OF THE CELL LINE TO THE PROVIDER. AND THIS IS JUST A COUPLE OF CLAUSES IN OUR TYPICAL DISTRIBUTION AGREEMENT WITH THE PROVIDER. LIKE I

SAID, OWNERSHIP REMAINS WITH THE ORIGINAL PROVIDER. IN MANY CASES WE PAY SORT OF A PORTION OF THE CHARGES THAT WE MAKE FOR DISTRIBUTION BACK TO THE ORIGINAL PROVIDER.

THIS IS A LIST THAT ARE IN WHAT WE CALL THE WISC BANK NOW THAT INCLUDES ALL THE ORIGINAL NATIONAL STEM CELL BANK CELL LINES, PLUS SOME GENETICALLY ENGINEERED VERSIONS OF THOSE SAME CELL LINES. YOU CAN SEE THE OWNERS ARE LISTED THERE ALSO, AND THEY'VE CHANGED, AS YOU RECOGNIZE FROM THE NAMES UP THERE. WE ALSO DISTRIBUTE SEVEN IPS CELL LINES, AND THESE WERE PRODUCED IN THE LAB OF JAMIE THOMSON. AND ALSO WE'VE EMBARKED ON A PROGRAM WITH A GROUP ON CAMPUS CALLED THE WAISMAN CLINICAL BIOMANUFACTURING FACILITY. DEREK HEI IS THE DIRECTOR OF THAT FACILITY, AND WE'RE PRODUCING GMP OR CLINICAL GRADE CELL LINES. WE HAVE AN H9 CELL LINE THAT'S AVAILABLE NOW. ANYBODY CAN PURCHASE EITHER CELL LINES OR RESEARCH BANKS THAT WERE DERIVED FROM THAT GMP CELL LINE. AND DEREK HAS RECENTLY COMPLETED A GMP H1 CELL LINE UNDER THE PACT AWARD, THE PACT GRANT THAT WAS MENTIONED EARLIER THAT WAS GIVEN TO THE UNIVERSITY OF WISCONSIN. AND HE'S EMBARKING ON THE PRODUCTION OF ADDITIONAL GMP LINES UNDER THE SAME PROGRAM.

JUST WANT TO GIVE YOU AN IDEA. THIS IS KIND OF A PRACTICAL ASPECT OF WHAT IT TAKES TO DO THIS KIND OF THING. EMBRYONIC STEM CELLS AND INDUCED PLURIPOTENT STEM CELLS BEHAVE VERY SIMILARLY IN CULTURE, AND THEY ALSO ARE MUCH MORE DIFFICULT TO CULTURE THAN MOST CELL LINES. SO TO MAKE THIS PROCESS SUCCESSFUL, WE HAVE TO DEVELOP RIGOROUS PROCEDURES THAT CONTROLS EACH STEP IN THE MAKING OF THE CELL LINE.

THIS IS JUST ONE PAGE OF FOUR WORK-FLOW PAGES THAT WE USE ON A DAILY BASIS. IN THIS CASE IT'S THE PRODUCTION OF THE MASTER CELL BANK, AND THERE'S ACTION ITEMS AND THERE'S QUALITY ASSURANCE CHECKPOINTS, THERE ARE DECISION POINTS WHERE A TEST COULD BE POSITIVE OR NEGATIVE, AND THAT WILL CAUSE THE THING TO STOP, AND CONTROLLING ALL THE ASPECTS OF THAT, INCLUDING THE DOCUMENTS, IS A QUITE DETAILED PROCESS. SO THAT WHEN WE ARE DONE, WE HAVE A CELL LINE, WE HAVE A VIAL OF CELLS THAT WE KNOW IS CAPABLE OF PRODUCING A GOOD CULTURE IN YOUR LAB. AND WE BACK THAT UP WITH A VERY DETAILED TECHNICAL SUPPORT AND ALSO ALL THE SOP'S AND PROCEDURES THAT WE RECOMMEND FOR USE.

THE CHARACTERIZATION OF BANKS IS PRETTY STANDARD. OUR MASTER CELL BANKS FOR THE RESEARCH

ARE ANYWHERE FROM A HUNDRED TO 200. FOR THE GMP BANKS, THEY'VE TYPICALLY BEEN THREE TO 500 VIALS. IT'S DONE WITH WCVF AT THE UNIVERSITY. WE DO THE TYPICAL THINGS. WE DO IDENTITY, CELL RECOVERY, WE LOOK FOR CONTAMINATIONS. WE DID A LOT OF ADVENTITIOUS AGENT TESTING MORE SO THAN WE'RE DOING NOW FOR NEW CELL LINES BECAUSE OF THE ORIGINAL NATIONAL STEM CELL BANK REQUIREMENTS FOR US TO TEST FOR MOUSE, BOVINE, AND PORCINE VIRUSES, AND SO THAT WAS A VERY EXPENSIVE ENDEAVOR, BUT WE DON'T DO ALL THOSE TESTS NOW BECAUSE IT'S NOT NECESSARILY REQUIRED FOR RESEARCH. HOWEVER, FOR THE GMP BANKS, THOSE AND MORE TESTS ARE DONE.

WE ALSO ORIGINALLY DID -- WE LOOKED FOR VIRUSES. IN THE CENTER IMAGE ON THE RIGHT, THAT'S A MOUSE VIRUS THAT HAPPENED TO COME OUT OF ONE CELL LINE. AND THEN, OF COURSE, WE LOOK FOR GENETIC STABILITY. THESE CELLS ARE EXTREMELY VULNERABLE TO GENOMIC ABNORMALITIES, AND SO THE TYPICAL WAY OF LOOKING AT GENOMIC ABNORMALITIES IS TO LOOK AT THE KARYOTYPE OR G-BANDING, AND THAT PICKS UP A LOT OF THINGS, BUT IT'S NOT SUFFICIENT TO LOOK AT TO FIND WHAT ARE TURNING OUT TO BE VERY SIGNIFICANT CHANGES IN THE GENOME THAT ARE NOT DETECTED BY G-BANDING; FOR EXAMPLE, DELETIONS OR ADDITIONS.

SO, FOR EXAMPLE, WE HAD A CASE RECENTLY WHERE WE HAD A PLURIPOTENT STEM CELL LINE FROM A FRAGILE X LINEAGE. AND, OF COURSE, THE FRAGILE X WOULDN'T SHOW UP ON THE -- DIDN'T SHOW UP ON THE KARYOTYPE, BUT WE DID FIND A DELETION IN THE CHROMOSOME 15, NOT USING KARYOTYPE, BUT USING THIS NEW METHOD OF TESTING THAT WE'RE USING ROUTINELY NOW, SO AN ARRAY GENOMIC -- COMPARATIVE GENOMIC HYBRIDIZATION. SO IT'S BECOMING MORE OF A REQUIRED STEP IN THE ANALYSIS OF THESE CELL LINES.

CHAIRMAN LO: DO YOU DO ANY GENOME SEQUENCING OR SNP'S PROFILING?

DR. FORSBERG: NO, WE DON'T DO ANY SEQUENCING PER SE. WE DID A LOT OF EXPRESSION ANALYSIS ON THE ORIGINAL NATIONAL STEM CELL BANK CELL LINES. WE'LL PROBE FOR SPECIFIC GENOMIC CHANGES WE SEE IN CGH USING FISH, BUT THAT'S ONLY IF WE NOTICE SOMETHING ON THE CGH ANALYSIS.

DR. LORING: I JUST WANTED TO COMMENT. CGH AND SNP GENOTYPING ARE JUST DIFFERENT RESOLUTION GENOME MAPPING. SO CGH IS NOT QUITE AS SMALL A RESOLUTION AS SNP GENOTYPING, BUT A LOT OF PEOPLE USE IT FOR ESSENTIALLY AN INTERIM METHOD THAT GIVES YOU MORE INFORMATION THAN A KARYOTYPE.

DR. FORSBERG: THIS SLIDE IS SIMPLY A

FLOWCHART FOR THE GMP PROCESS, LIKE WAS MENTIONED EARLIER. WE PRODUCE MASTER CELL BANKS. WE HAVE RESEARCH BANKS PRE- AND POST-GMP PRODUCTION. SOMETIMES WE FOUND THAT CLIENTS WANT TO, BEFORE WE EVEN EMBARK ON A GMP PROJECT, THEY WANT TO LOOK AT THE CELL LINE TO SEE IF IT BEHAVES LIKE THEY THINK IT SHOULD, AND BEFORE THEY EVEN PAY FOR THE GMP BANK. AND THEN, OF COURSE, AFTER THEY'RE DONE, THEY WANT TO DO SOME MORE TESTING, SO WE OFTEN MAKE A RESEARCH BANK. WE HAVEN'T DONE THIS YET, BUT WE ANTICIPATE MAKING WORKING BANKS FOR -- CLINICAL GRADE WORKING BANKS FOR USE IN SOME CLINICAL STUDIES.

AND THIS IS WHAT WE JUST TALKED ABOUT IN TERMS OF QUALITY CONTROL ON GENOMIC STABILITY. THAT JUST GIVES YOU A LITTLE MORE DETAIL ON THIS ARRAY CGH PROCESS. WE USED A VARIETY OF DIFFERENT TYPES OF ARRAYS OR DENSITY OF ARRAYS. DEPENDING ON WHICH ONE YOU CHOOSE, YOU CAN LOOK AT CHANGES AS SMALL AS 10, 20 KB VERSUS THE SMALLEST CHANGE YOU CAN SEE TYPICALLY IN A G-BAND IS 5 MEGABASES, SO IT'S MUCH HIGHER RESOLUTION.

AND THAT'S ESSENTIALLY ALL I WANTED TO SAY. I DID WANT TO SAY A LITTLE BIT ABOUT CONSENTS. THE CONSENTS THAT WE REQUIRE AND THAT THE NIH

REQUIRES ARE THAT ALL IDENTIFIERS BE REMOVED. SO THAT'S ONE OF THE THINGS THAT MAKES THE WHOLE PROCESS A LITTLE BIT EASIER. I KNOW THAT'S SPECIFIC FOR WHAT WE'RE DOING, BUT REMOVING THE IDENTIFIERS ELIMINATES THE POSSIBILITY OF RECONSENT ISSUES.

JUST AS AN EXAMPLE, FOR THE PROCESS OF GETTING APPROVAL AT THE NIH, I'VE GOT A LIST OF THE DOCUMENTS THAT WERE SENT FOR THE CELL LINES, THE H7, H9, 13, AND 14. THESE WERE A BIT IN THE NEWS PRIOR TO THIS APPROVAL. AND IT WAS INTERESTING BECAUSE THERE WERE TWO RELATIVE APPROVALS BY THE NIH. ONE WAS THE WORKING GROUP ROUTE, WHICH REQUIRED TWO COMMITTEES TO REVIEW THE DATA AND THEN MAKE A RECOMMENDATION TO THE DIRECTOR OF NIH. AND THAT'S HOW THE H1 LINE WAS ORIGINALLY APPROVED; HOWEVER, WE SUBMITTED THESE UNDER THE ADMINISTRATIVE ROUTE, WHICH IS ALL DONE BY IN-HOUSE PEOPLE AT THE NIH. I CAN TELL YOU THAT THERE ARE HUNDREDS OF PHONE CALLS AND E-MAILS GOING ALL AROUND THE WORLD BEFORE WE GOT ALL THESE DOCUMENTS. THOSE ARE THE DOCUMENTS WE ENDED GETTING AND SENT IN AND ALLOWED US TO GET APPROVAL OF THOSE CELL LINES.

JUST QUICKLY, WE'RE DERIVING NEW EMBRYONIC STEM CELL LINES. WE DO IT IN A FACILITY, OF COURSE, THAT HAS NO CONNECTION TO UNIVERSITY AND IT'S

ADMINISTRATIVELY AND PHYSICALLY SEPARATE FROM OUR OTHER LABS FOR ISSUES REGARDING FUNDING OF -- FEDERAL FUNDINGS OF DERIVING NEW EMBRYONIC STEM CELL LINES. WE USE THE SAME QUALITY ASSURANCE PROGRAMS THAT WE APPLY TO OUR NORMAL BANKING. IN THIS CASE IT SHOWS EMBRYOS GOING THROUGH TWO DIFFERENT ROUTES OF EXPANSION. AND THE TWO DIFFERENT ROUTES ARE TWO DIFFERENT LOCATIONS FOR SECURITY PURPOSES IN TERMS OF STERILITY, BUT ALSO FOR CHANGING THE CONDITIONS OF THE CULTURE.

WE KNOW THAT THERE'S A LOT OF INTEREST IN DERIVATIONS DONE IN AS WELL-DEFINED CONDITIONS AS POSSIBLE WITHOUT ANY ANAL COMPONENTS. AND BUT THERE IS A WAY TO TRANSITION INTO THOSE SAME CONDITIONS THAT THE FDA SEEMS TO BE PRETTY HAPPY ABOUT. THEY HAVE APPROVED THE H1 LINE PRODUCED ON MOUSE FEEDER CELLS, BUT WE EXPECT IT WILL BE EASIER TO GET THE TESTING DONE IF WE GO THROUGH A MORE DEFINED ROUTE. SO WE'RE DOING MULTIPLE ROUTES OF EXPANSION WHEN WE DO A DERIVATION.

RIGHT NOW WE HAVE FIVE NEW EMBRYONIC STEM CELL LINES UNDER MORE DEFINED CONDITIONS AND WE'RE CHANGING THE CONDITIONS AND IMPROVING THOSE CONDITIONS AS WE GO ALONG.

ONE THING I WANT TO EMPHASIZE, THAT THIS

WHOLE PROCESS REQUIRES A HUGE AMOUNT OF CONTROL OVER THE PROCESS, THE DOCUMENTATION. AND THIS IS JUST AN ILLUSTRATION OF THE KIND OF DOCUMENTS THAT WE KEEP AND WHERE WE KEEP THEM AND EXACTLY WHAT THE ACTION IS THAT WE'RE DOCUMENTING. THESE ARE CONTROLLED DOCUMENTS UNDER A CONTROLLED DATABASE SYSTEM.

A PORTION OF THESE DERIVATIONS WILL BE HELD BACK NOT FOR GENERAL USE NECESSARILY, ALTHOUGH MOST OF THEM WILL END UP -- THEY'LL ALL END UP IN THE NIH REGISTRY, AND WE WILL MAKE MOST OF THEM AVAILABLE TO ANYBODY WHO WANTS THEM; HOWEVER, THEY'RE GOING TO HOLD SOME BACK FOR POTENTIAL COMMERCIAL CLIENTS WHO ARE INTERESTED IN EXCLUSIVITY.

AND ONE OF THE ISSUES THAT COMES UP IN DERIVING NEW CELL LINES HAS TO DO WITH WHEN THE EMBRYOS WERE MADE IN VITRO, AND EMBRYOS BEFORE THIS DATE ON MAY 25, 2005, THE TESTING REQUIREMENTS ON THE DONORS IS A LOT DIFFERENT THAN AFTERWARDS. SO IT TURNS OUT THAT THE EMBRYOS THAT WE HAVE, WE HAD AROUND 900, THEY WERE ALL PRODUCED BEFORE MAY 25TH, SO WE DON'T HAVE TO DO ALL THE DONOR TESTING. NOW, HOWEVER, IF YOU MAKE A NEW EMBRYONIC STEM CELL LINE WITH A NEW EMBRYO AFTER THAT DATE, THERE'S A LOT OF DONOR TESTING THAT NEEDS TO BE DONE, WHICH MAY

IMPACT THE IDENTITY ISSUES. LOT OF INFORMATION HAS TO BE SUBMITTED TO THE FDA IF YOU WANT TO USE THEM FOR CLINICAL USE.

AND LAST SLIDE ESSENTIALLY, THE MOST IMPORTANT PART OF ALL THIS IS KEEPING TRACK OF EVERYTHING. WE HAVE LOTS OF CELL LINES. WE EXPECT MORE, AND THERE'S REQUIREMENTS OF DOCUMENTATION FOR CLINICAL GRADE AND JUST THE NORMAL DISTRIBUTION LINES IS HIGH, SO WE TRACK EVERY ASPECT OF IT ELECTRONICALLY, INCLUDING ALL THE GENOMIC INFORMATION WE GATHER FROM OUR CYTOGENETICS GROUP.

THAT'S ALL I HAD TO OFFER TODAY.

CHAIRMAN LO: GREAT. THANKS. QUESTIONS FOR DR. FORSBERG?

DR. TAYLOR: A FAST ONE. SO TRACEABILITY, ARE YOU HEARING ANYTHING FROM THE FDA ABOUT MAINTAINING THE ABILITY TO KEEP TRACEABILITY GOING FORWARD THROUGH TIME, OR ARE THEY SETTLING FOR ONE-TIME TRACEABILITY AT THE TIME OF DONATION?

DR. FORSBERG: TRACEABILITY TO WHAT?

DR. TAYLOR: FOR EXAMPLE, THERE'S BEEN SOME DISCUSSION ABOUT, PARTICULARLY GIVEN THE ISSUE OF PHENOTYPIC MANIFESTATIONS THAT MIGHT BE LATER IN LIFE THAN THE DONATION WAS MADE, ABOUT MAINTAINING SOME KIND OF ABILITY TO RECONTACT AN OTHERWISE

HOPEFULLY ANONYMOUS DONOR SO YOU CAN ACTUALLY SEE WHAT THEIR MEDICAL RECORDS WERE AT THE TIME.

DR. FORSBERG: NO. THEY'RE TOTALLY SEPARATED. THE ORIGINAL DONORS ARE UNIDENTIFIED, UNIDENTIFIABLE.

DR. TAYLOR: SO ONE-TIME INFORMATION AND SCREENING AND THAT'S ALL.

DR. PETERS: CORRECT ME. DID I HEAR YOU SAY THAT YOU HAVE SOME RECENTLY DERIVED HESC CELL LINES ON MOUSE FEEDER TRAYS?

DR. FORSBERG: NO. THESE ARE NOT ON MOUSE FEEDERS. THESE ARE DONE UNDER MORE DEFINED CONDITIONS. WE'RE CHANGING. PEOPLE THAT WORK IN THIS FIELD KNOW THAT WE'RE LOOKING FOR SYNTHETIC SUBSTRATES AND NON-ANAL COMPONENT MEDIA AND THINGS LIKE THAT. THAT'S EXACTLY WHERE WE'RE HEADED. IT'S A STEPWISE PROCESS TO MAKE SURE IT WORKS EFFICIENTLY AND WE GET STABLE KARYOTYPES AND THAT SORT OF THING.

DR. CIBELLI: THANKS FOR YOUR TALK. I DO HAVE A QUESTION ON RESTRICTIONS, THAT YOU SAID WICELL DOESN'T HAVE ANY RESTRICTIONS FOR RESEARCH. I BELIEVE THAT I HAVE TO SIGN EVERY YEAR A PIECE OF PAPER YOU SEND TO US SAYING THAT ONE OF THE RESTRICTIONS, COUPLE OF RESTRICTIONS --

DR. FORSBERG: I MISSPOKE. WE OBVIOUSLY

DO NOT -- I THINK WE'RE UNIQUE IN THE EMBRYONIC STEM CELL FIELD THAT WE DON'T ALLOW NUCLEAR TRANSFER OR CLONING. IT'S NOT STATED AS CLONING, BUT IT'S DEFINITELY CLONING. AND ALSO MAKING CHIMERIC EMBRYOS.

DR. CIBELLI: I THINK THAT'S RELEVANT FOR THIS GROUP. IN A SENSE WE CAN LEARN FROM THAT.

DR. FORSBERG: THAT'S OUR RESTRICTION. IT WASN'T NECESSARILY THE RESTRICTION OF THE CELL LINE PROVIDERS.

DR. CIBELLI: ANOTHER QUESTION I HAVE IS IN YOUR CONVERSATION WITH CLIENTS, THAT THEY HAVE ALREADY SUPPOSEDLY CONTACTED THE FDA, DO YOU HAVE A SENSE THAT THE FDA WILL REQUIRE THEM TO DO PRECLINICAL STUDIES WITH CELLS THAT HAVE BEEN PRODUCED UNDER NORMAL LABORATORY PRACTICES OR GOP OR GMP?

DR. FORSBERG: THAT'S A GOOD QUESTION. I DON'T THINK THEY'LL NECESSARILY REQUIRE GMP. THEY WOULD PREFER THAT, BUT THEY DON'T NECESSARILY REQUIRE IT. IF YOU ARE GOING TO SEND AN IND, AND IF IT'S DONE WITH GMP CELL LINES AND ONES THAT WOULD BE USED IN A PATIENT, I WOULD HIGHLY RECOMMEND IT.

DR. TAYLOR: DO YOU MAINTAIN -- I THINK MY UNDERSTANDING IS YOUR HOPE IS TO BE REALLY A

DISTRIBUTION CENTER FOR MANY DONORS, INCLUDING CHILDREN'S HOSPITAL, WHICH I HOPE YOU ARE TOO. DO YOU HAVE ANY BANKING AND DISTRIBUTION PURPOSES IN THESE CELL LINES WITH ONLY A BLANKET OR GENERAL RESTRICTION, BLANKET OR GENERAL CONSENT?

DR. FORSBERG: YOU MEAN WITHOUT THE CLONING?

DR. TAYLOR: I'M REFERRING BACK TO OUR PREVIOUS DISCUSSION. ONE COULD ENVISION IMPLEMENTING A CONSENT MODEL WHERE THERE'S SIMPLY SORT OF A GENERAL CONSENT ASKING TO DO FURTHER RESEARCH. MY QUESTION IS DO YOU HAVE ANY STEM CELL LINES, WHETHER OR NOT ORIGINATED BY WICELL, THAT ARE THOSE WHERE THE ONLY CONSENT IS A GENERAL OR BLANKET CONSENT? OR DO THEY HAVE OTHER ADD-ONS, YOU WILL DO THIS, YOU WON'T DO THIS, YOU CAN USE IT FOR THIS?

DR. FORSBERG: THESE CONSENTS THAT WE HAVE FOR THE LINES THAT I SHOWED HERE ARE ALL FROM EMBRYOS PRODUCED IN THE LATE '90S OR EARLY 2000, SO ALL THE CONSENTS ARE ALL DIFFERENT.

DR. TAYLOR: SO MY NEXT QUESTION IS SPECULATIVE, BUT I WILL ASK IT. IF YOU WERE TO TAKE THE POSITION, AS A NATIONAL OR INTERNATIONAL BANK, THAT THE ONLY STEM CELLS THAT YOU WOULD -- OR IPS CELLS THAT YOU WOULD HANDLE AND DISTRIBUTE WERE ONES

WHICH HAD NO RESTRICTIONS, BUT ONLY A GENERAL SORT OF BLANKET CONSENT, WHAT WOULD BE THE IMPACT ON THE SCOPE OF YOUR DISTRIBUTION AND BUSINESS?

DR. FORSBERG: YOU MEAN IF WE ACCEPTED IPS CELL LINES WITH NO RESTRICTIONS?

DR. TAYLOR: IF YOUR RULE WERE THE ONLY ONES WE WILL ACCEPT FROM OTHERS AND DISTRIBUTE WERE ONES WHICH HAVE A GENERAL BLANKET CONSENT, WE WON'T HANDLE ANY RESTRICTIONS. IF YOU HAVE RESTRICTIONS, GOODBYE TO A DEPOSITOR. WHAT WOULD BE THE IMPACT ON THE BANK?

DR. FORSBERG: I'M NOT QUITE SURE --

DR. OLSON: WHAT PERCENTAGE OF YOUR LINES WOULD FALL UNDER THE CATEGORY OF HAVING RESTRICTIONS, TO USE YOUR HYPOTHETICAL, RIGHT?

DR. TAYLOR: ACTUALLY IT'S A VERY PRACTICAL QUESTION. ONE IDEA THAT CERTAINLY COULD BE APPEALING TO SOME WOULD BE TO IMPLEMENT A RULE WITH A VERY GENERAL BLANKET OPEN-ENDED CONSENT. I CONSENT TO ANY FURTHER RESEARCH, JUST THAT. IT WOULD MAKE LIFE EASIER FOR A LOT OF PEOPLE. NOW, YOU HAVE MANY DIFFERENT INSTITUTIONS THAT YOU'RE APPROACHING TO BE POTENTIAL DEPOSITORS TO YOUR BANK. AND YOU'RE APPROACHING THEM PRESUMABLY BECAUSE OF THE VALUE, PUBLICATION VALUE AND SO ON, OF LINES

THAT THE SCIENTISTS HAVE GENERATED AT THESE DIVERSE INSTITUTIONS. SO IN A SENSE YOU'RE SUBJECT TO WHATEVER THOSE INSTITUTIONS ARE IMPLEMENTING WITH RESPECT TO RESTRICTIONS.

LET'S SUPPOSE YOU DECIDED YOU WERE GOING TO BE A LAW INTO YOURSELF, AND YOU SAID THE ONLY ONES WE'RE GOING TO TAKE ARE ONES WITHOUT ANY SPECIFIC RESTRICTIONS, AND YOU ARTICULATED THAT RULE. DO YOU HAVE ANY SENSE OF WHAT THE IMPACT WOULD BE ON YOU AS A BANK ABOUT THE DIVERSITY OF LINES? WHAT IT WOULD DO TO YOUR BUSINESS?

DR. FORSBERG: PEOPLE HAVE ATTACHMENTS TO THESE CELL LINES WHETHER THEY'RE IPS OR NOT, AND THEY OFTEN ATTACH THEIR PERSONALITIES ALMOST TO THESE CELL LINES. AND SO I WOULD REALLY PREFER TO HAVE A UNIFORM CONSENT, A UNIFORM MTA OR MOU. AND OUR MOU, WHICH IS WE ALWAYS GIVE THEM THE SAME MOU, BUT THEY ALWAYS NEGOTIATE SOMETHING DIFFERENT, A LITTLE BIT DIFFERENT, BUT WE TRY TO STICK TO THE MAIN CLAUSES.

DR. TAYLOR: LET ME PUT IT A LITTLE DIFFERENTLY. LET'S SUPPOSE THAT, CONTRARY TO RAY'S POSITION, THAT YOU LET ALL THESE INSTITUTIONS DO WHATEVER THEY WANTED, BUT THEY HAD TO INDEMNIFY. LET'S SUPPOSE THAT YOUR VIEW WERE THAT YOU JUST

WEREN'T GOING TO IMPLEMENT ANY RESTRICTIONS FROM UPSTREAM. I GUESS THE QUESTION IS A BIT LOADED BECAUSE I ACTUALLY THINK FROM MY EXPERIENCE THAT YOU WOULD HAVE NO ELIGIBLE STEM CELL LINES TO DISTRIBUTE. THERE WOULD BE NONE LEFT BECAUSE I THINK THEY ALL COME WITH RESTRICTIONS. IT WOULD BE NICE TO GET A UNIFORM PLACE, BUT THE PROBLEM IS WE ALL ARE STUCK WITH THE PROBLEM OF HAVING TO DISTRIBUTE LINES WITH VERY DIFFERENT KINDS OF RESTRICTIONS.

DR. FORSBERG: EVERYBODY HAS DIFFERENT EXPECTATIONS WHAT'S GOING TO HAPPEN TO THOSE CELL LINES TOO FROM AN OWNER STANDPOINT.

DR. TAYLOR: SO IT'S NOT JUST THE RESEARCH SUBJECTS, PARTICIPANTS, WHO HAVE THEIR OWN RESTRICTIONS. SOME INSTITUTIONS DO TOO, SOME LEGISLATURES, LIKE THE WISCONSIN LEGISLATURE IMPOSED THEIR OWN. SO DIVERSITY AT THIS POINT IS A FACT OF LIFE IF YOU WANT TO HAVE A COMPREHENSIVE STEM CELL BANKING DISTRIBUTION.

DR. FORSBERG: THAT POINTS OUT THAT YOU REALLY HAVE TO HAVE A TEAM THAT CAN NEGOTIATE THOSE CHANGES AND IMPLEMENT THEM AFTERWARDS, EVEN DURING THE REDISTRIBUTION PART.

DR. TAYLOR: WHICH DOESN'T MEAN WE SHOULD

BE ON A PATH TO GET SOMEPLACE MORE UNIFORM, BUT AT LEAST RIGHT NOW.

MS. BAUM: WELL, MAYBE IT'S TIME FOR POINT, COUNTERPOINT BECAUSE WHAT I SEE IS A DISTINCTION IN THAT WE ARE NOW CREATING NEW LINES, NOT THAT HAVE THESE HISTORICAL PROHIBITIONS OR REQUIREMENTS. AND I THINK THAT WE HAVE A GOLDEN MOMENT TO DECIDE WHAT WE ARE GOING TO ACCEPT IN AN IPS BANK. AND I THINK THAT WE HAVE THE ABILITY TO SAY, LOOK, WE'RE NOT GOING TO TAKE AND DEVELOP UNLESS -- THOSE CELL LINES IN AN IPS CELL BANK UNLESS THEY ACTUALLY ARE PRISTINE IN TERMS OF WHAT WE CONSIDER A PRISTINE INFORMED CONSENT. THERE WILL BE MANY, MANY DONORS OUT THERE. WE COULD SELECT FROM THEM. THIS IS NOT LIKE A SITUATION WHERE WE HAVE TO ADDRESS AND DEAL WITH HISTORICAL INFORMED CONSENTS WHICH WERE ALL OVER THE MAP. WE CAN MAKE THE MAP, AND WE CAN MAKE IT THE WAY WE WANT TO MAKE IT, AND THEN WE CAN SELECT WHAT WE WANT TO SELECT.

MAYBE I AM NAIVE IN THAT, BUT HAVING BEEN AT A LARGE COMMERCIAL INSTITUTION IN THE PAST, I NEGOTIATED HUNDREDS AND HUNDREDS OF INFORMED CONSENTS. AND IF THEY DIDN'T FIT WITH OUR TEMPLATE, SOMETIMES WE JUST DIDN'T DO THE RESEARCH. WE JUST DIDN'T DO RESEARCH WITH THOSE ENTITIES, AND WE

PRETTY MUCH WERE ABLE TO GET A LOT OF CONFORMANCE AROUND AN INFORMED CONSENT.

DR. TAYLOR: JUST ONE FAST THING. I THINK THERE'S A DIFFERENCE BETWEEN THE LINES THAT CALIFORNIA MIGHT CHOOSE TO FUND ITSELF WHERE ONE MIGHT HAVE AMPLE AUTHORITY OVER THE INFORMED CONSENT. AND I IMAGINE TREMENDOUS STRIDES COULD BE MADE TOWARDS A UNIFORM CONSENT IN THAT CONTEXT. BUT THEN I GUESS I WOULD POINT OUT THIS. SO THE ISSCR HAS ITS OWN VERSION OF INFORMED CONSENT. IT DID SO AFTER NAS HAD WRITTEN -- NAS DID ITS OWN HIGHLY DETAILED PIECE. THE ISSCR BEING PLURALISTIC MODIFIED THOSE. AND WHAT DID CALIFORNIA DO? IT DID ITS OWN VERSION AS WELL.

SO THAT'S NOT A CRITICISM. IT'S JUST A POINT THAT UNFORTUNATELY OR FORTUNATELY THERE IS SOME PLURALISM AROUND THIS ISSUE, AND THE ABILITY FOR ANY SINGLE AGENT, PARTICULARLY IF THEY'RE SEEKING FROM OTHERS THE ABILITY TO DISTRIBUTE CELLS IN A SENSE WITHOUT FINANCIAL RETURN, WHAT KIND OF MARKET POWER DO THEY HAVE TO ADJUST THE WORLD'S VIEWS OF WHAT GOES INTO AN INFORMED CONSENT. UNLESS THERE'S PATHWAY OF THE SORT THAT RAY HAS SORT OF SAID WE NEED TO HAVE THAT GETS US THERE, TO ME, AT LEAST, IT'S A BIT UPHILL TO THINK THAT -- UNLESS ONE

IS JUST GOING TO SAY WE'RE ONLY GOING TO ACCEPT CERTAIN LINES. I THINK THAT'S TOUGH IF YOU HAVE A LOT OF PROMINENT INSTITUTIONS, UK HAS ITS OWN VERSION, DOING DIFFERENT THINGS. IT'S TOUGH. OBVIOUSLY YOU DON'T WANT TO INCLUDE UK LINES BECAUSE THEIR CONSENT IS DIFFERENT TOO. IT'S TOUGH.

DR. LORING: SO I JUST HAVE A COMMENT. WE'RE TALKING ABOUT AN IPS CELL BANK, NOT A HUMAN EMBRYONIC STEM CELL BANK. SO THAT MEANS ALL THESE CELLS CAN BE MADE TOMORROW. I MEAN THERE'S NO SHORTAGE OF IPS CELL LINES. SO I AGREE WITH YOU, THAT YOU CAN IMPOSE WHATEVER INFORMED CONSENT IT IS THAT YOU WANT GOING FORWARD. WE CAN JUST PUT ALL THE ES CELL STUFF BEHIND US NOW. THE IP CLIMATE IS A LOT CLEARER NOW. AT THIS VERY MOMENT IT'S JUST EXACTLY THE RIGHT TIME TO START SOMETHING LIKE THIS.

DR. TAYLOR: JUST THIS POINT THOUGH. IF THAT WERE REALLY COMPLETELY TRUE, THEN YOU WOULDN'T ACTUALLY NEED A BANK. THERE'S AN ASSUMPTION ABOUT THE COMPLETE FUNGIBILITY OF LINES, ALTHOUGH THEY MAY BE CHARACTERIZED IN DIFFERENT WAYS. MAYBE I'M MISSING SOMETHING. I MIGHT BE MISSING SOMETHING.

DR. LORING: I MEANT THE VARIETY OF LINES AND THE DISEASE-SPECIFIC LINES. THOSE COULD BE REMADE IF THEY HAD BEEN MADE UNDER OTHER

CIRCUMSTANCES BECAUSE THERE'S NOT JUST ONE PATIENT THAT HAS A DISEASE. YOU WANT SOMETHING GENERALIZABLE, SO OBVIOUSLY YOU WANT MORE THAN ONE LINE FROM THAT. SO IF THERE ARE LINES THAT DON'T COMPLY, THEY CAN JUST SIMPLY BE REJECTED BY THE BANK, BUT YOU STILL WILL NEED A BANK BECAUSE YOU DON'T WANT PEOPLE ALWAYS MAKING NEW LINES IF THERE ARE ALREADY SOME AVAILABLE.

DR. TAYLOR: I AGREE WITH YOU COMPLETELY EXCEPT THAT, AGAIN, THE DIVERSITY OF OPINIONS AROUND GENERAL VERSUS SPECIFIC, I HAVEN'T ACTUALLY STATED MY OWN OPINION, IS SO SUBSTANTIAL YOU MIGHT STILL FIND YOURSELF IN A POSITION WHERE YOU'RE THE WORLD'S STRANGER WITH RESPECT TO ESSENTIAL ELEMENTS. SO A GOOD EXAMPLE IS THIS ISSUE OF COMMERCIALIZATION WHERE SOME PEOPLE LIKE ME THINK IT'S A GREAT THING TO SAY WE HAVE NO PROGRAMS TO REIMBURSE, BUT THERE ARE OTHERS NOW TAKING A VERY DIFFERENT VIEW.

DR. CYPRESS: I WANT TO GO BACK TO THE THEME ABOUT STANDARDIZATION BECAUSE I THINK THAT'S REALLY WHAT THIS IS ALL ABOUT. AND I WANT TO MAKE A COUPLE OF POINTS THAT I MIGHT HAVE MISSED IN MY FIRST. WHEN WE TALK ABOUT STANDARDIZATION, WE'RE NOT ONLY TALKING ABOUT MATERIALS. WE'RE ALSO TALKING ABOUT DATA. WE ALWAYS SAY THAT AT ATCC A

STANDARD IS THE MATERIAL AND THE ASSOCIATED DATABASE. SO THIS GROUP SHOULD PUT SOME ATTENTION TO THE ISSUE OF STANDARDIZATION OF INFORMATION AND DATA THAT ACCOMPANIES THE MATERIAL. THAT'S VERY, VERY IMPORTANT.

AS THIS DISCUSSION IS DEVELOPING HERE, WE ALSO REALIZE THAT WE NEED TO STANDARDIZE THE PROCESS, WHICH IS WHAT ISO IS ALL ABOUT. YOU NEED TO STANDARDIZE THE PROCESS OF HOW YOU'RE GOING TO MANAGE THE ACQUISITION AND DISTRIBUTION, AND YOU SHOULD TRY TO DO IT IN A WAY THAT BENEFITS THE SCIENTIFIC COMMUNITY IN THE BEST POSSIBLE WAY. I USED TO USE THE TERM "SCIENTIFIC PHILANTHROPY" FOR PEOPLE WHO DEPOSITED THINGS IN COLLECTIONS BECAUSE I THINK WE'VE LOST SOME OF THAT THEME WITH THIS TECH TRANSFER MANIA THAT WE HAVE AND ALL THE REST OF THE THING THAT GOES ALONG.

BUT I THINK THERE ARE THREE AREAS OF STANDARDS THAT NEED TO BE ADDRESSED, WHICH IS GOING TO HAPPEN IN THIS SDO PROCESS THAT I'VE TALKED ABOUT OR DISTRIBUTED TO YOU, IS THE DATA, THE MATERIAL, AND THE PROCESSES ARE ALL GOING TO TRY TO BE STANDARDIZED. AND SO WE WOULD HAVE UNIVERSAL TOOLS, SO TO SPEAK, THAT PEOPLE COULD USE AND THAT INSTITUTIONS COULD WORK MORE EASILY WITH EACH OTHER.

MAYBE THAT'S A PIE-IN-THE-SKY DREAM AND UTOPIA, BUT I THINK IT'S POSSIBLE IF THE LARGER INSTITUTIONS THAT ARE GOING TO BE THE MAJOR PLAYERS SET THE TONE AND THEN THE OTHERS WILL COME ALONG AND FOLLOW THEM. THAT'S WHAT I'M THINKING ABOUT.

DR. WAGNER: JUST TO FOLLOW UP ON THAT POINT, AND I THINK WOULD BE IMPORTANT IF CIRM DECIDES TO DEVELOP A BANK, AND THAT IS THAT I HAVEN'T HEARD ANYONE TALK ABOUT ANY INSTRUCTIONS TO THE RECIPIENTS OF THE CELL LINES. BECAUSE, FOR EXAMPLE, IF WICELL OR ANY OTHER BANK GIVES A VIAL OF CELLS TO AN INVESTIGATOR, WHAT WE DON'T KNOW IS REALLY WHAT HAPPENED TO THE CELLS AFTER THEY LEFT YOUR BANK. SO, FOR EXAMPLE, IF THEY START DOING MULTIPLE PASSAGES OR OVER TIME A GROUP OF STUDIES MAY BE DONE AND PASS INTO THE NEXT GENERATION OF CELLS, BUT TWO YEARS FROM NOW THEY'VE JUST KEPT PROPAGATING THOSE CELLS, YOU HAVE NO IDEA WHAT THE QUALITY CONTROL IS OF THAT CELL THAT THEY'RE REPORTING DATA ON.

SO WHAT I MEAN BY THAT IS THAT THERE MAY BE CERTAIN INSTRUCTIONS TO SAY ONCE YOU GET THIS VIAL, YOU MAKE YOUR OWN WORKING CELL BANK AT ONE PASSAGE. ALL STUDIES ARE DONE AT A CERTAIN PASSAGE. I'M BEING SOMEWHAT VAGUE BECAUSE I DON'T KNOW

EXACTLY WHERE YOU MIGHT PUT LIMITS, BUT IT JUST CANNOT BE CONTINUALLY PASSAGED AND TO THINK THAT YOU HAVE THE SAME CELL LINE THAT YOU HAD WHEN YOU ORIGINALLY SENT THEM THE FIRST VIAL. BECAUSE YOU DON'T KNOW WHETHER OR NOT THEY'VE ACCUMULATED GENETIC ABNORMALITIES OR SOME OTHER EVENT HAS OCCURRED.

SO, AGAIN, GOING BACK TO THE LAST POINT, THAT IS, THAT, YOU KNOW, YOU WANT TO GET DATA BACK PERHAPS, BUT YOU ALSO HAVE TO GIVE SOME INSTRUCTION AS TO HOW THESE CELLS WOULD BE MANIPULATED ONCE -- AT LEAST KNOW THAT THE STARTING POPULATION WAS WHAT WE ALL THINK IT SHOULD HAVE BEEN. DOES THAT MAKE SENSE?

DR. LORING: THERE IS A SOLUTION FOR THAT, AND IT'S PEER REVIEW AND PEER PRESSURE. AND I THINK -- I KNOW --

DR. WAGNER: IT'S FAILED IN THE PAST.

DR. LORING: I KNOW. BUT THERE ARE MORE AND MORE REVIEWERS NOW WHO ARE QUESTIONING THE PASSAGE NUMBER OR THE AGE OF THE CELLS. THEY'RE ASKING PEOPLE TO DO SNP GENOTYPING ON THE CELLS.

DR. WAGNER: SO THEN WHAT YOU WOULD REQUIRE IS AT LEAST TO HAVE CELLS STORED SO THAT YOU KNOW AT THAT PARTICULAR PASSAGE NUMBER, YOU CAN GO

BACK AND SAY THIS IS THE CGH RESULT OR THIS IS THE WHATEVER.

DR. LORING: THAT'S GOOD IN PRINCIPLE, BUT YOU'VE GOT TO REALIZE THAT REALISTICALLY RESEARCHERS ARE NOT GOING TO DO THAT. THEY'RE GOING TO TAKE THE SIMPLEST PATH. SO THAT MEANS THE INFORMATION WILL NOT BE AS VALUABLE, BUT YOU CAN MAKE SORT OF THE BANK MORE VALUABLE BY OFFERING THE CELLS AT A VERY LOW PRICE SO THAT PEOPLE CAN BUY THEM AGAIN AND AGAIN AND AGAIN SO THEY CAN REFRESH THEIR STOCKS. AND YOU HAVE RECOMMENDATION DON'T PASS THESE THINGS MORE THAN 20 TIMES. SO I THINK THERE ARE SOLUTIONS TO THAT. ALSO THERE'S A LOT OF PEER PRESSURE. THERE'S A LOT OF PEER PRESSURE TO HAVE LINES THAT GET USED.

SO I DON'T THINK THERE'S -- IF I HAD A LINE, I'D SEND IT TO ATCC IN A SECOND BECAUSE I WOULD LIKE FOR OTHER PEOPLE TO GET IT. SO I DON'T THINK THAT THERE WILL BE A LOT OF PROBLEMS WITH PARTICULAR INFORMED CONSENT. I THINK WE WILL CAVE.

DR. WAGNER: MY ONLY POINT IS I THINK THAT CIRM HAS AN OPPORTUNITY NOW, IF THEY'RE GOING TO DO IT, TO REALLY SET A STANDARD SO THAT YOU GET DATA THAT IS MORE LIKELY TO BE OF BENEFIT TO SOCIETY. AND TO JUST MAKE THE COMMENT THAT, WELL,

INVESTIGATORS AREN'T GOING TO DO IT, WE HAVE THE OPPORTUNITY OF SAYING, YES, WE'LL MAKE THESE LINES AVAILABLE. YOU GO A CERTAIN PASSAGE. WE KNOW THAT IT HAS A CERTAIN QUALITY. AND THEN WHEN YOU NEED TO RENEW THEM, THEY'RE AVAILABLE.

DR. LORING: IF YOU ONLY CHARGE LIKE $50 A VIAL OR SOMETHING, YEAH. IT'S CHEAPER FOR ME TO BUY ANOTHER VIAL OF CELLS THAN IT IS FOR ME TO CREATE A BANK AND USE IT.

DR. TROUNSON: I JUST WANT TO AGREE WITH RAY REALLY ABOUT THE STANDARDIZATION. THAT'S THE REASON WHY WE'RE TRYING TO PRETHINK THIS IN THE BEGINNING IN ORDER TO REALLY APPROACH IT WITH A STANDARDIZED PROCEDURE SO THAT YOU CAN DO COMPARISONS WITH THE MATERIAL THAT'S BEEN DERIVED IN EXACTLY THE SAME WAY.

SO WHATEVER STANDARD THAT WE HAVE, IF WE'RE ABLE TO GET THIS UP AT THE TIME, IT WOULD BE HOPEFULLY TO HAVE A METHOD THAT REALLY DIDN'T INTRODUCE ANY VIRAL OR EXTRA GENE INTO THE GENOME, BUT WAS ABLE TO CONVERT THOSE CELLS RELATIVELY EFFICIENTLY. THESE KIND OF THINGS ARE EVOLVING NOW QUITE QUICKLY.

ON THE OTHER SIDE OF IT, WE WOULD BE ABLE TO HAVE SOME SAY, I THINK, FOR CIRM GRANTEES. IT'S

POSSIBLY DIFFICULT TO ENSURE THAT YOU CAN HAVE, IF YOU PROVIDED THEM TO PEOPLE WHO WEREN'T CIRM GRANTEES, TO HAVE THE SAME DEGREE OF CONTROL OVER THAT, JOHN, I THINK. YOU COULD MAKE SOME RECOMMENDATIONS; BUT ONCE PEOPLE HAVE THE LINES, THEY WOULD POSSIBLY WANT TO MAKE THE COMPARISONS IN THEIR OWN WAY USING THEIR OWN PROCEDURES, AND IT MIGHT BE MORE DIFFICULT. BUT IF WE ARE ABLE TO USE IT THROUGH GRANTEES, THEN I THINK WE CAN MAKE VERY STRONG RECOMMENDATIONS AND KEEP THE DATA IN A PRISTINE STATE AND MAKE IT MUCH MORE USEFUL AS YOU SAY.

I THINK THAT'S THE HUGE ADVANTAGE OF BEING ABLE TO SET UP A SUBSTANTIAL BANK, THAT, NO. 1, IT WILL BE VERY ATTRACTIVE. IT WILL DO THE KIND OF THINGS THAT PATRICK WANTS US TO DO, TRYING TO GET SOME STANDARD INTO THE SYSTEM. I'M NOT REALLY WANTING TO TAKE CELLS IN THAT ARE MADE IN ALL SORTS OF DIFFERENT WAYS. I WANT TO GET THEM FROM CLINICIANS FROM THE NEAT MATERIAL, IF IT'S SKIN BIOPSY OR WHATEVER WE DECIDE, HANDLED IN EXACTLY THE SAME WAY. GET IT TO US AND THEN MADE BY ONE FACILITY AND, THEREFORE, HAVE A STANDARDIZED CELL LINE, WHICH IN DUE COURSE WE MAY PROVIDE THAT SERVICE OURSELVES OR LOOK TO SOME OTHER COMMERCIAL

NONPROFIT PROVIDER TO ENABLE THE DISTRIBUTION FROM THEN ON.

SO I THINK WE HAVE A CHANCE IF WE THINK THROUGH THIS PROPERLY. I THINK THIS DAY HAS BEEN WORTHWHILE JUST TO GET SOME OF THE POINTS THAT ARE FLYING THROUGH AND GET US A LITTLE MORE MATURE BEFORE WE TAKE A PROPOSAL FORWARD TO THE ICOC.

CHAIRMAN LO: I'VE GOT A NUMBER OF PEOPLE. DR. CYPRESS AND THEN DR. KIESSLING.

DR. CYPRESS: BY THE WAY, I PREFER RAY. I THINK ROBERT TAYLOR ON TO -- IT'S ROBERT TAYLOR, RIGHT? JOHN. SORRY, JOHN. ANYWAY, I THINK YOU'RE REALLY ONTO SOMETHING. AND IT'S SOMETHING WE'VE BEEN TALKING ABOUT AT ATCC FOR QUITE A WHILE. AND THAT IS THE ISSUE OF THE STATE OF THE MATERIALS AFTER THEY'RE DISTRIBUTED FROM A BANK. THERE ARE WAYS TO DEAL WITH IT. WE TALK ABOUT IT IN ARTICLE. ONE, EDITORS OF JOURNALS COULD DEMAND THAT THE MATERIAL BE DOCUMENTED, AND IT'S A SIMPLE DOCUMENTATION.

NOW, GO BACK TO THE POINT. IF YOU'RE THE DONOR OF THE MATERIALS AND YOU ARE GOING TO BE DISTRIBUTING IT TO ALL MEMBERS OF CIRM, SAY, FOR EXAMPLE, AND YOU ARE GOING TO BE SUBSIDIZING IT. REMEMBER, I TALKED ABOUT SUBSIDIZATION WHEN IT HAS

TO BE DEALT WITH. HECK, YOU CAN DEMAND CERTAIN THINGS THAT HAS TO BE DONE WITH THAT MATERIAL, LIKE DOCUMENTATION OF PASSAGES, DOCUMENTATION OF CONTAMINATION, BEFORE YOU ALLOW THIS MATERIAL TO BE PUBLISHED OR USED WITH YOUR NAME ON IT BECAUSE, AFTER ALL, IT CAME FROM CIRM. SO THAT'S ONE OF THE WAYS YOU COULD DO IT.

YOU ALSO CAN GO THE ROUTE THAT LAURIE TALKED ABOUT. YOU CAN HAVE AN EXCHANGE PROGRAM AT A VERY LOW COST.

DR. LORING: JEANNE.

DR. CYPRESS: GETTING EVERYTHING RIGHT. YOU COULD HAVE AN EXCHANGE PROGRAM WITH THE BANK WHERE AFTER X NUMBER OF PASSAGES WHICH YOU RECOMMEND IS A POINT OF WHERE YOU'VE LOST CONSTITUALITY, THAT YOU TRADE IT IN. OR YOU CAN ASK THE BANK TO CHECK YOUR MATERIALS AGAIN FOR THESE VARIOUS CRITERIA. I REALLY BELIEVE YOU'RE ONTO SOMETHING THAT WE'VE BEEN THINKING ABOUT. I THINK IT'S A STEP THAT WE OUGHT TO TAKE.

ONE MORE POINT. I ONCE ASKED OR I DIDN'T ASK, HE ASKED ME, THE LATE NOBEL LAUREATE JOSHUA LEDERBERG, WHO WAS ON OUR BOARD, HE ONCE SAID TO ME, "WHAT'S THE VALUE OF A BANK?" AND HE SAID, "RAY, YOU HAVE TO THINK ABOUT EVERYTHING IN ECONOMIC

TERMS." I SAID FINE. I WENT UP TO MIT AND I GOT THE WHIZ KIDS UP THERE IN ECONOMICS DEPARTMENT TO ASK THE QUESTION, AND THEY DID A MASSIVE STUDY WITH A BUNCH OF POST DOCS AND EVERYTHING. THEY CAME BACK WITH SOME GREAT ANSWERS. WHEN YOU DEPOSIT IN A BANK, WHETHER WISCONSIN, ATCC, OR CORYELL, OR ANY OTHER INTERNATIONAL BANK, A COUPLE OF VERY INTERESTING THINGS HAPPEN.

FIRST, YOU GET A FIVEFOLD INCREASE IN COMMERCIALIZATION. THIS IS DOCUMENTED, HARD ECONOMIC DATA, PUBLISHED AT MEETINGS. AND SECOND, THE INSTITUTION GETS AN EXTENDED CITATION TIME OF THE MATERIAL. IN OTHER WORDS, AND THIS IS IMPORTANT BECAUSE IN ACADEMIA, RECOGNITION OF THE INSTITUTION AND RECOGNITION OF THE SCIENTIST FOR THE WORK THEY'VE DONE IS VERY IMPORTANT. IT'S NOT ALL MONEY. OKAY. AND THAT IS PROBABLY ONE OF THE MOST POTENT FACTS, AND HE TALKS ABOUT IN HIS BOOK, THIS IS SCOTT STERN, THE ECONOMIST FROM MIT, WHO'S SINCE GONE TO NORTHWESTERN, AND HE TALKS ABOUT THE EFFECT ON THE RESEARCH PROCESS AND ITS LONGEVITY BECAUSE OF THE ROLE OF BANKS.

SO THERE'S A NUMBER OF VERY IMPORTANT ANSWERS TO THE QUESTION THAT LEDERBERG ASKED BESIDES THE QUALITY ISSUE. I THINK THIS IS ANOTHER FACTOR

WHY CIRM HAS TO BE LOOKING AT A BANKING APPROACH AND PUTTING IN THE RIGHT STRUCTURE.

AND FINALLY, THERE'S NO REASON WHY THE BANK COULDN'T BE IN CALIFORNIA. I LEAVE YOU THAT ONE.

DR. KIESSLING: I JUST ACTUALLY WANTED TO FOLLOW UP SOMETHING THAT DR. LORING SAID AND JOHN MENTIONED. WHEN I REVIEW PAPERS NOW THAT ARE WORKING ON CULTURED CELLS, I'M BEGINNING TO ASK THE AUTHORS TO PROVIDE INFORMATION ABOUT HOW THEY CHARACTERIZED THE CELL LINES DURING THE COURSE OF THOSE EXPERIMENTS. AND I DON'T KNOW EXACTLY WHAT THE ANSWER SHOULD BE. I THINK THAT CANCER CELL LINES ARE PARTICULARLY PROBLEMATIC, AND THERE'S A LOT OF WORK DONE ON CANCER CELL LINES. I THINK IF REVIEWERS, IF THE PEER REVIEW SYSTEM WORKED, AND IF REVIEWERS TURNED BACK TO EVERY AUTHOR HOW WAS THIS CELL LINE CHARACTERIZED ON THIS PARTICULAR SET OF EXPERIMENTS, THAT WOULD GO A LONG WAY TOWARDS SOLVING SOME OF THIS.

DR. LORING: MY ONLY RESPONSE IS I AGREE. I THINK, ESPECIALLY WITH THE CANCER LINES, EVEN IDENTITY OF THE CELLS HAS BEEN QUESTIONED. WE NEED TO ANTICIPATE THAT IN THIS FIELD AND MAKE SURE THAT WE START FROM THE VERY BEGINNING KNOWING THAT THERE

ARE ABSOLUTE IDENTIFIERS.

DR. WAGNER: I JUST WANT TO END THIS PART PERHAPS. THAT IS, IF WE'RE GOING TO MOVE TO CLINICAL USE OF THESE CELL LINES IN ANY WAY, SHAPE OR FORM POTENTIALLY IN THE FUTURE, THIS IS GOING TO BE KEY. IF YOU WANT TO TALK ABOUT GLP DATA AND ALL THAT, YOU HAVE TO BE ABLE TO HAVE THIS INFORMATION DONE IN A CERTAIN WAY TO BE ABLE TO EVEN GET APPROVAL FOR CERTAIN THERAPIES OR DIAGNOSTIC REAGENTS. SO FOR CERTAIN STUDIES THAT MOVE ON TO THAT DIRECTION, YOU'RE GOING TO HAVE TO BE ABLE TO KNOW EXACTLY WHAT PASSAGE AND HOW THEY WERE CHARACTERIZED.

AND, AGAIN, I THINK CIRM HAS THE ABILITY TO, ESPECIALLY WITHIN CIRM-FUNDED PROJECTS, IF YOU WANT TO GET THE MOST EFFECTIVENESS OUT OF THE MONEY YOU'RE INVESTING, THIS IS SOMETHING THAT I THINK IS GOING TO BE KEY.

CHAIRMAN LO: I WANT TO SORT OF GO BACK TO AN ISSUE WE HAD RAISED BEFORE AND TAKE ADVANTAGE OF OUR GUESTS. WE HAD SORT OF MENTIONED REALLY ONLY IN PASSING THE ISSUE OF RETURNING INFORMATION FROM THE GENOMIC SEQUENCING BACK TO THE ORIGINAL DONORS. DO WE EVER CONCEIVE OF DOING THAT? UNDER WHAT CIRCUMSTANCES? WHO HAS TO REVIEW IT, OKAY IT? AND

AS YOU KNOW, THERE'S A LOT OF DISAGREEMENT IN GENOMIC BIOBANKS AS TO HOW THEY'RE GOING TO HANDLE IT RANGING FROM SOME SAYING ABSOLUTELY NEVER TO SOME STUDY SAYING THAT WE'LL GIVE YOU A CD OF WHATEVER WE FIND. IT'S LIKE YOU SIGNED UP FOR 23ANDME.

SO I WAS GOING TO ASK DR. LORING SORT OF HOW SHE'S HANDLING THIS IN THE STEM CELL LINES SHE'S DERIVING WHERE SHE'S ACTUALLY DOING THE VERY RICH SNP'S DATA.

DR. LORING: THIS IS VERY TIMELY BECAUSE WE'VE BEEN IN OUR ETHNIC DIVERSITY PROJECT, WE, OF COURSE, THE SCIENTIFIC COMMUNITY IS VERY ETHICALLY DIVERSE, AND SO A LOT OF THE PEOPLE WHO HAVE VOLUNTEERED ARE ACTUALLY SCIENTISTS. THERE'S ONE THAT JUST CAME UP WHO VOLUNTEERED, BUT ONLY UNDER THE CIRCUMSTANCES THAT WE PROVIDED HIM HIS DATA BACK. SO I CONTACTED MY IRB AND ASKED THEM IF THAT WAS OKAY. AND THEY SAID ALL YOU NEED TO DO IS TO ADD ANOTHER CLAUSE TO YOUR IRB. IT'S PERFECTLY LEGITIMATE. I MEAN TO YOUR INFORMED CONSENT.

SO THEY WILL APPROVE IT. MY IRB AT LEAST WILL APPROVE THE RETURN OF THE DATA, WHICH THAT'S THE BEST I CAN DO AS A RESEARCHER. I ASKED THEM AND THEY SAID YES. I CAN SEE WHY HE WANTS IT. THAT'S HIS MOTIVATION FOR DOING IT IS TO GET HIS SNP DATA.

CHAIRMAN LO: SO TO PRESS A LITTLE BIT, AGAIN, TO GO BACK TO SOME OF THE ORIGINAL -- WELL, THE ORIGINAL RESEARCH ON BRCA, THE IDENTIFICATION OF BRCA, THERE WERE A LOT OF CONCERNS ABOUT GIVING PEOPLE INFORMATION BACK. AS SHERRY POINTED OUT, A REAL INSISTENCE ON COUNSELING BEFORE THEY GOT THE RESULTS AND AFTER THEY GOT THE RESULTS. OBVIOUSLY IF IT'S A SCIENTIST, YOU CAN SAY, WELL. HOW ABOUT PEOPLE WHO ARE LAYPEOPLE WHO DON'T HAVE THAT SORT OF SCIENTIFIC KNOWLEDGE? WHAT'S GOING TO BE YOUR POLICY IN TERMS OF ASSESSING THEIR ABILITY TO UNDERSTAND OR ASSESSING THEIR ABILITY TO UNDERSTAND THE IMPLICATIONS OF GETTING THAT INFORMATION BACK?

DR. LORING: I UNDERSTAND. AND I PROBABLY SHOULD HAVE BEEN MORE CLEAR. OUR INFORMED CONSENT AS IT IS NOW SAYS THAT WE WILL BE DOING GENOME SEQUENCING. WE WILL BE, BUT WE WILL NOT RETURN THAT INFORMATION TO YOU. SO THAT'S WHY I HAD TO GO BACK TO THE IRB AND ASK FOR AN EXCEPTION TO THAT BECAUSE THAT WAS OUR STANDARD POLICY BECAUSE WE'RE NOT IN THE GENETIC COUNSELING BUSINESS. WE PROMISED THEM THAT WE WOULD KEEP HIS SAMPLES ANONYMOUS, WHICH, OF COURSE, WE WILL. WE EXPLAIN HOW WE'RE GOING TO DO IT WHICH, OF COURSE, WE WILL DO.

SO I THINK -- THIS JUST CAME UP. THIS IS

JUST VERY, VERY RECENT. THIS IS A VERY PROMINENT SCIENTIST WHO SHALL REMAIN NAMELESS, BUT HE WANTS TO JOIN OUR STUDY. SO IT SEEMED REASONABLE TO ME. THAT'S WHY I ASKED BECAUSE IF THEY HAD SAID NO, I WOULD HAVE SAID NO TO HIM, BUT THEY DIDN'T THIS TIME.

DR. WAGNER: I HAVE TO SAY THAT'S PROBABLY NOT VERY RESPONSIBLE FROM THE IRB'S POINT OF VIEW. AND THE REASON BEING -- DON'T JUST SAY THAT BECAUSE THE SCIENTIST REALLY ALSO PROBABLY HAS NO IDEA, IF IT'S A BASIC SCIENTIST, REALLY WHAT THE IMPLICATIONS ARE. AND SO A GENETICS COUNSELOR IS REALLY THE ONLY WAY YOU COULD EVER DO ANYTHING LIKE THAT BECAUSE YOU HAVE NO IDEA WHAT YOU MIGHT FIND AND WHAT THE IMPLICATIONS MIGHT BE. IT COULD BE HORRENDOUS. AND NOT REALLY UNDERSTANDING REALLY WHAT THE QUESTION WAS WHAT MIGHT HAVE HAPPENED. I CAN TELL YOU THAT THERE'S OTHER CIRCUMSTANCES WHERE THIS HAS OCCURRED. THIS IS NOT A NEW QUESTION.

BUT ON THE OTHER HAND, I THINK I PERSONALLY DON'T HAVE A PROBLEM WITH SAYING, YES, THEY HAVE ACCESS TO THE DATA, BUT ONLY AFTER YOU GUARANTEE THE COUNSELING BECAUSE, YOU KNOW, YOU CAN'T BE THE COUNSELOR EITHER BECAUSE YOU ARE NOT A TRAINED GENETICS COUNSELOR. SO WHAT ARE YOU GOING

TO DO IF IT COMES BACK THAT THERE IS BRCA 2? THEN WHAT?

DR. LORING: WE HAVE TO COME BACK TO THE COMMERCIAL GENOTYPING SERVICES. THE WATER IS ALREADY UNDER THIS BRIDGE. SO NOW IT'S OUR DECISION TO ACT LIKE THEM OR TO ACT IN A DIFFERENT WAY. THAT WAS THE QUESTION BEFORE THE IRB. CAN WE RETURN DATA WITH -- AND YOU CAN DOWNLOAD ALL OF YOUR SNP GENOTYPING. IT'S GOING TO BE EXACTLY THE SAME THING AS IF HE PAID 23ANDME TO GET HIS GENOTYPE. IT'S ALMOST THE SAME MICROARRAY THAT THEY USE, VERY SIMILAR. SO HE'S NOT GOING TO FIND OUT ANYTHING HORRENDOUS BECAUSE THOSE ARE NOT -- THAT INFORMATION IS NOT AVAILABLE IN THE SNP GENOTYPING AREAS. ALL THOSE THINGS ARE BLOCKED, AND WE CAN'T SEE THEM EITHER. SO RIGHT NOW THERE ARE SOME SAFEGUARDS. BUT THINGS LIKE CYSTIC FIBROSIS, THEY ARE AVAILABLE AND YOU CAN SEE THEM, SO YOU CAN FIND OUT IF YOU'RE A CARRIER.

DR. WAGNER: SURE. IT'S JUST THAT SOMEONE NEEDS TO EXPLAIN TO THEM WHAT THE REAL RISK IS.

DR. LORING: IN THIS PARTICULAR CASE, THIS PARTICULAR INDIVIDUAL IS PERFECTLY CAPABLE OF UNDERSTANDING IT. YOU'RE RIGHT. OUR STANDARD IS TO NOT RETURN ANY GENETIC INFORMATION. SO THIS IS AN

EXCEPTION. WE MAY NEVER MAKE ANOTHER ONE AGAIN.

DR. ISASI: WHAT IS INTERESTING IS THAT NAS GUIDELINES, THE 2008 VERSION, TALKS ABOUT BANKS AND REGISTRIES. YOU HAVE EXPLICIT PROTOCOL FOR HANDLING THE RETURN OF WHAT THEY CALL CLINICALLY SIGNIFICANT INFORMATION TO DONORS. AND I WONDER IF THE BANKERS, ANY OF YOU HAVE IN YOUR PROTOCOLS STIPULATIONS LIKE THAT OR ANYBODY IS FOLLOWING OR TAKING NOTE OF NAS GUIDELINES.

DR. WAGNER: I GUESS I MISSED PART. WHAT EXACTLY ARE YOU ASKING?

DR. ISASI: YOU WERE TALKING ABOUT GETTING INDIVIDUAL RETURN OF RESEARCH TO DONORS OR CONVEYING INFORMATION COMING FROM THE STUDIES. AND I HAVE SEEN LITTLE NOTICE, FOR EXAMPLE, NAS GUIDELINES, THE 2008 VERSION THAT JUST CAME, IT CALLS FOR BANKS AND REGISTRIES TO HAVE A PROTOCOL ESTABLISHED FOR HOW TO HANDLE INDIVIDUAL RETURN OF RESULTS AND HOW TO HANDLE CLINICAL SIGNIFICANT INFORMATION IS HOW THEY CALL IT. I SEE SOMETHING -- SIMILAR PROVISION IN THE UK STEM CELL BANK. BUT I WONDER FOR THE BANKERS HERE WHETHER THERE IS SUCH A PROTOCOL EVER ADOPTED OR SOME RESEARCH PROJECTS.

DR. WAGNER: CERTAINLY IN THE SETTING OF NOT EMBRYONIC STEM CELLS OR IPS CELLS, BUT IN THE

SETTING OF CORD BLOOD TRANSPLANTATION WHERE THERE'S A LARGE REPOSITORY OF UMBILICAL CORD BLOOD FOR WHICH A SIMILAR TYPE OF CONCERN IS WE ACTUALLY DO HAVE GENETIC TESTING PERFORMED ON THE SAMPLES, AND WE ALSO DO INFORM THEM THAT WE'RE GOING TO DO SUCH, BUT SPECIFIC GENETIC TESTING. IT'S NOT LIKE A GENOMEWIDE GENETIC TESTING. AND SO THEY'RE INFORMED THAT WE WILL HAVE THE POTENTIAL FOR GIVING THEM INFORMATION BACK, BUT THEY HAVE AN OPT-OUT CLAUSE. SO THEY CAN ELECT TO SAY I'M NOT GOING TO -- I DON'T WANT THE INFORMATION, BUT THE DEFAULT IS THEY GET THE INFORMATION BACK, BUT IT'S VERY SPECIFIC GENETIC TESTING.

I THINK FOR THE NAS GUIDELINES, IF I RECALL CORRECTLY, SINCE I'M PART OF THAT COMMITTEE, THEY'RE JUST SAYING THAT YOU MUST HAVE A PLAN OF HOW TO HANDLE IT RATHER THAN SPECIFYING WHAT THE PLAN SHOULD BE.

CHAIRMAN LO: I THINK THE IDEA WAS YOU WANT TO HAVE THOUGHT THIS OUT IN ADVANCE WHEN YOU SET UP THE BANK RATHER THAN HAVE SOMETHING COME UP WHERE SOMEBODY SAYS, MY GOSH, LOOK AT THAT SEQUENCE. THEY HAVE A REALLY DELETERIOUS MUTATION AND NOT TO HAVE A PROCESS THOUGHT OUT.

THE NAS GUIDELINES HAD TO DO WITH

CLINICALLY SIGNIFICANT RESULTS, WHATEVER THAT MEANS. I ASSUME PROBABLY MEANS IF YOU HAPPEN TO NOTICE BRCA 1 OR 2, THAT'S CLINICALLY SIGNIFICANT. BUT THE OTHER EXTREME, I THINK DR. LORING'S EXAMPLE IS COMMON, THAT PEOPLE SAY, GLAD TO JOIN YOUR STUDY, BUT LET'S HAVE A LITTLE QUID PRO QUO. I'D LOVE TO HAVE MY DVD WITH MY ENTIRE GENOMIC SEQUENCE. I'M GOING TO MAKE A POSTER OUT OF IT FOR MY LIVING ROOM. WE'VE HAD PEOPLE SAY ALL KINDS OF THINGS ABOUT THEY WANT INFORMATION WHETHER OR NOT IT MEANS ANYTHING.

DR. TAYLOR: I'M BEING A LITTLE BIT QUIET HERE BECAUSE I ACTUALLY HAVE A PAPER ON THIS TOPIC COMING OUT ON JUNE 16TH IN *SCIENCE TRANSLATIONAL MEDICINE*. ONE OF THE DIFFERENCES HERE IS THERE'S A DIFFERENCE BETWEEN PROBABILISTIC INFORMATION POSSIBLY ASSOCIATED WITH SOME GENE AND VALIDATED CLINICALLY SIGNIFICANT INFORMATION FOR CONDITIONS THAT ARE BOTH SEVERE AND TREATABLE. SO THE CLASSIC STANDARD HERE IS VALID TEST, SEVERE, TREATABLE, OTHERWISE YOU SHOULDN'T KNOW AS A PARTICIPANT, BUT THAT STANDARD IS REALLY UNDER RECONSIDERATION BY THE NHLBI RIGHT NOW.

THERE CERTAINLY IS A GENERAL REVIEW AMONG RESEARCH ETHICISTS THERE'S AN OBLIGATION TO PROVIDE MEANINGFUL RESULTS. BUT WHAT ARE MEANINGFUL

RESULTS? THERE'S A RECENT PAPER, MAYBE END OF LAST YEAR, THAT SAYS NOTHING MOTIVATES PARTICIPATION AS MUCH, LITERALLY NOTHING, NOT EVEN FOUR TIMES AS MUCH AS MONEY, HUMONGOUS AMOUNTS OF MONEY, NOTHING MOTIVATES PARTICIPATION AS MUCH AS PROMISING RESULTS BACK.

DR. ISASI: CAN YOU REPEAT WHICH JOURNAL IS COMING?

DR. TAYLOR: *SCIENCE TRANSLATIONAL MEDICINE*.

CHAIRMAN LO: PAT, ARE THERE CLEAR ISSUES HERE OF HAVING TO HAVE THE TEST REPEATED ON A CLEAR CERTIFIED LINE?

DR. TAYLOR: SURE. AS YOU KNOW, NO TEST, NO SUCH TEST CAN BE USED FOR PURPOSES OF DIAGNOSIS AND TREATMENT BY A CLINICIAN, ALL THOSE CAVEATS ARE IMPORTANT, WITHOUT IT'S BEING VALIDATED.

CHAIRMAN LO: OTHER QUESTIONS, COMMENTS? ALAN, ARE WE FULFILLING YOUR HOPES WHEN YOU SET THIS UP? ARE THERE THINGS YOU WANT US TO SORT OF TRY AND TACKLE BEFORE DINNER?

DR. TROUNSON: I THINK IT'S BEEN VERY USEFUL. THANKS, BERNIE AND TO ALL THE STANDARDS WORKING GROUP, BUT ALL THE COLLEAGUES THAT JOINED US IN A VERY FREEWHEELING DISCUSSION. AND I THINK ALL

OF THOSE ISSUES, INCLUDING THE REALLY DEPTH OF THE IP ISSUES THAT WE NEED TO THINK ABOUT AS WELL, THEY'RE ALL CRITICAL COMPONENTS. AND SO IF WE CONTINUE TO DEVISE THIS OPPORTUNITY, WE WILL BE DRAWING ON, I THINK, SOME OF THE EXPERTISE THAT'S HERE IN TRYING TO FORMULATE SOMETHING WHICH WE THINK WOULD BE A RESOURCE FOR MANY DECADES OF RESEARCH. AND HOPEFULLY THAT WOULD BE VERY MEANINGFUL TO CALIFORNIA, BUT ALSO TO THE REST OF THE WORLD.

IF WE CAN MAKE IT EMPHATICALLY USABLE AND SHOW SOME LEADERSHIP HERE IN GETTING SOMETHING EXTREMELY VALUABLE AND STANDARDIZED THAT DERIVES REALLY GOOD QUALITY DATA, THEN I THINK WE CAN BE THANKED FOR A VERY LONG TIME FOR A RESOURCE THAT WAS OPPORTUNE AT THE TIME. SO ALL OF THIS WE WILL COMPUTE AND TAKE FORWARD. WE'LL CERTAINLY RETURN WITH QUESTIONS, I'M SURE, SAYING, WELL, WE HADN'T ACTUALLY THOUGHT OF THAT, BUT WHAT DOES THE STANDARDS COMMITTEE THINK OF THIS PARTICULAR SITUATION. BUT I THINK WE HAVE ENOUGH INFORMATION NOW TO SORT OF PROGRESS OUR THINKING IN THIS AREA. AND I THINK IT'S BEEN VERY, VERY USEFUL, AND WANTED TO THANK GEOFF AND YOU, BERNIE, AND SHERRY FOR OPENING UP THE OPPORTUNITY TO WORKSHOP THE IDEA A LITTLE BEFORE WE GOT TOO DEEP IN THE WATER AND WERE

TRYING TO CREATE SOMETHING WHERE WE HADN'T PRETHOUGHT SOME OF THESE ISSUES THROUGH. I THINK IT'S BEEN VERY, VERY USEFUL FOR THE WHOLE TEAM, AND I WANT TO PARTICULARLY THANK EVERYBODY WHO HAS SPENT THEIR TIME TODAY IN HELPING MAKE CONTRIBUTIONS TO THIS. IT'S BEEN VERY USEFUL FOR US.

CHAIRMAN LO: SO I ALSO WANT TO ADD MY THANKS TO OUR GUESTS FOR COMING AND SHARING THEIR KNOWLEDGE AND EXPERTISE AND VIEWPOINTS.

I JUST WANT TO MAKE SURE WE WERE ALL CLEAR ON WHAT'S GOING TO HAPPEN NEXT SINCE I LOOK TO GEOFF BECAUSE GEOFF IS THE EFFECTOR ARM OF THIS. THERE WILL BE SOME SORT OF REPORT ON THE WORKSHOP LIKE OTHER WORKSHOPS THAT WILL BE ON THE WEB SITE. WE'VE ALREADY TASKED GEOFF WITH SORT OF ASSEMBLING INFORMATION ABOUT WHAT'S CURRENTLY BEING DONE IN TERMS OF REGULATIONS, GUIDELINES FROM OTHER BODIES, COURT CASES, BEST PRACTICES OF OTHER SORT OF BANKS OF VARIOUS OTHER KINDS OF BIOLOGICAL MATERIALS TO HELP INFORM THE DISCUSSION PARTICULARLY ON THE ISSUES THAT WE'VE ALREADY LOOKED AT.

I WANT TO ASK ALAN. THERE'S OBVIOUSLY A LOT OF ISSUES YOU AND YOUR TEAM ARE GOING TO BE THINKING ABOUT AS YOU MOVE FORWARD ON THIS. I'M SORT OF THINKING ABOUT SORT OF THE MATCH BETWEEN

YOUR NEEDS AND OUR SORT OF EXPERTISE, THAT GOING BACK IN HISTORY AT THE VERY START OF CIRM THERE'S A SEPARATE IP WORKING GROUP, WAS THAT WHAT IT WAS CALLED, THAT REALLY DEALT WITH THOSE VERY COMPLICATED AND DIFFICULT ISSUES. AND THEY HAD A LOT OF EXPERTISE ON IP, WHICH I THINK MOST OF US REALLY DON'T HAVE. JEFF, I DON'T KNOW IF YOU AND OTHERS ARE ACTUALLY ON -- FRANCISCO AND JEFF ARE ON THAT COMMITTEE, BUT I THINK THE REST OF US, I DON'T KNOW ABOUT PROFESSOR ROBERTS, BUT THE REST OF US ARE SORT OF THIS IS NOT OUR AREA.

SO GIVEN THAT I THINK THAT'S BEEN IDENTIFIED AS AN IMPORTANT ISSUE THAT NEEDS TO BE SORT OF WORKED OUT, DO YOU HAVE THOUGHTS ON RECONVENING OR GOING BACK TO SOME OF THAT COMMITTEE, OR DID YOU WANT TO SORT OF RELY ON THIS GROUP TO SORT OF THINK THAT THROUGH? I'M JUST CONCERNED ABOUT OUR COMPOSITION ISN'T REALLY OPTIMAL FOR THAT.

MR. SHEEHY: ACTUALLY IT MIGHT NOT BE A BAD IDEA. THE IP COMMITTEE IS SUPPOSED TO -- I THINK WE HAD A DECISION YESTERDAY THAT THEY WERE GOING CONVENE A MEETING. I THINK THE ITEM THAT THEY WERE GOING TO LOOK AT IS PRETTY PERFUNCTORY. AND SO THIS MIGHT BE A GOOD THING AT LEAST FOR THEM TO START TO WORK ON. I THINK IT PROBABLY IS BETTER.

WE'VE GOT A DIFFERENT TYPE OF EXPERTISE. WE DON'T HAVE MARY MAXON ANYMORE UNFORTUNATELY WHO WAS INVALUABLE. THAT'S HOW WE DID LAST TIME. IT'S UP TO -- I DON'T KNOW WHAT ALAN THINKS.

DR. TROUNSON: I THINK THAT WE FORTUNATELY HAVE ELONA BAUM WHO IS VERY GOOD IN THIS RESPECT AND HAS COME OUT OF A VERY MAJOR ORGANIZATION THERE. SO I THINK WE CAN SORT OF DEVELOP SOME THOUGHTS IN THIS DIRECTION, AND THE IP TASK FORCE WILL BE ABSOLUTELY ESSENTIAL FOR US TO TRY IT OUT. WE'VE GOT QUITE A LOT OF COMPONENT PARTS TO PUT TOGETHER, THE SCIENCE PART, THE ORGANIZATIONAL PART. WE'LL FIGURE OUT WHETHER THE ICOC IS SUPPORTIVE OF US MOVING IN THIS DIRECTION, AND WE'LL HAVE TO PUT A DETAILED CASE IN FRONT OF THEM.

BUT AT LEAST I THINK IT'S BEEN USEFUL TO REALLY HEAR FROM THE SPECTRUM THAT WE'VE HEARD FROM, TO BE HONEST. AND SOME OF THE INPUTS THAT HAVE COME FROM THE STANDARDS GROUP HAS BEEN TERRIFIC. I THINK IT'S BEEN A GREAT TO AND FRO BETWEEN OUR EXPERTS AND YOURSELVES. AND SO THIS IS REALLY HELPFUL, BUT I THINK THIS IS THE CIRM WAY OF DOING THINGS WHERE THE PUBLIC HAVE HAD THE OPPORTUNITY TO COME ALONG AND LISTEN. WE HAVEN'T SORT OF BEEN IN THE BANKING BUSINESS UP UNTIL NOW, AND I THINK THAT'S PROBABLY

BEEN THE RIGHT DECISION. LET'S WORK ON THIS A LITTLE FURTHER NOW. I FEEL ENCOURAGED THAT THERE'S A FAIR BIT OF SUPPORT FROM THE STANDARDS GROUP TO EXPLORE THIS, BUT EXPLORE IT IN A WAY WHICH REALLY GETS THE MAJOR BENEFITS FROM AN ACTIVITY THAT CIRM COULD PUT TOGETHER. SO I THINK WE WILL. I THINK WE'LL NEED TO GET THE SCIENCE RIGHT. WE NEED TO GET SOME OF THE ORGANIZATIONAL THOUGHTS A BIT MORE MATURE AND THEN BRING THEM TOGETHER WITH THE SUGGESTIONS THAT YOU'VE MADE TO US. AND WE'RE CLEARLY GOING TO BE TALKING TO YOU INDIVIDUALS AND OUR EXPERT PANELISTS THAT HAVE JOINED US TODAY TO GET SOME CLARITY OF SOME OF THOSE ISSUES. THERE'S A LOT OF THEM.

THE DIVERSITY ISSUE IS A DEEP PLUMBING WELL WHERE WE'VE STARTED TO WORK INTO THAT SPACE. AND THE MORE WE LOOK, IT IS A VERY TRICKY BUSINESS, AS YOU SAY, DR. ROBERTS. SO WE KNOW THOSE THINGS NEED TO BE WELL THOUGHT THROUGH. AND IF WE'RE GOING TO ENCOURAGE A BROAD SPECTRUM OF CALIFORNIANS TO BE INVOLVED, WE NEED TO MAKE SURE WE'VE GOT ALL OF THE ABILITIES TO DO THAT. PROVIDING CONSENTABLE INFORMATION TO THE BROAD POPULATION, VERY IMPORTANT MATTER. WE'LL KEEP YOU INFORMED AS WELL.

CHAIRMAN LO: I THINK I SPEAK FOR THE

COMMITTEE, THAT WE'VE ALWAYS REGARDED OUR WORK AS A WORK IN PROGRESS. SO I THINK WE LOOK FORWARD, ALAN, TO WORKING WITH AND YOUR TEAM AS YOUR IDEAS DEVELOP TO SORT OF CONTINUE WHENEVER IT WOULD BE HELPFUL TO SORT OF PROVIDE YOU FEEDBACK AND THOUGHT. AND I THINK, AGAIN, IT'S GOING TO BE A STEPWISE PROCESS. SO I THINK IN THIS REPORT WE CAN JUST IDENTIFY SOME ISSUES AND CONCERNS.

I THINK THE NEXT STEP WOULD BE TO MAKE SURE THAT WE'VE IDENTIFIED IMPORTANT POINTS TO CONSIDER AND PRECEDENTS OR BEST PRACTICES AND PROBLEMS PREVIOUSLY ENCOUNTERED OR SHORTCOMINGS IN CURRENT APPROACHES. AND THEN I DON'T THINK WE'RE GOING TO BE ABLE TO SOLVE THE PROBLEMS FOR YOU IN A MONTH OR SIX MONTHS, BUT I THINK, AS YOU MATURE THE SORT OF SCIENTIFIC AND ORGANIZATIONAL ASPECTS, WE CAN THEN SORT OF MOVE FORWARD TO ADDRESS SOME OF THESE ETHICAL ISSUES IN MORE SPECIFICITY. I THINK THESE ARE -- IT'S AN IMPORTANT SORT OF IDEA FOR A PROJECT THAT HAS A LOT OF POTENTIAL BENEFIT, AND I THINK WE WOULD ALL LOOK FORWARD TO CONTINUING TO WORK WITH YOU AND TO SORT OF THINK THROUGH SOME OF THESE ISSUES AND MAKE SURE WE GET IT RIGHT.

ANY OTHER COMMENTS, ISSUES? I THINK WE'VE HAD A VERY PRODUCTIVE DAY, AND I SORT OF

SHORTCHANGED YOU ON YOUR MORNING BREAK. SO UNLESS THERE ARE BURNING THINGS PEOPLE WANT TO SAY --

DR. WAGNER: I'M GOING TO MAKE ONE COMMENT BECAUSE I WAS JUST LOOKING AT IT. I'VE BEEN ON THE HUMAN EMBRYONIC STEM CELL ADVISORY COMMITTEE AT THE NAS FOR A WHILE. TODAY WE ACTUALLY DISSOLVED. SO IT NO LONGER EXITS. HOWEVER, THE ONE THING I DIDN'T REALIZE. THE FIRST REPORT CAME OUT ON SEPTEMBER 11, 2001. SO THIS JUST CAME OUT. I JUST GOT THIS E-MAIL JUST REMINDING US OF THAT.

CHAIRMAN LO: I HOPE IT'S NOT RAINING OUTSIDE. WE HAVE DINNER AT SIX; IS THAT CORRECT, PAT, IN THE SAME ROOM WHERE WE HAD LUNCH? THE 30TH FLOOR. WE'RE GOING UPSTAIRS. IT'S A GREAT VIEW. SO THAT'S OUR REWARD.

AND OTHERWISE, I WANT TO THANK ALL OF YOU FOR COMING AND THANK YOU FOR YOUR IDEAS, AND WE'LL BE BACK IN TOUCH.

(THE MEETING WAS THEN CONCLUDED AT 05:07 P.M.)

REPORTER'S CERTIFICATE

I, BETH C. DRAIN, A CERTIFIED SHORTHAND REPORTER IN AND FOR THE STATE OF CALIFORNIA, HEREBY CERTIFY THAT THE FOREGOING TRANSCRIPT OF THE PROCEEDINGS BEFORE THE SCIENTIFIC AND MEDICAL ACCOUNTABILITY STANDARDS WORKING GROUP OF THE INDEPENDENT CITIZEN'S OVERSIGHT COMMITTEE OF THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE IN THE MATTER OF ITS REGULAR MEETING HELD AT THE LOCATION INDICATED BELOW

SAN FRANCISCO MARRIOTT UNION SQUARE
480 SUTTER STREET
SAN FRANCISCO, CALIFORNIA
ON
WEDNESDAY, MAY 26, 2010

WAS HELD AS HEREIN APPEARS AND THAT THIS IS THE ORIGINAL TRANSCRIPT THEREOF AND THAT THE STATEMENTS THAT APPEAR IN THIS TRANSCRIPT WERE REPORTED STENOGRAPHICALLY BY ME AND TRANSCRIBED BY ME. I ALSO CERTIFY THAT THIS TRANSCRIPT IS A TRUE AND ACCURATE RECORD OF THE PROCEEDING.

BETH C. DRAIN, CSR 7152
BARRISTER'S REPORTING SERVICE
1072 BRISTOL STREET
SUITE 100
COSTA MESA, CALIFORNIA
(714) 444-4100