BEFORE THE

INDEPENDENT CITIZENS' OVERSIGHT COMMITTEE
TO THE
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE
ORGANIZED PURSUANT TO THE
CALIFORNIA STEM CELL RESEARCH AND CURES ACT

REGULAR MEETING

LOCATION:	LUXE HOTEL 11461 SUNSET BOULEVARD LOS ANGELES, CALIFORNIA
DATE:	WEDNESDAY, DECEMBER 11, 2013 THURSDAY, DECEMBER 12, 2013 9 A.M.
REPORTER:	BETH C. DRAIN, CSR CSR. NO. 7152
BRS FILE NO.:	95381 & 95494

I N D E X

I N D E X (CONT'D.)

LOS ANGELES, CALIFORNIA; DECEMBER 12, 2013

9 A.M.

CHAIRMAN THOMAS: OKAY. I'D LIKE TO WELCOME EVERYBODY TO DAY TWO OF OUR TWO-DAY SESSION. YESTERDAY WE HAD OUR WORKSHOP. TODAY WE HAVE ONE MORE ITEM FROM THAT, WHICH WE'LL GET TO IN A BIT, BUT IN ADDITION THE FULL DAY'S AGENDA ON A BUNCH OF OTHER ITEMS. DO WE NEED TO RECALL -- MARIA, DO WE NEED TO REDO THE PLEDGE OF ALLEGIANCE? NO. WE'RE GOOD. GOT TO GET THE PROCEDURE RIGHT.

MS. BONNEVILLE: LARS BERGLUND.

DR. BERGLUND: YES.

MS. BONNEVILLE: LINDA BOXER.

DR. BOXER: HERE.

MS. BONNEVILLE: DAVID BRENNER.

DR. BRENNER: HERE.

MS. BONNEVILLE: SUE BRYANT. ANNE-MARIE DULIEGE.

DR. DULIEGE: HERE.

MS. BONNEVILLE: MARCY FEIT. LEON FINE.

DR. FINE: HERE.

MS. BONNEVILLE: ELIZABETH FINI.

DR. FINI: HERE.

MS. BONNEVILLE: JUDY GASSON. MICHAEL

GOLDBERG.

MR. GOLDBERG: HERE.

MS. BONNEVILLE: SAM HAWGOOD.

DR. HAWGOOD: HERE.

MS. BONNEVILLE: STEPHEN JUELSGAARD.

DR. JUELSGAARD: HERE.

MS. BONNEVILLE: TED KRONTIRIS.

DR. KRONTIRIS: HERE.

MS. BONNEVILLE: SHERRY LANSING. BERT LUBIN. FRANCISCO PRIETO. ROBERT QUINT.

DR. QUINT: HERE.

MS. BONNEVILLE: AL ROWLETT.

DR. ROWLETT: HERE.

MS. BONNEVILLE: JOAN SAMUELSON. JEFF SHEEHY.

MR. SHEEHY: HERE.

MS. BONNEVILLE: OSWALD STEWARD. JONATHAN THOMAS.

CHAIRMAN THOMAS: HERE.

MS. BONNEVILLE: ART TORRES.

MR. TORRES: HERE.

MS. BONNEVILLE: CARL WARE. DONNA WESTON.

DR. WESTON: HERE.

MS. BONNEVILLE: DIANE WINOKUR.

MS. WINOKUR: HERE.

CHAIRMAN THOMAS: FOR THE RECORD, JEFF JUST WALKED IN.

DR. BRYANT: ALSO I WAS ON MUTE. SORRY. THIS IS SUE.

CHAIRMAN THOMAS: OKAY. ALL RIGHT. THANK YOU, EVERYBODY.

WE ARE GOING TO TAKE AN ITEM OR TWO OUT OF ORDER BECAUSE WE HAVE SOME FOLKS HERE WHO ARE GOING TO PRESENT, SO WE'LL PROCEED FIRST TO ITEM 14, WHICH IS CONSIDERATION OF AUDIT RESULTS FROM MACIAS, ET AL.

MR. GODSEY: GOOD MORNING, EVERYONE. MY NAME IS JIM GODSEY. I'M THE PARTNER FROM MGO. I'LL SUMMARIZE OR SHORTEN IT TO MGO. AND WE ARE HERE TO PRESENT THE RESULTS OF OUR EXAMINATION OF THE FINANCIAL STATEMENTS OF THE INSTITUTE FOR THE PERIOD ENDING JUNE 30, 2013.

WE'VE CONDUCTED -- OUR AUDIT WAS CONDUCTED IN ACCORDANCE WITH GENERALLY ACCEPTED AUDITING STANDARDS AND INCLUDED RESPONSIBILITIES UNDER GOVERNMENTAL AUDITING STANDARDS. BASED UPON OUR AUDIT, WE HAVE ISSUED OUR REPORT DATED OCTOBER 15, 2013. THAT IS, THE REPORT IS UNMODIFIED. MANY OF YOU HAVE GONE THROUGH THIS A NUMBER OF TIMES. THIS IS A NEW CHANGE. WE USED TO REFER TO THIS AS

UNQUALIFIED. THERE WAS SO MUCH QUESTIONS ABOUT A NEGATIVE IN THE UNQUALIFIED ASPECT OF IT, WE SIMPLIFIED EVERYTHING. NOW WE'RE CALLING IT UNMODIFIED. WE STILL HAVE A NEGATIVE, AND IT'S STILL A CLEAN OPINION. SO THIS IS THE OPINION THAT YOU WOULD EXPECT TO SEE, WANT TO SEE, ON YOUR FINANCIAL STATEMENTS, INDICATING THOSE FINANCIAL STATEMENTS HAVE BEEN PREPARED IN ACCORDANCE WITH GENERALLY ACCEPTED ACCOUNTING STANDARDS.

IN ADDITION, WE HAVE ISSUED OUR REPORT ON INTERNAL CONTROLS IN ACCORDANCE WITH GOVERNMENTAL AUDITING STANDARDS. THOSE STANDARDS REQUIRE THAT WE UNDERSTAND THE INTERNAL CONTROLS NECESSARY TO PLAN THE AUDIT ENGAGEMENT AND DETERMINE WHAT ADDITIONAL AUDIT STEPS, PROCEDURES WE WILL APPLY. THAT IS LESS THAN WHAT WOULD BE REQUIRED TO ISSUE AN OPINION ON THOSE FINANCIAL -- ON THE INTERNAL CONTROLS. SO IN ACCORDANCE WITH THOSE STANDARDS, WE'VE ISSUED OUR REPORT. WE HAVE NOT PROVIDED AN OPINION, NOT REQUIRED, AND WE IDENTIFIED THAT THERE WERE NO SIGNIFICANT DEFICIENCIES OR MATERIAL WEAKNESSES IDENTIFIED IN THE SYSTEM OF INTERNAL CONTROLS FOR THE PERIOD ENDING JUNE 30, 2013.

I HAVE A COUPLE OF OTHER REQUIRED, WHAT WE REFER TO AS REQUIRED COMMUNICATIONS. AGAIN, THIS IS

JUST TO EMPHASIZE THAT THESE FINANCIAL STATEMENTS ARE MANAGEMENT RESPONSIBILITIES. THEY ARE REPRESENTATIONS MADE BY MANAGEMENT, AND MANAGEMENT IS RESPONSIBLE FOR THE SELECTION OF THE APPROPRIATE ACCOUNTING PRINCIPLES THAT ARE USED TO PREPARE THOSE. WE REVIEW THOSE ACCOUNTING PRINCIPLES. WE CONCUR WITH MANAGEMENT THAT THEY WERE THE APPROPRIATE PRINCIPLES FOR THE INSTITUTE, AND THAT THEY WERE CONSISTENTLY APPLIED FROM ONE PERIOD TO THE NEXT.

WE DID NOT IDENTIFY -- WE IDENTIFIED NO TRANSACTIONS THAT THERE WAS NOT SUBSTANTIVE AUTHORITY FOR THAT TYPE OF ATTRACTION. AND BASED UPON OUR AUDIT, WE BELIEVE THAT ALL TRANSACTIONS, ALL SIGNIFICANT TRANSACTIONS, WERE RECOGNIZED IN THE APPROPRIATE ACCOUNTING PERIOD.

WE DID NOT EXPERIENCE ANY UNUSUAL DIFFICULTIES DURING THE PERFORMANCE OF THE AUDIT. MANAGEMENT HAS BEEN TREMENDOUSLY RESPONSIVE TO US. ALL QUESTIONS THAT WE HAD WERE ANSWERED. THERE WERE ABSOLUTELY NO RESTRICTIONS PLACED ON US DURING THE COURSE OF THE AUDIT.

WE DID NOT HAVE ANY DISAGREEMENTS, PROFESSIONAL DISAGREEMENTS, AS FAR AS ACCOUNTING PRINCIPLES WITH MANAGEMENT. AND WE HAVE RECEIVED

WRITTEN CONFIRMATION FROM MANAGEMENT, WHAT WE REFER TO AS THE MANAGEMENT LETTER, DATED OCTOBER 15TH AS WELL, INDICATING THAT EVERYTHING THAT IS IN THE FINANCIAL STATEMENTS IS PROPERLY STATED IN THE FINANCIAL STATEMENTS AND THAT ALL TRANSACTIONS THAT SHOULD BE INCLUDED HAVE, IN FACT, BEEN INCLUDED.

AND THE LAST ITEM I WOULD SHARE WITH YOU ALL IS THAT THERE WAS NO PRECONDITIONS TO US BEING SELECTED AS THE EXTERNAL AUDITORS FOR THE INSTITUTE. THERE WERE NO CONDITIONS, NO AGREEMENTS AS TO IF WE SELECT YOU, WILL YOU HANDLE CERTAIN TRANSACTIONS THIS WAY OR THAT WAY. SO NO PREEXISTING CONDITIONS.

THE REST OF THIS IS INCLUDED IN OUR LETTER. SO IF YOU HAVE ANY FURTHER QUESTIONS OR DETAILS, WE CAN REFER TO THAT. THAT'S MY FORMAL PRESENTATION. IF THERE'S ANY QUESTIONS THAT I CAN ANSWER, I'D LIKE TO DO THAT AT THIS TIME.

CHAIRMAN THOMAS: ANY QUESTIONS FROM MEMBERS OF THE BOARD? I'D LIKE TO THANK YOU AND WOULD LIKE TO PARTICULARLY THANK CHILA FOR HER INCREDIBLE WORK IN HELPING TO COORDINATE ALL OF THIS AND JUST ALL THE FINANCIAL WORK SHE DOES THROUGHOUT THE YEAR, WHICH IS SO FIRST-RATE AND IS REFLECTED HERE IN THIS REPORT. SO, CHILA, THANK YOU VERY MUCH.

DO YOU HAVE A COMMENT, MR. GOLDBERG?

MR. GOLDBERG: YES. I JUST WANTED TO SECOND THAT. MY APPRECIATION AND CONGRATULATIONS TO, OF COURSE, CHILA, WHO HAS KIND OF QUARTERBACKED THIS, BUT ALSO TO ALAN AND THE ENTIRE STAFF BECAUSE IT REQUIRES ALL OF YOU TO BE ABLE TO GENERATE THIS KIND OF SUPERB ACCOUNTING AND AUDIT PERFORMANCE.

WHAT WE LIKE AT THE FINANCE SUBCOMMITTEE IS TO BE AS UNDER THE RADAR AS POSSIBLE TO THE REST OF YOU. AND THANKS FOR ALLOWING US TO BE THAT FOR THIS BOARD, SO IT DOESN'T HAVE TO SPEND ITS TIME ON DEALING WITH UNTIDY AND IMPROPER ISSUES. IT'S AN EXTRAORDINARY THING IN AN ORGANIZATION THIS LARGE AND COMPLEX TO HAVE THE LONG RECORD OF CLEAN OPINIONS AND UNMODIFIED OPINIONS THAT WE'VE HAD. AGAIN, HATS OFF TO ALL OF THOSE PEOPLE RESPONSIBLE FOR THAT. THANK YOU.

CHAIRMAN THOMAS: THANK YOU. MR. HARRISON, WE JUST ACCEPT THE REPORT, CORRECT? OKAY. THANK YOU VERY MUCH.

MR. GODSEY: THANK YOU. GOOD MORNING.

CHAIRMAN THOMAS: OKAY. LET'S GO ON. WE HAVE ONE ISSUE REMAINING FROM YESTERDAY THAT WE DIDN'T GET TO IN OUR WORKSHOP, WHICH WOULD NOW LIKE TO ADDRESS. DR. TROUNSON IS GOING TO SPEAK ABOUT

THE HAPLOTYPE BANK.

DR. TROUNSON: HI. JUST BEFORE I START, I WANTED TO SAY THAT DURING MY TIME HERE, THE SIX YEARS, WE'VE HAD ABSOLUTELY CLEAN AUDIT REPORTS ON EVERY OCCASION. SO BOTH CHILA AND MARGARET FERGUSON, WHO WAS HERE BEFORE CHILA, AND DURING MY TIME WERE ASTONISHINGLY GOOD IN ACTUALLY DOING THIS JOB. AND I THINK THEY'RE ABSOLUTELY FANTASTIC PEOPLE, AND THEY COME FROM AN EXPERIENCE AND A BACKGROUND WHICH IS SUPERB.

BUT I ALSO WANTED TO THANK MICHAEL GOLDBERG, WHO SAT IN THE FINANCE CHAIR DURING MY TIME HERE. AN EASIER PERSON TO WORK WITH, THERE'S NONE. IN THAT SENSE IT'S MADE THIS PART OF IT SEEM REALLY, REALLY EASY. SO I DON'T THINK THERE HAS BEEN A SINGLE ISSUE, PERHAPS EXCEPT THE ODD COMMENT SOMEWHERE ABOUT TRAVEL EXPENSES FROM SOMEWHERE ELSE, BUT THE FINANCES HAVE BEEN EXEMPLARY. SO THANKS TO ALL THE STAFF, ALL OF THEM, WHO DO THIS GREAT WORK, AND FOR THE FINANCE COMMITTEE IN SUPPORTING US IN DOING THAT. REALLY WANTED TO THANK YOU, MICHAEL. IT'S REALLY MEANT A LOT FOR ME FOR THAT SIX YEARS TO HAVE YOU THERE. WONDERFUL.

SO THIS IS A LEFTOVER FROM YESTERDAY. AND I WANTED TO BRING SOMETHING TO YOUR ATTENTION

BECAUSE I THINK IT'S VERY IMPORTANT AND SOMETHING THAT'S REALLY WORTH CONSIDERING. THE FIRST FEW SLIDES DON'T RELATE TO THE ISSUE AT ALL, BUT I THOUGHT, BECAUSE IT COULD BE CONFOUNDED WITH WHAT WE ALREADY DO WITH THE IPS CELL BANK, I'LL JUST REMIND YOU THAT WE ARE FUNDING AN IPS CELL BANK FOR RESEARCH. AND WE'VE BEEN THROUGH THAT, AND THAT'S BEING ESTABLISHED AT THE BUCK INSTITUTE NOW WITH THE DERIVERS THERE AND THE BANK WILL BE THERE.

AND SO THIS IS REALLY ABOUT DISEASE MODELING AND TARGET DISCOVERY FOR COMPLEX DISEASES. AND IT'S REALLY A RESEARCH ACTIVITY WHERE TISSUE COLLECTION FOR SOME VERY SPECIFIC COMPLEX DISEASES AND THE DERIVATION AND BANKING IS HAPPENING SO THAT WE CAN EXPLORE THE ISSUES OF DISEASE PHENOTYPE COMPARED TO A NORMAL PHENOTYPE TO TRY AND FIND WHAT IS GOING WRONG, PARTICULARLY IN GENETIC PATHWAYS, WITH THESE INDIVIDUALS.

WE'VE ALREADY UNDONE SOME THINGS. AND THE ISSUE OF AUTISM IS CURRENTLY BEING UNDONE BY THIS RESEARCH. SCHIZOPHRENIA, MANY DIFFERENT THINGS ARE BEING UNDONE, BEING ELABORATED, THE CAUSES ARE BEING ELABORATED BY THIS KIND OF RESEARCH. SO WE WOULD HOPE IN THE FUTURE THAT WE WOULD GET INSIGHTS INTO THE DISEASE MECHANISMS AND TARGET DISCOVERIES

THROUGH THAT BANK. AND SO THESE ARE THE CONDITIONS THAT WE'VE BEEN COLLECTING TISSUE FROM: NEURODEVELOPMENT DISORDERS IN JUVENILE; IDIOPATHIC AUTISM; THAT IS, AUTISM OF UNKNOWN CAUSE. IDIOPATHIC, IDIOPATHIC IS UNKNOWN CAUSE. FAMILIAL DILATED CARDIOMYOPATHY; VIRAL HEPATITIS, THAT IS, SOME PATIENTS ARE MUCH MORE SUSCEPTIBLE THAN OTHERS TO VIRAL HEPATITIS. AND WE WANT TO TRY AND UNDERSTAND WHAT THAT IS SO THAT WE CAN HELP PROTECT THOSE PEOPLE WHO ARE PARTICULARLY SENSITIVE TO INFECTIONS. AND WE HOPE THAT THAT WORK WILL RESULT IN SOME HELP IN INFECTIOUS DISEASES.

IDIOPATHIC PULMONARY FIBROSIS OF THE LUNGS, A TERRIBLE CONDITION FOR WHICH THERE IS NO TREATMENT CURRENTLY AND ONE THAT I USED TO WORK ON. SO I KNOW REAL PROBLEMS IN THAT DISEASE. BLINDING EYE DISEASES, WHICH WE REALLY DON'T KNOW MUCH OF THE CAUSE OF. AND, OF COURSE, THE BIGGY IN MANY RESPECTS IS ALZHEIMER'S DISEASE, A GROWING EPIDEMIC.

SO THIS IS ABOUT RESEARCH. I WANT TO TALK TO YOU ABOUT SOMETHING ELSE BECAUSE THE WAY WE NEED TO DELIVER OUR THERAPIES, UNLESS THEY ARE AUTOLOGOUS, THAT IS, YOU'RE TAKING IN YOUR OWN CELLS, THERE'S A PROBLEM BECAUSE THE BODY WILL REJECT THOSE CELLS. AND MAYBE UNDER SOME CONDITIONS

IN THE EYE YOU CAN GIVE LOCAL IMMUNOSUPPRESSION THAT WILL KEEP ALLOGENEIC CELLS FROM BEING LOST AND PERHAPS IN THE CENTRAL NERVOUS SYSTEM, BUT THERE IS EVIDENCE -- THERE IS SOME EVIDENCE THAT ALLOGENEIC CELLS WILL BE LOST EVEN FROM THE CENTRAL NERVOUS SYSTEM.

IMMUNOLOGICAL REJECTION IS A THING WHICH IS CUTTING OFF AND WILL CONTINUE TO CUT OFF OUR ABILITY TO DELIVER CELL THERAPIES TO THE PATIENT POPULATIONS OF CALIFORNIA AND THE WORLD. SO WE COULD USE INDIVIDUALIZED IPS CELLS; THAT IS, TAKE A CELL FROM YOU AND USE IT IN AN AUTOLOGOUS MANNER. THAT'S CERTAINLY A POSSIBILITY FOR THE FUTURE. BUT MOST PEOPLE IN THE CLINICAL MEDICINE BELIEVE THIS IS NOT REALLY FEASIBLE BECAUSE OF THE COST. AND THE OTHER IMPORTANT THING IS THE TIME IT TAKES TO GET A MATURE CELL FROM A PATIENT THROUGH TO AN IPS CELL AND THEN THROUGH DIFFERENTIATION INTO THE CELL TYPE THAT YOU WANT. SO THAT PERIOD OF TIME CAN BE AS LONG AS NINE OR TWELVE MONTHS.

NOW, THAT ISN'T GOING TO HELP SOME PATIENTS THAT ARE CONSIDERABLY WORSE OFF AFTER 12 MONTHS, AND IN MANY CASES YOU REALLY WANT TO BE ABLE TO DO THIS QUICKLY AND EFFECTIVELY WITH YOUR PATIENTS. SO IT'S KIND OF UNLIKELY THAT WE'LL DO IT

IN AN AUTOLOGOUS MANNER FOR THE COST AND TIME.

SOMATIC CELL NUCLEAR TRANSFER IS ANOTHER POSSIBILITY, BUT IT HAS EXACTLY THE SAME PROBLEMS OF DERIVATION, PERHAPS A LITTLE BIT SHORTER, BUT THERE ARE REAL ISSUES OF BEING ABLE TO DO THAT WITH THE MATERIALS THAT ARE CURRENTLY AVAILABLE. SO THAT'S NOT REALLY AN OPTION EITHER.

WE COULD GENETICALLY MANIPULATE IPS CELLS TO REDUCE THEIR IMMUNOGENICITY. AND SO THIS IS A REALLY -- AND I KNOW THAT THERE ARE PAPERS IN THE PRESS AND RESEARCHERS WERE ABLE TO FIND WAYS IN WHICH YOU CAN KNOCK OUT THE ANTIGENS WHICH THE BODY RECOGNIZES AS A FOREIGN. SO YOU CAN ACTUALLY DO THAT. THE PRIMARY PROBLEM IS IF THOSE CELLS THEN BECOME CANCEROUS OR BEEN INFECTED, THERE'S NO WAY THE BODY CAN STOP IT. SO YOUR IMMUNE SYSTEM NEEDS TO BE EFFECTIVE FOR ALL THE CELLS IN YOUR BODY. SO IF YOU'VE KNOCKED OUT THE ABILITY FOR THE CELLS TO IN ANY WAY RECOGNIZE THAT, THERE'S A POTENTIAL THERE THAT'S PROBABLY NOT GOING TO BE A GOOD IDEA. AND IT'S CERTAINLY A CONCERN IN THE FIELD AMONGST IMMUNOLOGISTS, THAT WE SHOULD BE REALLY, REALLY CAREFUL ABOUT KNOCKING OUT INMATE IMMUNITY FOR THESE KIND OF CELLS. SO THAT'S A POSSIBILITY, BUT NOT LIKELY RIGHT NOW.

INDUCTION OF IMMUNE TOLERANCE, WE'VE BEEN FUNDING IT. THERE'S A LOT OF WORK THAT'S BEEN GOING ON IN THE FIELD. WE STILL DON'T HAVE AN IMMUNE TOLERANCE WAY OF DOING IMMUNE TOLERANCE. IT JUST DOESN'T EXIST YET, NOT YET. MAYBE IT WILL COME, BUT IT'S NOT THERE. SO TO EDUCATE THE BODY THAT YOU ARE GOING TO PUT CELLS IN AND THOSE CELLS WILL BE ACCEPTED WITHOUT THE ATTENDANT DIFFICULTIES OF CONTROLLING WHAT HAPPENS TO THOSE CELLS AFTERWARDS, THAT'S STILL AN OPTION.

SO WHAT CAN WE DO NOW IS THAT COULD ENABLE US TO TRANSPLANT THESE CELLS WITHOUT THE CURRENT ISSUES OF THE LONG-TERM, LIFETIME IMMUNOSUPPRESSION, WHICH IN ITSELF IS INCREDIBLY DANGEROUS AND ALSO BRINGS SECONDARY EFFECTS TO THE PATIENTS. THE ONE THING THAT WE SCIENTISTS AGREE WITH INTERNATIONALLY IS THAT AN HLA MATCHING BANK, A BANK OF CELLS WHICH ARE MATCHED TO THE PATIENTS ACROSS THE MAJOR HISTOCOMPATIBILITY ANTIGENS, WOULD BE VERY EFFECTIVE. SO IF WE CAN MATCH EMBRYONIC STEM CELL OR CAN MATCH IPS CELLS TO THE PATIENT ACROSS THE MAJOR HISTOCOMPATIBILITY ANTIGENS, THEN MAYBE SOME LIGHT IMMUNOSUPPRESSION WOULD BE NECESSARY FOR THE MINOR ANTIGENS OR PERHAPS NOT ANYTHING AT ALL.

SO A NUMBER OF US INTERNATIONALLY HAVE

ARGUED THAT WE SHOULD CREATE A NATIONAL OR INTERNATIONAL STEM CELL BANK OF HAPLOTYPE IPS CELLS THAT IS COMPRISED OF EMBRYONIC STEM CELLS, BUT THAT'S VERY, VERY DIFFICULT TO DO, OR IPS CELLS SELECTED TO BE IMMUNOLOGICALLY COMPATIBLE WITH A LARGE PROPORTION OF THE POTENTIAL RECIPIENT POPULATION.

HOW LARGE WOULD THAT POTENTIAL STEM CELL BANK NEED TO BE TO MATCH EVERYBODY? SO THIS IS A REALLY IMPORTANT QUESTION. SO IF YOU LOOK AT POPULATING AN IPS BANK TO FACILITATE THIS MATCH, YOU NEED TO THINK ABOUT THE REALLY MAJOR HISTOCOMPATIBILITY ANTIGENS WHICH ARE CAUSING THE TROUBLE. AND THEY'RE THE HLA-A'S, THE -B'S, AND THE -DR COMBINATIONS, AND THERE'S A LARGE NUMBER OF THEM. SO YOU'VE GOT THREE TYPES OF ANTIGENS THAT YOU'VE GOT TO BE CAREFUL ABOUT.

AND IF WE GET GENETICISTS WHO HAVE BEEN LOOKING AT THE UTILITY OF EACH OF THE THEORETICAL HOMOZYGOUS COMBINATIONS BECAUSE WHAT YOU DON'T WANT IS TO DOUBLE THE COMPLEXITY BY HAVING THE GENES ON ONE SIDE DIFFERENT THAN THE GENES ON THE OTHER. SO IF YOU CHOOSE TO BE HOMOLOGOUS, YOU WILL HAVE THE SAME SET OF GENES. SO SOME PEOPLE ARE HOMOLOGOUS ACROSS THESE GENES, AND THESE ARE THE ONES, IF WE

COULD FIND THEM, WOULD BE REALLY VALUABLE. AND I'LL DEMONSTRATE THIS IN A MINUTE.

SO WE CAN DETERMINE WHICH OF THESE USEFUL THEORETICAL COMBINATIONS COULD EXIST AMONGST THE 22 MILLION HLA-TYPED VOLUNTEERS THAT ARE ON THE BONE MARROW BANKS WORLDWIDE. AND THERE'S A BONE MARROW REGISTRY WHICH TELLS YOU WHAT THEY ARE. AND IF YOU WORK THAT PROCESS THROUGH, YOU CAN COME TO AN UNDERSTANDING OF HOW MANY CELLS THAT YOU MIGHT NEED.

SO IN THE CASE WHERE THEY'VE DONE THESE CALCULATIONS FOR THE JAPANESE POPULATION, AS SHOWN IN THIS FIGURE HERE, SO ON THE X AXIS IS THE NUMBER OF HOMOLOGOUS COMBINATIONS THAT YOU NEED ACROSS THOSE TO GIVE YOU COVERAGE FOR 90 PERCENT OF THE POPULATION. AND IT IS ONLY 50 CELL TYPES, ONLY 50, WILL COVER 90 PERCENT OF THE JAPANESE POPULATION. SO THAT'S A RELATIVELY HOMOGENEOUS POPULATION IN JAPAN, RELATIVELY. BUT 50 OF THEM WILL COVER 90 PERCENT OF THAT POPULATION.

SO IF YOU LOOK AT THE UNITED KINGDOM, WHICH IS A MORE DIVERSE POPULATION, WHAT WOULD IT TAKE THERE? SO IF YOU LOOK AT THE THEORETICAL CALCULATIONS, TO GET 90 PERCENT, LOOKS TO BE AROUND ABOUT 120 CELL LINES. SO MORE THAN DOUBLE, BUT 120 OF THESE CELL LINES WOULD COVER 90 PERCENT OF THE

WHOLE OF THE UNITED KINGDOM. AND IT'S QUITE A MIXED POPULATION IN THE UNITED KINGDOM. AND IT COMES DOWN TO LOOKING AT WHAT THEY ACTUALLY ARE. SO IF YOU TAKE THE DATA FROM THE BONE MARROW BANKS, IT COMES OUT PRETTY MUCH EXACTLY TO WHAT YOU PREDICT. ROUNDABOUT 120 CELL LINES WILL COVER 90 PERCENT OF THE UNITED KINGDOM.

WE HAVEN'T DONE THE CALCULATIONS YET FOR CALIFORNIA OR FOR OTHER POPULATIONS YET, BUT IT WOULD BE A FAIR THING TO BELIEVE THAT IT WOULD BE CERTAINLY LESS THAN 200 AND PROBABLY LESS THAN 150 CELL LINES WOULD COVER 90 PERCENT OF CALIFORNIA PATIENTS. WE CAN DO THOSE CALCULATIONS. WE CAN GET SOMEBODY. IT'S NOT THAT DIFFICULT TO DO. YOU NEED TO KNOW WHAT ARE THE BONE MARROW VARIANCES IN CALIFORNIA. AND THERE WILL BE, OF COURSE, A LOT OF LATIN PATIENTS IN THAT. SO I DON'T MEAN LATIN. I MEAN HISPANIC POPULATION. SO YOU COULD LOOK AT THAT AND FIND OUT WHAT WOULD TAKE. AND I PREDICT IT WOULD BE CERTAINLY LESS THAN 200 AND PROBABLY AROUND 150 OR LESS TO DO THAT.

SO LET ME GIVE YOU THE EXAMPLE. HERE, LOOKING AT THAT TIME THE UK, THREE OF THESE HOMOZYGOUS CELL TYPES SHOWN THERE. SO A1, B8, C7, DR17, AND DQ2. THE NUMBER OF POTENTIAL HLA-MATCHED

DONORS ARE GREATER THAN 20,000 ON THE WORLD BONE MARROW BANKS. SO IT'S A RELATIVELY COMMON HLA TYPE. IT WOULD MATCH 17 PERCENT OF ALL THE PATIENTS IN THE UK. SO THAT ONE ALONE WILL MATCH 17.

AND THEN AS YOU MOVE DOWN IN THE LIST, THE NEXT ONE WILL MATCH 11 PERCENT OF THE POPULATION. SO IT'S A LITTLE BIT LESS COMMON. AND THEN THE NEXT ONE WOULD MATCH 9 PERCENT. WITH THOSE THREE, YOU'VE GOT 35 PERCENT OF THE POPULATION. SO YOU CAN SEE YOU CAN BUILD THIS UP. AND IF YOU TAKE THE FIRST 15, YOU GET TO 60 PERCENT OF THE POPULATION. SO THE ONES THAT ARE MORE DIFFICULT TO GET, ARE THE RARER, THE RARER HAPLOTYPES, BUT THEY CAN BE FOUND. SO WORLDWIDE WE WANT TO SET UP BANKS AROUND THE WORLD THAT WILL ENABLE EVERYBODY TO ACCESS THESE CELL LINES FOR CELL THERAPIES IN THE FUTURE.

SO WHAT SHOULD WE DO? WHAT SHOULD CIRM DO? I THINK CIRM OUGHT TO BE PART OF THIS. I THINK WE ARE THE STEM CELL LEADERS IN THE FIELD. WE OUGHT TO BE PART OF IT. AND HOW COULD WE BE PART OF IT? WELL, I THINK WE COULD ACTUALLY FIND OUT THE PATIENTS WHO ARE HERE IN CALIFORNIA, AND WE COULD USE, FOR EXAMPLE, THE ALPHA STEM CELL CLINICS WHO'VE GOT ALL THE PEOPLE THAT YOU NEED TO GO TALK TO THE PATIENTS AND GET THEIR CONSENT TO DONATE FOR THE

GLOBAL GOOD.

AND I THINK IF YOU HAD IN MIND THAT YOU COULD MAKE A BANK OF 150 TO 200, AT THE MAXIMUM, SO IT MIGHT BE 150, MIGHT BE 200, TO COVER 90 PERCENT OF CALIFORNIA, THAT WOULD TAKE SOME TIME BECAUSE THE RARE ONES ARE MORE DIFFICULT TO FIND, BUT IT WOULD MAYBE TAKE TWO OR THREE YEARS, THREE OR FOUR YEARS TO GET IT ALTOGETHER, BUT YOU WOULD GET IN THE BEGINNING A COVERAGE OF QUITE A FEW OF THEM JUST WITH THE MORE COMMON HAPLOTYPES. AND IF WE SHARED IT ACROSS THE WORLD, WE COULD GET THOSE MORE EXTREMELY UNCOMMON ONES.

SO I'M SUGGESTING THAT WE COULD HELP -- WE COULD GET THE STEM CELL -- THE ALPHA STEM CELL CLINICS TO HELP ON THE PATIENT SIDE TO TALK TO THOSE WHO HAVE GOT THESE HAPLOTYPES. THE BONE MARROW BANKS ARE VERY OPEN TO THIS. I THINK THE PATIENTS YOU COULD GET TO TALK TO WOULD BE VERY SUPPORTIVE GENERALLY, I THINK, IN PROVIDING THOSE CELLS FOR THE COMMON GOOD OF ALL PEOPLE.

AND THEN YOU NEED SOMEONE TO DERIVE THE IPS CELLS, AND THEN THEY NEED TO BE BANKED SOMEWHERE. AND THE BANK SHOULDN'T BE WHAT WE'RE USING FOR OUR CURRENT BANK, BUT IT NEEDS TO BE A BIOBANK. AND OUR ALPHA CLINICS ARE GOING TO HAVE TO

HAVE BIOBANKS ASSOCIATED WITH THEM BECAUSE THEY'RE INVOLVED IN CELL THERAPY. SO I THINK THIS ACTIVITY COULD WELL AND TRULY BE UTILIZED THROUGH OUR ALPHA STEM CELL CLINICS, BUT WE NEVER HAVE GIVEN THE THOUGHT TO THIS BEFORE THIS TIME. I THOUGHT AS I'M APPROACHING THE TIME WHEN I'M LEAVING, I'M ACTUALLY CURRENTLY ON THE GLOBAL STEERING COMMITTEE OF TEN TO TWELVE PEOPLE WHO ARE TRYING TO ORGANIZE THIS ACROSS THE GLOBE.

I THINK IT MIGHT TAKE TEN TO $12 MILLION TO SET UP THIS BANK HERE IN CALIFORNIA. AND THIS WOULD GIVE YOU PRETTY GOOD COVERAGE OF CALIFORNIA, AND THEN WE'D BLEND IT IN WITH THE GLOBAL BANKS. I THINK YOU WOULD BE ABLE TO ACCESS EVEN THOSE MORE RARE TYPES OF HAPLOTYPES. SO I WANTED TO GIVE YOU THAT INFORMATION AS PART OF YESTERDAY. WE'RE NOT ASKING YOU FOR THAT MONEY NOW BECAUSE WE REALLY HAVEN'T SAT DOWN AND TRIED TO DO THE CALCULATION SPECIFICALLY. AND WE WOULD HAVE TO DO SOME GENOTYPING ASSOCIATED WITH THIS BECAUSE YOU WOULDN'T WANT TO PUT CELLS IN THE BANK THAT HAD THE RIGHT HAPLOTYPE, BUT HAD SOMETHING WRONG WITH AN ONCOGENE OR A DISEASE, A KNOWN ERROR IN A DISEASE GENE. THAT COULD BE FOOLISH TO HAVE THEM BANKED. SO WE'D NEED TO DO SNP ANALYSIS TO MAKE SURE WE WEREN'T PUTTING

THE SO-CALLED WRONG ONES, IF YOU LIKE, IN A BANK.

SO THERE WOULD BE SOME GENOTYPING ASSOCIATED WITH IT AS WELL. AND WE HAVEN'T REALLY HAD THE TIME TO SIT DOWN AND DO THAT. WE WOULD PROBABLY TRY AND WORK THIS THROUGH TO BRING IT TO YOU HOPEFULLY BEFORE I LEAVE WITH THE HELP OF NATALIE DEWITT AND MIKE YAFFE, PUT A PROPOSAL BACK TO THE BOARD. SO THIS WAS FOR INFORMATION. I'M HAPPY TO ANSWER QUESTIONS. I THINK THIS IS THE KIND OF LEADERSHIP CIRM SHOULD SHOW GLOBALLY. IT'S KIND OF UP TO YOU TO THINK ABOUT AND EVENTUALLY RESPOND WHEN WE BRING SOMETHING FORWARD. BUT I THOUGHT AS PART OF YESTERDAY'S DISCUSSIONS THAT MAYBE YOU OUGHT TO CONSIDER THAT THIS MIGHT HAPPEN SOONER. AND IF I TURNED UP HERE IN MARCH WITH THAT AND HAVING NOT TOLD YOU, I THINK YOU QUITE RIGHTLY WOULD SAY WHY DIDN'T YOU SAY SOMETHING ABOUT IT BACK IN DECEMBER. I'M OPEN TO QUESTIONS IF YOU LIKE.

CHAIRMAN THOMAS: OKAY. THANK YOU, ALAN.

DR. DULIEGE: THANK YOU. INDEED IT'S A BRILLIANT IDEA. AND SO THANK YOU TO YOU AND THE CIRM TEAM. AND I ALSO APPRECIATE THAT YOU ARE THINKING GLOBALLY, NOT JUST ABOUT CALIFORNIA OR THE U.S. POPULATION.

HOW ACTIVE ARE OTHER COUNTRIES BEYOND

JAPAN AND UK IN THIS EFFORT?

DR. TROUNSON: VERY ACTIVE. THEY'RE VERY ACTIVE IN GERMANY, IN FRANCE, AND CHINA, KOREA. THEY'RE ALL WANTING TO BE PART OF THIS. AND SO WE ARE ALSO NOW TALKING TO INDIA BECAUSE THE INDIAN SUBCONTINENT IS PRETTY BIG. AND THEN I'VE ALSO TALKED TO THE QATAR FOUNDATION BECAUSE I WANTED TO MAKE SURE WE COVERED THE AFRICAN POPULATIONS. AND QATAR IS TRYING TO TAKE A LEADERSHIP IN REGENERATIVE MEDICINE AND KNOW THEY ARE VERY POSITIVE ABOUT IT. I WILL BE MEETING THEM IN APRIL AGAIN, AND WE EXPECT THEM TO DO THIS.

WE WOULD BE -- WE'RE ALL TRYING TO SORT OF GET A LITTLE BIT OF MONEY TO HELP MAKE SURE THAT WE KEEP THE GLOBAL COMPONENT ACTIVE SO THAT WHEN WE DERIVE THEM, WE DO IT IN A WAY WHERE EVERYBODY CAN ACCEPT THE CELLS, NOT JUST CALIFORNIA, BUT THEY'RE MADE IN A WAY WHICH WOULD BE ACCEPTABLE INTO CHINA, INTO THE UK, INTO WHEREVER. SO IT NEEDS PEOPLE TO SORT OF WORK TOGETHER TO ENABLE THAT YOU CAN SHIP THESE CELLS AROUND FOR THE PATIENTS. THEY NEED TO BE MADE UNDER CERTAIN CONDITIONS AND BEST PRACTICES AND SO FORTH. SO WE WOULD BE LOOKING FOR A LITTLE BIT OF MONEY FROM EVERYBODY TO HELP MAKE SURE THAT THAT GLOBAL INITIATIVE KEEPS THE THING TOGETHER SO

WE CAN ACCESS EVERYBODY.

BUT THEY'RE VERY ACTIVE. THE FRENCH PEOPLE HAVE STARTED, THE JAPANESE PEOPLE HAVE STARTED THEMSELVES. WE HAVEN'T, BUT I'M SUGGESTING THAT WE SHOULD. THE UK WILL BE STARTING SHORTLY, I THINK, AND SO ON. SO IT WILL BE A GLOBAL MOVEMENT, AND I THINK, AS YOU SAY, I THINK WE SHOULD BE PART OF IT.

DR. BRENNER: I THINK IT WOULD HELPFUL, IF POSSIBLE, TO DO THE CALCULATION OF HOW MANY WE NEED BEFORE WE HAVE TO VOTE WHEN WE COME WITH IT BECAUSE WE NEED TO KNOW WHAT THE NUMBER IS.

DR. TROUNSON: I THINK WE WOULD TRY TO DO IT. THERE ARE SOME CLINICAL GENETICISTS WHO PROBABLY HAVE INFORMATION, DAVID, AND WE CAN GET TO IT REASONABLY QUICKLY BECAUSE I'M IN CONTACT WITH THE PEOPLE WHO HAVE MADE CALCULATIONS BOTH IN JAPAN AND IN THE UK. AND I'D GET MICHAEL AND NATALIE TO SORT OF, IN MY ABSENCE, SORT OF WORK WITH THOSE PEOPLE TO GET THE NUMBERS IF WE CAN. I'M PRETTY SURE IT'S GOING TO BE LESS THAN 200, AND PROBABLY AROUND 150. LET'S SAY IT'S A LITTLE BIT MORE DIVERSE THAN THE UK. I'M NOT SURE IT IS, BUT WE SHOULD FIND OUT.

DR. HAWGOOD: ALAN, I AGREE WITH

ANNE-MARIE THAT THIS SOUNDS LIKE A BRILLIANT IDEA. IT'S VERY MUCH AN IPS CELL IDEA. HOW MANY OF EITHER OUR PROTOCOLS OR PROTOCOLS AROUND THE WORLD THAT ARE HEADED FOR THE CLINIC ARE IPS CELL BASED VERSUS EMBRYONIC STEM CELL BASED? THIS DOESN'T REALLY ADDRESS ANY ISSUES WITH THE EMBRYONIC CELLS.

DR. TROUNSON: THE ONLY ONE THAT'S MOVING INTO CLINICAL TRIAL THAT I KNOW OF RIGHT NOW IS THE JAPANESE WORK ON THE EYE, SAM. BUT WE WOULD EXPECT IT TO BE STRONGLY REPRESENTED IN THE FUTURE. THE THING ABOUT THIS IS WE NEED TO GET STARTED BEFORE THEY'RE READY TO COME ON BOARD BECAUSE OTHERWISE TO SET IT UP AFTERWARDS IS GOING TO DELAY ANY KIND OF APPLICATION OF IT, AND WE SHOULDN'T DO THAT.

DR. HAWGOOD: I AGREE WITH THAT, BUT IT IS, IN ESSENCE, A PROJECT THAT IS MAKING A BET ON IPS CELLS.

DR. TROUNSON: YES.

DR. HAWGOOD: THE SECOND IS JUST A TECHNICAL QUESTION. THE GENOTYPING, WHICH MAKES ABSOLUTE SENSE, BUT MY ASSUMPTION IS, AND CORRECT ME IF I'M MISSING A TECHNICAL ISSUE, THAT THE HAPLOTYPING AND THE GENOTYPING, IN EFFECT, COULD BE ONE STEP.

DR. TROUNSON: THAT WOULD BE ONE STEP. I

THINK THE SNP ANALYSIS TO MAKE SURE THAT WE DON'T HAVE DISEASE-RELATED GENE ABERRATIONS IN SOME OF THE OTHER MAJOR DISEASES. THAT, I THINK, WOULD BE WORTH KNOWING.

DR. HAWGOOD: WOULDN'T YOU GET THAT FROM A FULL DEEP SEQUENCING?

DR. TROUNSON: YOU WOULD. I DON'T THINK YOU'D DO A DEEP SEQUENCE ON IT. I THINK THAT'S TOO COSTLY AT THE PRESENT TIME, BUT A MORE SHALLOW LOOK WOULD PROBABLY BE APPROPRIATE AT THIS POINT IN TIME. IN THE FUTURE WE CAN ALWAYS GO BACK AND REDO A DEEPER SEQUENCE IF NECESSARY, BUT I THINK A SNP ANALYSIS WOULD BE ALL THAT'S REQUIRED RIGHT NOW.

MR. SHEEHY: SO I NOTICE ON THE PAPER THAT MAHENDRA RAO WAS ONE OF THE AUTHORS. SO WHAT IS THE INVOLVEMENT OF NIH IN THIS?

DR. TROUNSON: NIH IS ONE OF -- THEY'RE ON THE STEERING COMMITTEE, JEFF. THEY'RE STRONGLY SUPPORTIVE. I DON'T REALLY KNOW ABOUT THE MONEY IN NIH. THINGS ARE PRETTY TIGHT OVER THERE. BUT WE DON'T KNOW THAT AT THIS STAGE, BUT THEY'RE INVOLVED IN THE STEERING COMMITTEE. THEY'RE VERY SUPPORTIVE. THEY WANT TO BE INVOLVED, YES. AT THIS STAGE THAT'S THEIR INVOLVEMENT.

MR. SHEEHY: IT JUST SEEMS TO ME THAT THIS

IS THE TYPE OF -- THIS IS REALLY NOT A STATE EFFORT. IF IT MAKES SENSE, I THINK CONTRIBUTING TO IT AND HELPING TO GET THIS OFF THE GROUND, I KNOW THE SEQUESTER IS INCREDIBLY CHALLENGING IN WASHINGTON, BUT I THINK THIS IS ONE THING THAT IF WE DO A PROPOSAL, THIS SHOULD BE VERY WELL INTEGRATED WITH FEDERAL EFFORTS BECAUSE ULTIMATELY THIS TYPE OF PROJECT, AS YOU MENTION, IS A NATIONAL GOVERNMENT PROJECT AND REALLY A GLOBAL PROJECT, AND WE SHOULD BE INTEGRATED WITH WHATEVER THE FEDERAL GOVERNMENT IS DOING SO THAT WE'RE NOT PAYING TO DUPLICATE THINGS.

IF THE FEDERAL GOVERNMENT IS MAKING LINES AND WE'RE MAKING THE SAME LINES, THAT'S NOT A GOOD USE OF CALIFORNIA TAXPAYER MONEY. SO IF THEY ARE CLEARLY PARTICIPATING, THEN THE PROPOSAL THAT COMES FORWARD SHOULD HAVE US INTEGRATED WITH THEM FROM THE START. AGAIN, IF THIS IS A GOOD PROJECT, I THINK I'D BE HAPPY PERSONALLY TO PARTICIPATE. BUT I REALLY DON'T WANT TO BE IN A SITUATION WHERE WE HAVE TWO BANKS MAKING THE SAME LINES. WE'RE PAYING FOR ONE AND THE FEDERAL GOVERNMENT IS PAYING FOR THE OTHER. AS WE WERE DISCUSSING AT LENGTH YESTERDAY, WE'RE ENTERING A REALM OF FINITE RESOURCES, SO LET'S ONLY DO THINGS ONCE IF WE CAN DO THEM ONCE.

DR. TROUNSON: YOU COULD TAKE THAT TO THE LIMIT AND SAY, WELL, IF YOU WAIT FOR ALL OF THEM TO SET UP THE BANKS, THEY'LL BE ACCESSIBLE THROUGH OTHER BANKS. SO THAT'S A POSSIBILITY. YOU WOULD WAIT TILL EVERYONE SET IT UP AND YOU WOULD PROBABLY FIND THAT YOU WOULD GET 90 PERCENT OF THEM THROUGH OTHER BANKS.

NIH AT THIS MOMENT HAVE NOT PUT A PROPOSAL ABOUT SETTING UP ANY BANKING AT THIS POINT IN TIME THEMSELVES. SO I DON'T KNOW.

MR. SHEEHY: DON'T WE HAVE -- AREN'T WE COLLABORATING WITH THEM ON SEVERAL THINGS?

DR. TROUNSON: OH, YES. WE ARE.

MR. SHEEHY: SO THEY ARE SETTING UP IPS CELL BANKS.

DR. TROUNSON: BUT NOT FOR THIS PURPOSE AT THIS STAGE THAT I KNOW OF.

MR. SHEEHY: BUT, AGAIN, THIS IS ABOUT COORDINATION. IF WE WERE TO SAY THAT WE'RE WILLING TO PUT UP MONEY, THAT MIGHT STIMULATE SOME ACTIVITY. I JUST WOULD NOT WANT US TO GET OUT THE GATE WITH SOMETHING WITHOUT HAVING EXPLORED EVERY OPPORTUNITY TO LEVERAGE OUR MONEY TO THE NTH DEGREE. AGAIN, WE TALKED ABOUT IT YESTERDAY. $10 MILLION COULD MAKE A BIG DIFFERENCE IN GETTING A THERAPY INTO A PATIENT

HERE IN CALIFORNIA AS OPPOSED TO DOING SOMETHING THAT HIGHLY DUPLICATIVE OF WHAT NIH IS DOING.

SO I THINK WE NEED TO BE CLEAR. DOES IT TAKE SO MUCH LONGER TO SYNCHRONIZE OUR EFFORTS WITH NIH? I DON'T THINK WE'RE GOING TO BE PUTTING THESE INTO PEOPLE TOMORROW.

DR. TROUNSON: WE ARE SYNCHRONIZED. AS I SAID, THEY'RE ON THE STEERING COMMITTEE, THE GLOBAL STEERING COMMITTEE. SO THEY'RE SYNCHRONIZED WITH WHAT EVERYBODY ELSE IS DOING. SO WE'RE TRYING TO GET THIS TO BE A GLOBAL INITIATIVE, SOMETHING THAT WE'RE READY FOR DELIVERY OF CELL THERAPIES TO PATIENTS FOR THE FUTURE. SO THEY ARE IN THAT INTERNATIONAL STEERING COMMITTEE. MAHENDRA RAO IS ON IT. WHEN HE'S NOT THERE, ONE OF HIS DEPUTIES IS THERE. SO THEY'RE PART OF DEVELOPING ALL OF THE PROCEDURES, RECOMMENDED PROCEDURES, AND SO FORTH MOVING FORWARD.

DR. KRONTIRIS: TECHNICAL QUESTION. HOW LONG, GIVEN CURRENT TECHNOLOGY, IS IT FROM GETTING THE SAMPLE TO HAVING A USABLE LINE?

DR. TROUNSON: AN IPS CELL LINE? IT'S AROUND ABOUT THREE MONTHS FROM GETTING A SAMPLE TO HAVING IT APPROPRIATELY CHARACTERIZED AND TESTED. AROUND THREE MONTHS.

DR. KRONTIRIS: GIVEN THE NATURE OF THE THERAPIES AND THE TIMELINE OF THE DISEASES, WOULD IT WE POSSIBLE TO HAVE THIS AS A VIRTUAL RESOURCE DEPENDING HEAVILY ON THE PREEXISTING TRANSPLANT DATABASE, BUT WITH A SUBINFORMATICS COMPONENT THAT DISEASE-BASED GROUPS WOULD BE ABLE TO FEED INTO AND GO TO THE DATABANK FOR INDIVIDUALS WHO COULD BE DONORS FOR SPECIFIC PATIENTS?

DR. TROUNSON: I THINK THE IDEA IS FOR EVERYBODY TO ACCESS THESE BANKS AS FREELY AS POSSIBLE, LIKE THE BONE MARROW BANKS, THAT THEY'D BE AVAILABLE.

DR. KRONTIRIS: BUT THE DIFFERENCE IS YOU WOULDN'T HAVE A BANK OF CELLS. YOU WOULD HAVE 22 MILLION PEOPLE WHO WOULD MADE INDIVIDUAL POINT OF CONTACT, SO TO SPEAK, CONTRIBUTIONS TO GIVEN PATIENTS.

DR. TROUNSON: MAYBE THE THREE MONTHS, WE TALKED ABOUT TAKING NINE MONTHS TO GET THE CELLS THAT YOU REALLY NEED FROM DIFFERENTIATION AFTER ALL OF THAT AND ALL THE TESTING AND SO ON. AGAIN, IF YOU DO IT ON AN INDIVIDUAL BASIS, IT'S STARTING TO BECOME MORE LIKE AN AUTOLOGOUS SYSTEM. SO IT'D BE BETTER TO HANDLE IT IN SOME SORT OF BULK PROCEDURES, I THINK.

MS. WINOKUR: IS THE CDC INVOLVED AT ALL, CENTER FOR DISEASE CONTROL?

DR. TROUNSON: NO. THEY'RE NOT SPECIFICALLY INVOLVED AT THIS POINT IN TIME. AS I SAID, THE NIH IS INVOLVED.

MS. WINOKUR: WELL, THE CDC HAS ESTABLISHED REGISTRIES FOR SOME OF THE DISEASES THAT WE'D BE INTERESTED IN.

DR. TROUNSON: I THINK WHAT WE NEED TO KNOW IS THE DATA OUT OF THE BONE MARROW BANKS, THE CORD BLOOD BANKS WHERE THEY'RE PUBLIC AND MAYBE THE APHERESIS DATA THAT'S AVAILABLE FOR PATIENTS. SO THOSE ARE THE DATABANKS THAT WE NEED TO ACCESS TO FIND THE INDIVIDUAL.

MS. WINOKUR: THEY COLLECT A VARIETY OF INFORMATION ON EACH REGISTRANT.

DR. TROUNSON: SO WE'RE LOOKING FOR THE SPECIFIC HAPLOTYPES RATHER THAN THE DISEASE PEOPLE. ANYWAY, I TAKE THE POINT. WE SHOULD LOOK AT EVERYBODY WHO WILL CONTRIBUTE TO THESE THINGS, BUT CURRENTLY WE HAVEN'T INCLUDED THEM IN THE ORGANIZATION. BUT THIS IS EARLY DAYS.

DR. BOXER: I THINK IT'S INCREDIBLY EXCITING TOO. I THINK THIS IS THE KIND OF THING THAT WE SHOULD BE A LEADER IN. I THINK JEFF'S POINT

ABOUT MAKING SURE THAT WE'RE COORDINATING WITH THE NIH AND GLOBALLY, AND I THINK YOU'VE SAID THAT, ALAN, IS CRITICALLY IMPORTANT.

ONE OTHER COMMENT AND THEN A QUESTION. SO I'M ASSUMING, YOU TALKED A LITTLE BIT ABOUT THE GENETIC SCREENING. AND OBVIOUSLY AS WE GAIN MORE INFORMATION, ALL THE DEEP SEQUENCING, I'M ASSUMING WE'D HAVE TO GO BACK AND LOOK AT THE STORED SAMPLES, AND SIMILARLY FOR POSSIBLE INFECTIOUS AGENTS BECAUSE, AGAIN, WE MAY BE PUTTING THESE INTO PEOPLE WITHOUT NORMAL IMMUNE SYSTEMS WHO'D BE AT RISK FOR THAT.

DR. TROUNSON: RIGHT. SO YOU WOULD HAVE TO COVER A LOT OF TESTING TO ENSURE THAT EVERYBODY WILL ACCEPT THEM. SO IT IS A VERY IMPORTANT POINT. SO THERE ARE CERTAIN TASK FORCES WITHIN THE GROUP SETTING UP TO LOOK AT DIFFERENT PARTS OF IT, THE CONSENT PART, THE DISEASE INFECTION PART, AND SO ON AND SO ON. SO IT WILL ALL HAVE TO COME TOGETHER IN AN APPROPRIATE PLAN. WE'LL WE CONTRIBUTING TO THAT CLEARLY. BUT IF THEY'RE NOT CONSISTENT, IT WILL BE VERY DIFFICULT FOR US TO SOURCE SOME SAMPLES.

DR. BOXER: MY QUESTION IS HOW MANY DIFFERENT TISSUE TYPES ARE WE ABLE TO DIFFERENTIATE THESE CELLS INTO NOW? I KNOW THAT'S ONGOING WORK.

DR. TROUNSON: IT'S ONGOING. WE'RE REALLY GOOD AT DOING SOME TISSUES AND STILL DEVELOPING CAPABILITIES FOR OTHER TISSUES. BUT ANYTHING YOU CAN DIFFERENTIATE AN EMBRYONIC STEM CELL INTO, YOU CAN DIFFERENTIATE AN IPS CELL INTO THESE DAYS. WHETHER THEY ARE EXACTLY EQUIVALENT OR NOT I THINK IS STILL A MATTER OF DEBATE SOMETIMES, BUT MORE AND MORE EVIDENCE IS THAT THEY APPEAR TO BE AT LEAST OPERATIVE IN ANIMAL TRANSPLANTS AT THE SAME LEVEL AS EMBRYONIC STEM CELLS. THEY'RE FUNCTIONALLY THE SAME, AND YOU'RE ABLE TO CORRECT MOST OF THE DISEASES THAT EMBRYONIC STEM CELLS CAN IN ANIMALS.

MR. ROWLETT: AGAIN, I APPRECIATE. THIS SOUNDS VERY EXCITING. I ALSO WANTED TO ACKNOWLEDGE THE REFERENCE TO MENTAL HEALTH DISORDERS, AUTISM AND SCHIZOPHRENIA SPECIFICALLY, AND THE POSSIBLE OUTCOMES FOR CITIZENS AFFLICTED WITH THOSE DISEASES.

IN REFERENCE TO MR. SHEEHY'S COMMENTS ABOUT FINITE RESOURCES, IT WOULD BE HELPFUL, WHEN YOU COME BACK, TO HEAR, GIVEN THE DUPLICATIVE NATURE OF THE WORK THAT NIH IS DOING AND WHAT CIRM MIGHT BE PROPOSING TO DO, HOW, GIVEN THAT, IT STILL MAKES SENSE BECAUSE OF OUR ABILITY TO INITIATE FAR QUICKER AND THE DIRECT BENEFIT FOR THE CITIZENS OF CALIFORNIA VERSUS THE NATIONAL AND GLOBAL LANDSCAPE

TO HEAR ABOUT THAT. AND HOW YOU THINK THAT IN SPITE OF SOME OF THE DUPLICATIVE NATURE OF THE WORK, US INITIATING THIS MIGHT RESULT IN NIH DOING SOMETHING A LITTLE BIT DIFFERENTLY THAT WOULD BENEFIT THE CITIZENS OF CALIFORNIA.

AGAIN, I'M GOING TO END WHERE I BEGAN. IT WAS VERY EXCITING TO HEAR THE REFERENCE TO MENTAL HEALTH AND HOW THAT MIGHT BENEFIT CITIZENS OF THE STATE.

DR. TROUNSON: RIGHT. SO AS I SAID, AT THE MOMENT, I DON'T KNOW REALLY WHAT THEY'RE PROPOSING TO DO. THEY'RE HAVING SOME BUDGETARY ISSUES, AS YOU KNOW, AT THE PRESENT TIME. SO WE DON'T REALLY KNOW, BUT I IMAGINE THAT THEY WILL BECOME INVOLVED. AND AT WHAT TIME I'M NOT SURE.

CHAIRMAN THOMAS: LEON, THEN JEFF.

DR. FINE: MOST PATIENTS WHO WILL BE THE RECIPIENTS OF THESE CELLS WILL BE ON PHARMACOLOGICAL AGENTS FOR THE TREATMENT OF THEIR DISEASE. AND I THINK IT'S LIKELY THAT PHARMACOGENOMIC ANALYSIS WILL THROW OUT ALL SORTS OF POLYMORPHISMS THAT WILL INDICATE EITHER AN INCREASED OR DECREASED SENSITIVITY. IT MIGHT BE THAT THE GENETIC ANALYSIS GOING FORWARD MIGHT ACTUALLY HAVE TO HAVE THAT SORT OF INFORMATION BUILT IN IF PATIENTS ARE TO RECEIVE

CELLS OF ANOTHER GENOTYPE.

DR. TROUNSON: I THINK THAT'S TRUE. I THINK IN THE END THE MOST OPTIMUM CELL MIGHT BE TESTED FOR MANY DIFFERENT THINGS, AND MAYBE YOU WANT TO DEEP SEQUENCE. BUT WE'RE NOT ANTICIPATING THAT THE DEEP SEQUENCING WOULD BE NECESSARY RIGHT NOW BECAUSE OF THE COST INVOLVED. BUT THE COST OF DEEP SEQUENCING IS GOING DOWN AND WILL SORT OF FLATTEN TO AN ASYMPTOTIC VALUE SOMEWHERE, AND THEN YOU CAN MAKE A CALCULATION ABOUT HOW IMPORTANT THESE THINGS BECOME THEN. YES, I AGREE.

MR. SHEEHY: SO IS THERE A CLINICAL TRIAL IN PHASE I WITH AN ALLOGENEIC IPS CELL PRODUCT AT THIS TIME?

DR. TROUNSON: ALGOGENIC IPS CELLS, NO.

MR. SHEEHY: NO. MAYBE DR. FEIGAL COULD HELP WITH THIS TOO. ISN'T THE PATHWAY THAT WE WOULD FIRST MOST LIKELY MOVE CELLS THROUGH AN AUTOLOGOUS PATHWAY? AND HOW MANY TRIALS ARE THERE ACTUALLY UNDER WAY WITH AN AUTOLOGOUS PRODUCT?

DR. FEIGAL: WITH AN AUTOLOGOUS, THERE ARE TWO. THERE'S A GROUP IN JAPAN AND THERE'S A GROUP IN THE UNITED STATES. ONE IS WORKING ON PLATELETS TO TRY AND PRODUCE THAT. THE OTHER IS WORKING ON IPS TO TREAT A BLINDING EYE DISEASE. AND THEY'RE

ACTUALLY -- THEY'VE GONE THROUGH THE APPROVALS IN JAPAN. AND JAPAN, AS YOU MAY KNOW, RECENTLY CHANGED THEIR REGULATORY PATHWAYS SO THAT THEY CAN GET INTO THE CLINIC MORE QUICKLY. SO RIGHT NOW THERE'S TWO THAT ARE WORKING ON AN AUTOLOGOUS APPROACH.

MR. SHEEHY: I MEAN ONE OF THE BARRIERS TO EMBRYONIC STEM CELLS AS AN ALLOGENEIC PRODUCT, WE HAVEN'T REALLY OVERCOME THOSE, WHICH IS WHY IPS CELLS ARE SO ATTRACTIVE BECAUSE YOU CAN DO THAT AUTOLOGOUSLY.

SO THE QUESTION IS WHY WE NEED TO SPEND $10 MILLION SETTING UP A BANK WHEN, IF I'M BEING PRACTICAL, IT'S GOING TO TAKE AT LEAST A DECADE BEFORE AN AUTOLOGOUS PRODUCT, IF EVERYTHING GOES WELL, GETS THROUGH PHASE III AND WE HAVE ENOUGH CONFIDENCE TO EVEN PUT THESE CELLS INTO A HUMAN BEING FOR THERAPY, AND THEN WE WOULD START TO TALK ABOUT AN ALLOGENEIC PRODUCT. IN THAT DECADE THE TYPES -- HOW YOU WOULD BANK, DERIVE, ANALYZE THOSE CELLS, GIVEN THE PACE OF SCIENTIFIC DISCOVERY, SEEMS LIKE IT WOULD BE COMPLETELY DIFFERENT IN A LOT OF WAYS THAN WHAT WE'RE DOING NOW.

I THINK WE WOULD BE THROWING $10 MILLION OUT THE DOOR TO BUILD A BANK FOR PRODUCTS WE DON'T KNOW WHAT THEY'RE GOING TO LOOK LIKE. I WOULD JUST

FEEL MORE COMFORTABLE COMING BACK TO THIS. AGAIN, THIS IS EXACTLY ONE OF THE PROBLEMS THAT I'M HAVING IS THAT WE CONTINUE TO PUSH MONEY OUT THE DOOR FOR PROJECTS WITHOUT THINKING, AS DR. JUELSGAARD -- I MEAN AS MR. JUELSGAARD SAID, WHAT'S OUR OBJECTIVE? AND IF OUR GOAL IS TO GET PRODUCTS INTO PATIENTS, NONE OF THESE CELLS ARE GOING TO GET INTO A PATIENT FOR AT LEAST 25 YEARS.

YOU HAVE TO GET THE AUTOLOGOUS CELLS THROUGH. THEN YOU HAVE TO GET A CLINICAL TRIAL WITH THE ALLOGENEIC PRODUCT.

DR. TROUNSON: MAYBE I CAN RESPOND THIS WAY. WE'VE GOT EXAMPLES WHERE THAT'S REALLY NOT THE CASE. IN THE CASE OF THE CARDIAC CELLS THAT WE STARTED OFF THEY'RE AUTOLOGOUS CELLS IN OUR CLINICAL STUDIES HERE, THEY'VE BEEN CONVERTED TO ALLOGENEIC CELLS. THEY'VE MOVED DIRECTLY TO THOSE ALLOGENEIC CELLS BECAUSE THEY FOUND THAT THEY WERE MUCH BETTER AND MUCH LESS COSTLY AND JUST AS EFFECTIVE. WE DID THAT WITHIN A VERY SHORT TIME FRAME.

I EXPECT THAT THE JAPANESE ARE GOING TO MOVE VERY QUICKLY FROM BEING PATIENT SPECIFIC TO ALLOGENEIC. AND I THINK THE REST OF THE SCIENTIFIC WORLD ACTUALLY BELIEVES THE SAME. THAT'S REALLY THE BASIS OF WHAT WE WROTE ABOUT. AND WE DON'T EXPECT

THIS TO BE 25 YEARS, THAT'S FOR SURE. SO YOU CAN TAKE THAT POINT OF VIEW, BUT I JUST RESPECTFULLY DISAGREE.

DR. FEIGAL: I JUST WANT TO MAKE -- CAN I MAKE ONE COMMENT?

MR. SHEEHY: CAN I JUST RESPOND? NO. 1, THE CELLS THAT YOU'RE TALKING ABOUT ARE NOT PLURIPOTENT CELL PRODUCTS. SO PLURIPOTENT CELL PRODUCTS HAVE TO MAKE IT THROUGH THE REGULATORY PATHWAY INITIALLY. THIS ONE THEY GOT GOOD RESULTS, BUT THESE WERE ADULT CELLS.

AND THEN THE SECOND POINT IS THAT IT ONLY TAKES THREE MONTHS TO MAKE A LINE. SO IF WE PUT THIS OFF FOR A WHILE, WE CAN STILL MAKE THE LINES. I'M LUST LEERY ABOUT MAKING THIS BIG INVESTMENT UP FRONT.

DR. FEIGAL: THAT'S FINE. I THINK THE POINT THAT WAS TRYING TO BE MADE, AND THAT'S SEPARATE FROM THE POINT ABOUT THE BANK, IS THAT PEOPLE MAY SIMULTANEOUSLY LOOK ON MULTIPLE APPROACHES. SO HE DID GIVE THE EXAMPLE OF AN ADULT CELL LINE THAT STARTED WITH AUTOLOGOUS AND THEN WENT TO ALLOGENEIC. WE DON'T PERCEIVE THAT PEOPLE ARE GOING TO WAIT TILL THE END OF A TEN-YEAR PROCESS BEFORE THEY MIGHT TRY AN APPROACH WITH ALLOGENEIC.

SO I THINK PEOPLE DO TRY APPROACHES SIMULTANEOUSLY WITHOUT WAITING FOR THE FULL PATHWAY. YOU'RE ABSOLUTELY CORRECT. IPS, WHETHER IT'S AUTOLOGOUS OR WHETHER IT'S ALLOGENEIC, IF IT'S MANIPULATED, IT'S GOING TO GO THROUGH A REGULATORY PATHWAY. SO WE ARE TALKING ABOUT A GMP, A GOOD MANUFACTURING PROCESS, TO DEVELOP THESE CELL LINES.

SO TO DR. BOXER'S POINT, WE WOULD HAVE TO TEST FOR ADVENTITIOUS AGENTS OR OTHER TYPES OF INFECTIOUS AGENTS. THAT WOULD BE STANDARD. WE WOULD HAVE TO DO THAT.

MR. SHEEHY: ISN'T THE EXAMPLE OF CARDICELL, ONE OF THE REASONS THAT THEY WERE ABLE TO SWITCH IS THOSE CELLS ARE EVANESCENT, IF I REMEMBER THE WORD. AND WE WOULD NOT RELY ON THE EVANESCENCE OF A PLURIPOTENT CELL PRODUCT. I DON'T THINK THE FDA WOULD BE SO CASUAL ABOUT THAT.

DR. FEIGAL: JUST TO BE CLEAR, IT REQUIRED A SEPARATE -- IT DOES REQUIRE A SEPARATE IND TO GO FROM AUTOLOGOUS TO ALLOGENEIC.

CHAIRMAN THOMAS: OKAY. COULD I JUST -- SINCE THIS IS GOING TO BE BROUGHT BACK FOR FURTHER DISCUSSION IN A FEW MONTHS AND WE HAVE SOME OF THE TOPICS, ALAN, THAT I THINK WOULD NEED TO BE ADDRESSED AT THAT TIME, I THINK WE CAN JUST SORT OF

TAKE THIS UNDER ADVISEMENT. THANK YOU VERY MUCH FOR THE PRESENTATION.

JEANNE, IF YOU'RE QUICK. WE NEED TO MOVE ON.

DR. LORING: THIS IS JEANNE LORING FROM SCRIPPS RESEARCH INSTITUTE. I JUST WANT TO ADDRESS A COUPLE OF THE SCIENTIFIC QUESTIONS BECAUSE WE DO THIS SORT OF THING. FIRST OF ALL, THE COST OF DOING A SNP GENOTYPE IS AROUND $150 NOW FOR UP TO 5 MILLION SITES IN THE GENOME. THE COST OF A FULL GENOME SEQUENCE IS AROUND $3,000. SO IF YOU WANT TO TAKE THOSE INTO YOUR CONSIDERATION, I THINK WE CAN THINK ABOUT HOW MUCH WORK WE COULD DO ON EACH CELL LINE.

THE SECOND POINT IS THAT WE GOT GRANTS FROM THE BILL AND LINDA GATES FOUNDATION SEVERAL YEARS AGO TO CREATE AN ETHICALLY DIVERSE POPULATION OF STEM CELLS FOR PHARMACOGENETICS AND MAYBE TRANSPLANTATION. SO THE OUTCOME OF THAT, WE TRIED MANY TIMES TO GET FUNDING FROM NIH TO SUPPORT THIS FURTHER AND WERE UNSUCCESSFUL, NOT SURPRISINGLY. HOWEVER, ONE THING THAT CAME OUT OF THAT EFFORT IS A LINE THAT WE MADE WHICH HAS THE MOST COMMON EUROPEAN HAPLOTYPE, AND IT'S BEEN COMPLETELY SEQUENCED. AND WE ARE DISTRIBUTING IT UNDER AN MGA. SEVERAL OF THE

LABS IN CALIFORNIA ARE USING IT AS THEIR SORT OF EUROPEAN NONDISEASE CONTROL. SO THAT'S AVAILABLE TO ANY RESEARCHER.

CHAIRMAN THOMAS: THANK YOU. THAT'S VERY INTERESTING. WE APPRECIATE THAT. OKAY.

SO, ALAN, THANK YOU. I THINK WE HAVE A SENSE OF SOME OF THE ISSUES THAT WILL BE DISCUSSED WHEN WE REVISIT THIS DOWN THE ROAD.

WE'RE GOING TO MOVE NEXT INTO THE DISEASE TEAM ITEM. WE NEED TO TAKE A SHORT BREAK HERE BEFORE THAT. SO LET'S PLAN ON RECONVENING IN ABOUT FIVE MINUTES OR SO. THANK YOU.

(A RECESS WAS TAKEN.)

CHAIRMAN THOMAS: OKAY. WE'RE NOW GOING TO PROCEED TO ITEM 15, CONSIDERATION OF THE APPLICATIONS FOR THE LATEST ROUND OF THE DUANE ROTH DISEASE TEAM THERAPY DEVELOPMENT III AWARDS, OTHERWISE KNOWN AS DT III. BEFORE WE GET GOING, I JUST WANTED TO MAKE A FEW POINTS.

FURTHER TO THE PROCEDURES THAT WE PUT IN PLACE FOLLOWING THE IOM REPORT A YEAR AGO, WE HAVE A REVISED SET OF PROTOCOLS THAT WE HAVE BEEN USING THIS YEAR WITH RESPECT TO AWARDS THAT ARE BROUGHT BEFORE THIS BOARD. SO THE PROCEDURE THAT IS NOW IN PLACE, WHICH WE HAVE SUCCESSFULLY USED IN PREVIOUS

MEETINGS, WE HAVE APPLICANTS APPLY, THEY GO THROUGH THE SCREENING AND GRANTS WORKING GROUP PROCESS. THE GRANTS WORKING GROUP IS TASKED WITH PUTTING THE PROPOSALS IN EACH OF THEIR MEETINGS INTO THREE TIERS. TIER I IS RECOMMENDED FOR FUNDING, TIER II IS SUBJECT TO REVIEW BY STAFF, TIER III IS NOT RECOMMENDED FOR FUNDING.

THOSE PROJECTS THAT ARE IN TIER I NEEDN'T GO THROUGH ANY FURTHER ANALYSIS. THOSE PROJECTS THAT ARE IN TIER II ARE ROUTINELY NOW REVIEWED BY STAFF TO SEE IF THEY WOULD RECOMMEND MOVING ANY OF THOSE PROJECTS UP TO TIER I.; THAT IS TO SAY, INCLUDED IN THE RECOMMENDED FOR FUNDING CATEGORY. TIER IIIS ARE NOT ROUTINELY REVIEWED BY STAFF.

HOWEVER, THERE IS A WELL THOUGHT OUT APPELLATE PROCESS BY WHICH APPLICANTS WHO ARE EITHER IN TIER II AND NOT GOING TO BE RECOMMENDED FOR FUNDING OR THOSE IN TIER III MAY FILE AN APPEAL ON THE BASIS OF EITHER DISAGREEMENT IN FACT OR MATERIAL NEW INFORMATION. THAT APPEAL GOES TO STAFF. STAFF ANALYZES IT, AND TO THE EXTENT THEY FEEL THAT THE ISSUES RAISED IN THE APPEAL WARRANT RE-REVIEW, THOSE PROJECTS WOULD GO TO A SUBSET OF THE GRANTS WORKING GROUP FOR SUCH RE-REVIEW, AND THE RESULTS OF THAT WOULD BE INCLUDED IN THE FINAL TABULATION THAT GOES

TO THE BOARD.

THE REASON FOR THIS APPELLATE PROCEDURE IS PREVIOUSLY WE HAD HAD THE AVENUE OF EXTRAORDINARY APPEAL WHICH INVOLVED APPLICANTS COMING DIRECTLY TO THE BOARD WITHOUT REVIEW BY STAFF TO MAKE A CASE THAT THEIR PARTICULAR PROJECT SHOULD BE FUNDED. IT WAS THE CONSIDERED OPINION OF THE BOARD THAT THAT WAS NOT A PROCEDURE THAT LED TO CAREFUL AND CONSIDERED THOUGHT ON THE APPEAL ITSELF AND THAT, INSTEAD OF HAVING THAT EXTRAORDINARY PETITION AVAILABLE, IT MADE MUCH MORE SENSE TO HAVE THE APPEALS GO STRAIGHT TO STAFF FOR THEIR EVALUATION.

SO HAVING GONE THROUGH ALL THAT, THIS RESULTS IN A REVISED LIST OF TIERS THAT THEN GOES TO THE BOARD FOR ITS REVIEW. PREVIOUSLY IN THE GRANTS WORKING GROUP THERE HAD BEEN TWO ELEMENTS. THERE WAS THE SCIENTIFIC REVIEW FOLLOWED BY PROGRAMMATIC REVIEW, WHICH DEALS WITH ISSUES THAT AREN'T STRICTLY SCIENTIFIC, BUT PERTAIN TO THE ADVISABILITY OF INCLUDING A PARTICULAR APPLICATION IN THE RECOMMENDED CATEGORY.

AGAIN, AS PART OF THE RESPONSE TO THE IOM, WE HAVE SHIFTED THE PROGRAMMATIC REVIEW FROM THE GRANTS WORKING GROUP TO THE BOARD MEETING ITSELF SO THAT WE HAVE THE BENEFIT OF HAVING THAT DISCUSSION

AS A MATTER OF FIRST INSTANCE AT THE BOARD MEETING.

THE PATIENT ADVOCATES WHO WERE PREVIOUSLY RUNNING PROGRAMMATIC REVIEW IN THE GRANTS WORKING GROUP ARE STILL PARTICIPANTS IN THE PEER REVIEW ITSELF, ALTHOUGH NOT VOTING PARTICIPANTS ON EACH INDIVIDUAL ITEM SINCE THAT HAS NOW BEEN SHIFTED TO THE BOARD, BUT THEY HAVE THE FULL BENEFIT OF HAVING SAT THROUGH THE GRANTS WORKING GROUP AND ARE INTIMATELY ACQUAINTED WITH ALL OF THE ISSUES THAT NEED TO BE DISCUSSED AT THE BOARD LEVEL.

SO PROGRAMMATIC REVIEW HAS PROCEEDED AT THE BOARD. AND AT THE END OF THAT, THE BOARD THEN VOTES ON THE RECOMMENDED SLATE OF FUNDING THAT EMERGES FROM THE DISCUSSION FOLLOWING PROGRAMMATIC REVIEW. SO THAT IS NOW THE WAY WE DO THINGS.

I STRONGLY URGE ANY APPLICANTS IN THE ROOM TO NOT VIEW THE BOARD MEETING ITSELF AS AN INSTANCE OF FIRST APPEAL BECAUSE, WHILE THE SUBSTANCE OF WHAT MAY BE SAID COULD WELL HAVE MERIT, THAT IS THE NOT THE PROCEDURE WE HAVE IN PLACE. IN FACT, WE SPECIFICALLY DESIGNED IT TO AVOID THAT. SO PLEASE TAKE THAT UNDER ADVISEMENT.

HAVING SAID THAT, THOSE APPLICANTS WHO ARE HERE WILL HAVE THEIR OPPORTUNITY IN PUBLIC COMMENT TO STATE WHATEVER THEY WOULD LIKE TO ABOUT THEIR

PARTICULAR APPLICATION. MR. HARRISON, DID I LEAVE ANYTHING OUT?

MR. HARRISON: ONE CLARIFICATION AND ONE THING TO ADD. THE PATIENT ADVOCATES OF THE GRANTS WORKING GROUP DO PARTICIPATE IN THE VOTE TO RECOMMEND THE SLATE OF APPLICATIONS TO THE FULL BOARD. BASED ON THE IOM'S RECOMMENDATIONS, WE HAVE ALSO ESTABLISHED AN APPLICATION REVIEW SUBCOMMITTEE, WHICH IS COMPRISED OF ALL THE MEMBERS OF THE BOARD, BUT THE MEMBERS WHO ARE APPOINTED FROM INSTITUTIONS THAT RECEIVE CIRM FUNDING ARE NONVOTING MEMBERS. AND WHAT THAT MEANS IS THAT YOU HAVE THE ABILITY TO PARTICIPATE IN THE DISCUSSION OF AN APPLICATION, ASSUMING YOU DON'T OTHERWISE HAVE A CONFLICT OF INTEREST, BUT YOU MAY NOT VOTE. SO WHEN WE DO A ROLL CALL VOTE, YOUR NAMES WILL BE NOT BE CALLED.

AS ALWAYS, WE HAVE PROVIDED YOU WITH A LIST OF THE APPLICATIONS IN WHICH YOU HAVE A CONFLICT. SO BEFORE RAISING YOUR HAND TO OFFER COMMENT ABOUT A PARTICULAR APPLICATION, PLEASE CHECK YOUR LIST BEFORE SPEAKING. AND IF YOU FORGET, WE WILL POLITELY REMIND YOU.

CHAIRMAN THOMAS: THANK YOU, MR. HARRISON. WITH RESPECT TO THE PATIENT ADVOCATES OF THE GRANTS WORKING GROUP, THANK YOU FOR ADDING THAT. MY

COMMENT WAS THAT THEY DON'T VOTE ON INDIVIDUAL; WHEREAS, BEFORE THEY DID. BUT YOU'RE ENTIRELY CORRECT. THEY DO VOTE ON MOVING THE SLATE TO THE BOARD.

AND THE LAST ITEM MR. HARRISON DISCUSSED IS CRITICAL. IT WAS THE PRINCIPAL RESPONSE OR THE NO. 1 RESPONSE WE HAD TO THE IOM REPORT DEALING WITH THE ISSUES OF EVEN PERCEIVED CONFLICTS OF INTEREST ON MATTERS THAT COME BEFORE THE BOARD FOR VOTES ON AWARDS. SO IT'S A VERY IMPORTANT PART OF THE ENTIRE PUZZLE.

WITH THAT AS A VERY LENGTHY PRELUDE, LET'S NOW PROCEED TO --

MR. SHEEHY: CAN I JUST TALK A LITTLE BIT DEEPER ABOUT THE PROCESS SO EVERYBODY KNOWS EXACTLY WHAT'S GOING TO HAPPEN BEFORE WE START INTO THIS.

SO, NO. 1, IT WILL BE CONDUCTED MUCH IN THE SAME MANNER IN WHICH PROGRAMMATIC REVIEW WAS CONDUCTED AT THE WORKING GROUP, WHICH MEANS NO ITEM WILL COME UNDER DISCUSSION UNLESS THERE'S BEEN A MOTION BY AN ELIGIBLE MEMBER TO MOVE THIS IN EITHER DIRECTION, EITHER OUT OF FUNDING OR INTO FUNDING.

WE'LL START WITH TIER I, WE'LL GO TO TIER II, AND THEN WE'LL GO TO TIER III.

COULD MR. HARRISON PERHAPS CLEARLY

IDENTIFY THE MEMBERS WHO CAN MAKE MOTIONS?

MR. HARRISON: LET ME IDENTIFY THE MEMBERS OF THE APPLICATION REVIEW SUBCOMMITTEE. REMEMBER THAT THOSE OF YOU WHO ARE ON THE APPLICATION REVIEW SUBCOMMITTEE MAY STILL HAVE CONFLICTS OF INTEREST WITH RESPECT TO A PARTICULAR APPLICATION, SO YOU STILL NEED TO CONSULT YOUR LIST BEFORE OFFERING A MOTION OR A COMMENT.

THE MEMBERS OF THE APPLICATION REVIEW SUBCOMMITTEE ARE DULIEGE, FEIT, GOLDBERG, JUELSGAARD, LANSING, PRIETO, QUINT, ROWLETT, SAMUELSON, SHEEHY, STEWARD, THOMAS, TORRES, AND WINOKUR.

MR. SHEEHY: AND THE WAY IN WHICH WE'LL PROCEED IS A MOTION WILL BE MADE, THE BOARD WILL DISCUSS, AND THEN WE'LL TAKE PUBLIC COMMENT. IF THERE'S NO MOTION, ANY PUBLIC COMMENT ON ONE OF THOSE ITEMS WILL TAKE PLACE AFTER THE MOTION TO MAKE THE OMNIBUS APPROVAL OF THE GRANT APPLICATIONS. I WILL BE CHAIRING IT, AND THEN ON THOSE APPLICATIONS WHERE I HAVE CONFLICT, I'LL PASS TO DR. STEWARD. AND I THINK THAT'S PRETTY MUCH IT.

OH, ONE OTHER POINT. I WILL TAKE THE STAFF RECOMMENDATIONS AS MOTIONS FROM THE CHAIR. I THINK THAT'S APPROPRIATE. THE STAFF HAS MADE

RECOMMENDATIONS ON TIER II, AND THOSE SHOULD BE DISCUSSED BY THE BOARD AS A MATTER OF COURSE.

CHAIRMAN THOMAS: THANK YOU. OKAY. I THINK THE GROUND RULES ARE SET. I WILL NOTE THAT WE HAD A SET OF EARLY TRANSLATION AWARDS WITH THIS PROTOCOL, WORKED SWIMMINGLY, AND WE EXPECT IT WILL TODAY AS WELL.

OKAY. ON TO THE PRESENTATION ITSELF. WE HAVE KEVIN WHITTLESEA. DR. WHITTLESEA, PLEASE PROCEED.

DR. WHITTLESEA: THANK YOU, MR. CHAIRMAN. MEMBERS OF THE BOARD, LADIES AND GENTLEMEN, FOR THOSE OF YOU WHO I HAVE NOT HAD AN OPPORTUNITY TO MEET INDIVIDUALLY, I'M KEVIN WHITTLESEA, THE SCIENCE OFFICER LEADING THIS RFA, WHICH IS RFA 13-01, THE DUANE ROTH DISEASE TEAM THERAPY DEVELOPMENT AWARDS III.

I'M GOING TO TAKE JUST A FEW MINUTES, WALK YOU THROUGH THE GOALS AND OBJECTIVES OF THE RFA, THE PRIORITY AREAS OF THE RFA, SOME KEY ASPECTS OF THIS PARTICULAR CALL FOR APPLICATIONS, THE GRANTS WORKING GROUP COMPOSITION, AND THE REVIEW CRITERIA BY WHICH THE GRANTS WORKING GROUP CONSIDERED THE APPLICATIONS RECEIVED UNDER THIS CALL FOR APPLICATIONS. AND THEN I'M GOING TO TURN IT OVER TO DR. BETTINA STEFFEN,

WHO WILL PROVIDE INFORMATION ABOUT THE STAFF RECOMMENDATIONS WHICH WERE JUST REFERRED TO.

IN TERMS OF THE GOALS AND OBJECTIVES OF THIS RFA, AS YOU ALL ARE VERY FAMILIAR, THE DISEASE TEAM PROGRAM OVERALL HAS THE OBJECTIVE OF ADVANCING PRECLINICAL AND CLINICAL DEVELOPMENT OF NOVEL THERAPIES. NOW, THIS PARTICULAR CALL FOR APPLICATIONS, THE THIRD CALL WITHIN THE DISEASE TEAMS PROGRAM, AS I MENTIONED, IS THE DUANE ROTH DISEASE TEAM THERAPY DEVELOPMENT III AWARDS. THIS THIRD CALL HAD TWO KEY OBJECTIVES. THE FIRST, TO COMPLETE AN EARLY PHASE CLINICAL TRIAL WITHIN THE AWARD PERIOD. AND THOSE PROPOSED TRIALS WILL EVALUATE PRELIMINARY SAFETY AND ASSESS PRELIMINARY BIOLOGICAL EFFICACY AND BIOLOGICAL ACTIVITY IN HUMANS.

THOSE PROJECTS -- AND WE DID ALLOW UP TO 12 TO 18 MONTHS OF PRECLINICAL IND-ENABLING RESEARCH. THE IDEA IS THAT WE WEREN'T INTERESTED IN FUNDING PARTIAL CLINICAL TRIALS. WE WANTED TO ENSURE THAT WITHIN THE AWARD PERIOD THAT THE CLINICAL TRIAL PROPOSED COULD ACTUALLY BE COMPLETED. SO THAT 12- TO 18-MONTH WINDOW WAS TO ENSURE THEY WERE CLOSE ENOUGH TO THEIR IND FILING TO STILL HAVE SUFFICIENT TIME TO COMPLETE THAT TRIAL WITHIN THE

AWARD PERIOD.

SECONDLY, ONLY AVAILABLE FOR CIRM EARLY TRANSLATIONAL AWARDEES. WE HAD A PATHWAY WHEREBY THOSE APPLICANTS WHO WERE SUCCESSFUL IN THEIR ET AWARDS, COMPLETED THEIR MILESTONES, COULD THEN HAVE THE OPPORTUNITY TO FILE TO THIS CALL FOR APPLICATIONS WITH A DIFFERENT OBJECTIVE. RATHER THAN COMPLETING A CLINICAL TRIAL, IT WAS TO COMPLETE A WELL-SUPPORTED IND FILING WITHIN THE AWARD PERIOD.

SO TWO VERY DIFFERENT OBJECTIVES. I'M GOING TO SAY MORE ABOUT THAT EARLY TRANSLATIONAL AWARD PATHWAY LATER ON, BUT JUST WANTED TO MAKE CLEAR THAT THERE ARE TWO BUCKETS OF APPLICATIONS WITHIN THIS PARTICULAR CALL.

THE RFA PRIORITIES, WE IDENTIFIED THREE KEY PRIORITIES FOR THIS CALL FOR APPLICATIONS. THE FIRST IS PROPOSALS THAT INCLUDE A PHASE I OR PHASE II CLINICAL STUDY THAT COULD DEMONSTRATE CLINICAL PROOF OF CONCEPT IF SUCCESSFUL. THAT'S OBVIOUSLY A STRATEGIC PRIORITY RIGHT NOW, SO THAT WAS IDENTIFIED AS A PRIORITY WITHIN THIS RFA AS WELL.

SECOND IS PROPOSALS AIMED AT FURTHERING THE DEVELOPMENT OF SUCCESSFULLY COMPLETED CIRM-FUNDED PROJECTS. PROGRAMS THAT WE HAVE ALREADY INVESTED IN THAT ARE PERFORMING WELL, WANTED TO

ENSURE THEY HAVE THE OPPORTUNITY FOR CONTINUED FOLLOW-ON FUNDING TO ADVANCE THOSE PROJECTS INTO THE CLINIC.

LASTLY, PROPOSALS THAT CANNOT OR ARE UNLIKELY TO RECEIVE TIMELY OR SUFFICIENT FEDERAL FUNDING. THIS OBVIOUSLY IS SOMETHING THAT'S VERY MUCH IN THE SPIRIT OF PROPOSITION 71 AND WANTED TO ENSURE THAT THAT WAS CLEARLY REFLECTED WITHIN THIS RFA AS WELL.

WANTED TO SHOW YOU WHERE EXACTLY THIS RFA FALLS WITHIN THE CONTEXT OF OTHER EXISTING CIRM-FUNDED PROGRAMS WITHIN THE PORTFOLIO. THE DISEASE TEAM THERAPY III PROGRAM IS DESIGNED TO CAPTURE MATURE PROGRAMS AT OR CLOSE TO EARLY CLINICAL DEVELOPMENT STAGE. YOU WILL SEE THE CHEVRON DIAGRAM HERE WHICH YOU'RE VERY FAMILIAR WITH. YOU WILL SEE THIS CALL FOR APPLICATIONS IN THE BOTTOM RIGHT-HAND CORNER COLORED. THAT IS THIS PARTICULAR CALL FOR APPLICATIONS. YOU WILL SEE, AS I MENTIONED, IT DOES INCLUDE SOME PRECLINICAL ACTIVITIES LEADING UP TO AN IND FILING, BUT THE EMPHASIS THERE IS IN PHASE I AND PHASE II CLINICAL STUDIES AND THE COMPLETION OF A PROPOSED STUDY.

YOU WILL NOTE IN THE BOTTOM LEFT-HAND CORNER OF THE SLIDE A BOX WHICH STATES, NOTE THAT

EARLY TRANSLATIONAL ALLOWANCE PATHWAY APPLICANTS FIT ROUGHLY HERE, POINTING TO THE DISEASE TEAM I APPLICATION PROGRAM. WHAT THAT IS INTENDED TO REFLECT IS THOSE APPLICATIONS COMING THROUGH THE EARLY TRANSLATIONAL PROGRAM, WHICH I'VE ALLUDED TO, IN TERMS OF THEIR STAGE OF READINESS LOOK A LOT MORE LIKE THE DISEASE TEAM I PROGRAM, WHICH MANY OF YOU ARE VERY FAMILIAR WITH, THAT WITHIN THE AWARD PERIOD, THEIR OBJECTIVE IS AN IND FILING. SO THAT'S WHAT'S INTENDED TO BE CAPTURED THERE. IN TERMS OF THINKING ABOUT WHAT THOSE PROJECTS LOOK LIKE IN TERMS OF READINESS, THAT'S REALLY WHERE THEY FALL, BUT ARE INCLUDED WITHIN THIS RFA AS WELL.

IN TERMS OF THINKING ABOUT FOLLOW-ON FUNDING OPPORTUNITIES FOR EXISTING CIRM PROGRAMS, THESE ARE THE TWO PROGRAMS THAT REALLY WERE ELIGIBLE TO APPLY FOR THIS. THE EARLY TRANSLATIONAL AWARDS, WHICH I'VE ALREADY MENTIONED, ADDITIONALLY, THE DISEASE TEAM I PROGRAMS. THOSE PROGRAMS WERE FUNDED FOR FOUR YEARS WITH THE OBJECTIVE OF AN IND FILING. THOSE PROGRAMS THAT EITHER ALREADY HAVE OR ARE ON TRACK TO COMPLETE THAT IND FILING WITH TIMING SUCH THAT THEY WERE ABLE TO APPLY FOR THIS CALL FOR APPLICATIONS COULD THEN APPLY TO THIS PROGRAM TO REQUEST -- TO SEEK FUNDING FOR THEIR PROPOSED

CLINICAL TRIAL. SO THOSE ARE TWO DIFFERENT CIRM-FUNDED PROGRAMS. ACTIVE AWARDS OF THOSE PROGRAMS ARE MEETING THEIR MILESTONES, PERFORMING WELL, SUCCESSFUL PROGRAMS, HAVE THE OPPORTUNITY THEN APPLY TO THIS CALL FOR FOLLOW-ON FUNDING. SO JUST WANTED TO MAKE THAT VERY CLEAR.

IN TERMS OF ELIGIBILITY CRITERIA WITHIN THIS CALL FOR APPLICATIONS, A FEW KEY AREAS. WE DID HAVE SPECIFIC ELIGIBILITY CRITERIA. MUST HAVE AN ELIGIBLE THERAPEUTIC CANDIDATE. INSTITUTIONAL ELIGIBILITY, WE DID, AS PER MANY OF OUR PREVIOUS CALLS FOR APPLICATION, A LAB WITH NONPROFIT AND FOR-PROFIT INSTITUTIONS TO APPLY.

THE PRINCIPAL INVESTIGATOR OR PI MUST COMMIT 30-PERCENT EFFORT TO THE PROGRAM. SO A SUBSTANTIAL AMOUNT OF EFFORT REFLECTIVE OF THE AGGRESSIVE TIMELINES WE'RE PROPOSING AND KEY DELIVERABLES.

A PROJECT MANAGER DEDICATED TO THE PROJECT WITH NO LESS THAN 50-PERCENT EFFORT TO ENSURE THAT THE MILESTONES ARE MET AND MANAGING THESE LARGE COLLABORATIVE TEAMS.

ADDITIONALLY, WE HAVE THE OPPORTUNITY, NOT A REQUIREMENT, BUT THE OPPORTUNITY FOR ONE CO-PRINCIPAL INVESTIGATOR.

AND, FINALLY, A PARTNER PI. THIS RFA IS PARTICIPATING IN THE COLLABORATIVE FUNDING PARTNERSHIPS PROGRAM THAT YOU ALL ARE VERY FAMILIAR WITH. THE PARTICULAR AGENCIES THAT WILL PARTICIPATE IN THIS CALL FOR APPLICATIONS, THE UK, CHINA, ANDALUCIA, AND THE NIH.

I WANTED TO SAY A FEW WORDS ABOUT GRANTS WORKING GROUP EXPERTISE REFLECTIVE OF THE LATER STAGE OF THE PROJECTS COMING INTO THIS CALL FOR APPLICATIONS, THAT NECESSITATED EXPERTISE THAT WE'VE NOT INCLUDED IN OUR GRANTS WORKING GROUP BEFORE, BUT WERE APPROPRIATE BASED ON THE TYPES OF APPLICATIONS WE WERE SOLICITING WITH THIS RFA.

FIRST, DISEASE AREAS, IMPORTANT TO HAVE EXPERTISE IN THE DISEASES CAPTURED WITHIN THE POOL OF APPLICATIONS RECEIVED. PRODUCT DEVELOPMENT, REGULATORY PROCESS, PRECLINICAL STUDY DESIGN, INDIVIDUALS TO LOOK AT THE PHARMACOLOGY AND TOXICOLOGY OF THE DEVELOPMENT CANDIDATE PROPOSED. AND THEN IT'S THESE LAST TWO THAT I WAS REFERRING TO: CLINICAL TRIAL OPERATIONS AND BIOSTATISTICS. WE HAD NOT PREVIOUSLY INCLUDED THOSE IN OUR GRANTS WORKING GROUP. THOSE INDIVIDUALS WERE LOOKING AT THE PROPOSED CLINICAL STUDIES, AND THAT WAS REALLY A FOCAL POINT THAT WAS IMPORTANT EXPERTISE TO HAVE AT

THE TABLE BASED ON THE OBJECTIVES OF THESE PARTICULAR APPLICATIONS.

REVIEW CRITERIA USED BY THE GRANTS WORKING GROUP. THESE GENERAL BUCKETS WILL BE VERY FAMILIAR BASED ON PREVIOUS CALLS FOR APPLICATION THAT YOU ALL ARE VERY FAMILIAR WITH. FIRST, SIGNIFICANCE AND IMPACT. THREE KEY AREAS IDENTIFIED WITHIN SIGNIFICANCE AND IMPACT BEING EVALUATED. THE FIRST IS THE TARGET PRODUCT PROFILE. THIS IS THE ASPIRATIONAL GOAL OF THE TEAM, WHAT THEY WANT THEIR PRODUCT TO LOOK LIKE. THAT WAS AN IMPORTANT CONSIDERATION. IS IT RATIONAL AND IS IT ACHIEVABLE?

SECOND IS THE CLINICAL COMPETITIVENESS AND IMPACT. WHAT DOES THE COMPETITIVE LANDSCAPE LOOK LIKE FOR THE DISEASE AREA AND THE THERAPEUTIC APPROACH THEY'RE GOING AFTER? AND WHAT IS THE POTENTIAL IMPACT FOR THEIR THERAPY APPROACH TO HAVE TO THEIR TARGET PATIENT POPULATION.

RESPONSIVENESS TO THE RFA, PRIORITIES, ETC., HOW RESPONSIVE WAS THEIR THERAPEUTIC APPROACH TO THE PARTICULAR CALL FOR APPLICATIONS.

SECOND KEY IS SCIENTIFIC RATIONALE AND RISK BENEFIT. WITHIN THAT, WHAT IS THE PRECLINICAL AND/OR CLINICAL DATA THAT WAS PROVIDED WITH THEIR PACKAGE? HOW COMPELLING IS IT? AND WHAT DOES THE

RISK BENEFIT PROFILE LOOK LIKE IN TERMS OF THE PATIENT POPULATION TARGETED WITH THE PROPOSED THERAPEUTIC?

THIRD, THERAPEUTIC DEVELOPMENT READINESS. HOW FAR ALONG ARE THEY? THERE WERE A NUMBER OF KEY MILESTONES THAT WE WERE LOOKING AT, WHICH I'LL SAY A FEW WORDS ABOUT IN ONE OF MY LATER SLIDES.

DESIGN AND FEASIBILITY. THERE WERE THREE KEY AREAS LOOKED AT WITHIN DESIGN AND FEASIBILITY OF THE PROPOSED STUDY. FIRST WAS DEVELOPMENT PLAN TO END OF PHASE II. MOST OF THE APPLICATIONS RECEIVED WERE LOOKING AT PHASE I STUDIES. HOWEVER, WE WANT TO ENSURE THAT THE INVESTIGATORS HAVE PLANS BEYOND JUST COMPLETING A PHASE I STUDY. HAVE THEY THOUGHT ABOUT WHERE THEY'RE GOING AND WHAT THE PHASE II STUDY MIGHT ACTUALLY LOOK LIKE TO ENSURE THAT THERE IS A PLAN.

DEVELOPMENT PLAN TO END OF PHASE II. THE SECOND WAS THE PROJECT PLAN. AND THE THIRD IS OTHER KEY PROJECT COMPONENTS. WITHIN THAT, GRANTS WORKING GROUP WAS LOOKING AT THE PRECLINICAL PLAN, THE REGULATORY PATHWAY, THE MANUFACTURING PLAN, AND THE PROPOSED CLINICAL STUDY. FIFTH IS THE PI AND DEVELOPMENT TEAM. WITHIN THAT, THE EXPERTISE AND TRACK RECORD OF THE PRINCIPAL INVESTIGATOR, THE

DEVELOPMENT TEAM, AND THE PROPOSED LEADERSHIP PLAN, AND THE CLINICAL INVESTIGATOR AND THE PROPOSED CLINICAL SITES.

SIXTH WAS THE BUDGET. THIS WAS LOOKED AT INSOFAR AS THE BUDGET MIGHT IMPACT FEASIBILITY OF THE PROPOSED STUDIES.

SEVENTH WAS COLLABORATIONS, ASSETS, RESOURCES, AND ENVIRONMENT. WITHIN THAT, LOOKING AT COLLABORATIONS. IS THE RIGHT EXPERTISE AT THE TABLE?

NEXT IS LEVERAGED FUNDING FOR CLINICAL TRIALS, IF APPLICABLE. I'M GOING TO SAY A FEW WORDS ABOUT THAT IN ONE OF MY LATER SLIDES.

AND THEN CONTRACT SERVICES. CONTRACT MANUFACTURING ORGANIZATIONS, CONTRACT RESEARCH ORGANIZATIONS, CONSULTANTS. AGAIN, IS THE RIGHT EXPERTISE ON THE TEAM?

AND THEN LASTLY, RESOURCES AND ENVIRONMENT.

AND THEN THE EIGHTH CATEGORY IS INTELLECTUAL PROPERTY AND LICENSES. THIS WAS LOOKED AT FROM A HIGH LEVEL IN TERMS OF WERE THERE ANY IDENTIFIED KEY SHOW STOPPERS, RED FLAGS, PROBLEMS THAT MIGHT COME UP THAT WOULD PREVENT THIS THERAPEUTIC APPROACH FROM MOVING FORWARD. AGAIN,

CONSISTENT WITH SOME OF THE POINTS THAT I'VE ALREADY MADE. WE'RE NOT LOOKING AT NEAR TERM, JUST COMPLETING A PHASE I STUDY, BUT IS THERE A PLAN AND A PATHWAY TO MOVE THESE PRODUCTS BEYOND PHASE I TOWARDS COMMERCIALIZATION.

READINESS FOR CLINICAL TRIAL PROJECTS. THIS IS ONE THAT WE LOOKED AT VERY CLOSELY AND HAD KEY MILESTONES TO ENSURE THAT WE HAVE GOOD, INDEPENDENT WAYS OF ASSESSING WHERE THEY ACTUALLY ARE AND ARE THEY ACTUALLY READY TO MOVE INTO THE CLINIC. FOR EXAMPLE, ANY APPLICANT PROPOSING A PHASE II STUDY REQUIRED THE PROVISION OF PHASE I SAFETY DATA BY THE FULL APPLICATION SUBMISSION DATE. THAT'S TO ENSURE THAT WE ACTUALLY HAVE DATA IN HAND FOR THE GRANTS WORKING GROUP TO BE ABLE TO REVIEW AND LOOK AT SIGNALS OF SAFETY, ANY POSSIBLE PROBLEMS, AND WAS THAT ACCESSIBLE FOR THE PROPOSAL OF A PHASE II STUDY.

SIMILARLY, PROPOSING A PHASE I STUDY REQUIRED AN IND FILING BY THE LETTER OF INTENT SUBMISSION DATE. THAT GAVE US THE OPPORTUNITY TO SEEK COMMENTS FROM THE FDA, SEE IF THERE WERE ANY CLINICAL HOLD ISSUES, AND, AGAIN, MAKE SURE THAT THESE WERE PROJECTS THAT WERE READY TO GO, READY TO MOVE INTO THE CLINIC.

AND LASTLY, I DID MENTION THAT WE DID ALLOW UP TO 12 TO 18 MONTHS OF PRECLINICAL IND-ENABLING RESEARCH FOR PROJECTS COMING PROPOSING A PHASE I STUDY. THOSE APPLICANTS WE REQUIRED THE COMPLETION OF A PRE-IND MEETING WITH THE FDA BY NOT LATER THAN THE FULL APPLICATION SUBMISSION DATE. AGAIN, THAT PROVIDED US WITH THE OPPORTUNITY TO RECEIVE THOSE FDA MEETING MINUTES AND THAT CORRESPONDENCE, WHICH WE DID REQUIRE THEM TO PROVIDE TO CIRM, GAVE US THE OPPORTUNITY TO REVIEW THOSE COMMENTS, SEE IF THE FDA IDENTIFIED ANY KEY ISSUES, RED FLAGS, ADDITIONAL STUDIES THAT MIGHT BE REQUIRED WHICH COULD POTENTIALLY AFFECT THE TIMELINE AND FEASIBILITY OF THE PROJECT. AND THOSE PROJECTS, ADDITIONALLY, HAD TO DEMONSTRATE CLEAR EVIDENCE THAT A SINGLE THERAPEUTIC DEVELOPMENT CANDIDATE HAD BEEN SELECTED AND HAD TO SHOW CLEAR EVIDENCE THAT THEY'VE DEMONSTRATED PRECLINICAL PROOF OF CONCEPT IN THEIR TARGET DISEASE AND/OR INJURY IN A RELEVANT RESEARCH MODEL WITH THE ACTUAL PROPOSED THERAPEUTIC CANDIDATES.

THESE WERE CLEAR THINGS THAT WE COULD MONITOR, THEY HAD PROVIDE DEMONSTRATION OF, AND WE KNEW THAT THEY WERE ACTUALLY ON TRACK WHERE THEY SAID THEY WERE AND READY TO MOVE INTO THE CLINIC TO

COMPLETE THOSE PROPOSED TRIALS WITHIN THE AWARD PERIOD.

I WANTED TO SAY NOW A FEW WORDS ABOUT THE EARLY TRANSLATIONAL ALLOWANCE PATHWAY. I'VE MENTIONED THAT THIS WAS AN OPPORTUNITY AVAILABLE ONLY TO EXISTING CIRM EARLY TRANSLATIONAL AWARDEES. THE DEVELOPMENT OF THIS PATHWAY WAS TO ENSURE THAT THERE WAS AN OPPORTUNITY FOR SUCCESS FOR CONTINUED CIRM-FUNDED PROJECTS. SO EARLY TRANSLATION AWARDEES WITH A CURRENT PROJECT COULD APPLY WITH THE GOAL OF AN IND FILING WITHIN FOUR YEARS. I MENTIONED THIS IS ONLY AVAILABLE TO ET AWARDEES, AND THEY HAD TO EITHER HAVE ALREADY COMPLETED OR BE ON TRACK TO COMPLETE THEIR MILESTONES WITHIN THE APPLICATION CYCLE PERIOD. AND THEIR GOAL WAS THEN ONLY TO ACHIEVE AN IND FILING WITHIN THE AWARD PERIOD.

AND THERAPEUTIC APPROACH DEVELOPED UNDER AN ET AWARD WAS ELIGIBLE. HOWEVER, ONE EXCEPTION THAT WE MADE WAS ANY SMALL MOLECULE OR BIOLOGIC PROPOSED, IT HAD TO BE THE SAME DEVELOPMENT CANDIDATE DEVELOPED UNDER THE ET AWARD, BUT ANY SMALL MOLECULE OR BIOLOGIC HAD TO BE TARGETING AN ENDOGENOUS STEM CELL AND THE PRIMARY MECHANISM OF ACTION FOR REGENERATION AND REPAIR.

THE THOUGHT PROCESS THERE IS WE HAVE A

NUMBER OF PROGRAMS WITHIN THE EARLY TRANSLATIONAL PORTFOLIO THAT ARE USING STEM CELLS AS A DRUG SCREENING TOOL. AND IN THE CASE THAT THERE'S A HIT THAT COMES OUT OF THAT, THAT DRUG MAY NO LONGER BE TARGETING THE STEM CELL PATHWAY. SO IF THE STEM CELL COMPONENT OF THE PROJECT IS DONE, WE DID NOT WANT TO CAPTURE THOSE PROJECTS WITHIN THIS PARTICULAR CALL FOR APPLICATIONS. SO REALLY TARGETING STEM CELL PATHWAYS.

SO THAT WAS WHAT WE WERE LOOKING FOR WITHIN THE EARLY TRANSLATIONAL PATHWAYS. NOW, WE DID HAVE WITHIN THE RFA A LIST OF REQUIREMENTS THAT MUST HAVE BEEN MET BY THE APPLICANT. ESSENTIALLY, FOR EXAMPLE, HAVE THEY SELECTED A SINGLE THERAPEUTIC CANDIDATE? HAVE THEY SHOWN CLEAR PROOF OF CONCEPT? AND THE IDEA IS THAT THOSE CRITERIA WERE DESIGNED TO ENSURE THAT ANY ET APPLICANT COMING THROUGH THIS PATHWAY HAD THE ABILITY TO SUCCEED. THEY WERE FAR ENOUGH ALONG IN THEIR PROJECT. THEY WERE READY FOR A DEVELOPMENT PROGRAM. WE DIDN'T WANT TO FULLY SUPPORT THE ET PROGRAMS; HOWEVER, COMING INTO THIS APP, WE WANTED TO MAKE SURE THEY WERE READY TO GO.

LASTLY, BUDGET AND MECHANISM. THESE AWARDS ARE BETWEEN FIVE AND $20 MILLION OVER FOUR YEARS OR LESS. THIS BOARD APPROVED UP TO $100

MILLION COMMITTED FOR UP TO FIVE AWARDS. AWARDS CAN BE EITHER TO NONPROFIT INSTITUTIONS IN THE FORM OF GRANTS. FOR-PROFIT INSTITUTIONS APPLYING COULD CHOOSE A GRANT OR A LOAN.

I WANTED TO SAY A FEW WORDS ABOUT LEVERAGED FUNDING THAT WAS INCLUDED WITHIN THIS RFA. WE DID INCLUDE A PROVISION SUCH THAT ANY APPLICANT PROPOSING A CLINICAL TRIAL USING A SMALL MOLECULE OR BIOLOGIC HAD TO PROVIDE LEVERAGED FUNDING EQUIVALENT TO 25 PERCENT OF THE COST OF THE PROPOSED CLINICAL TRIAL. THE IDEA THERE IS THAT FOR SMALL MOLECULES OR BIOLOGICS, THERE ARE LOTS OF OPPORTUNITIES FOR OTHER FUNDING STREAMS. AND WE THOUGHT IT WAS IMPORTANT FOR THOSE COMING IN TO SHARE SOME SKIN IN THE GAME AND TO SAY THEY THOUGHT ABOUT THIS AND LOOKING AT ADDITIONAL POSSIBLE FUNDING OPPORTUNITIES BEYOND THE SCOPE OF JUST CIRM FUNDING. CELL THERAPIES WERE NOT SUBJECT TO THAT SINCE THAT'S AN AREA WHERE IT'S NEW, THERE ARE A LOT OF MANUFACTURING CHALLENGES, THEY'RE MORE COSTLY. THEY WERE NOT SUBJECT TO THE MATCHING REQUIREMENT. LEVERAGED FUNDING WAS EXPECTED FOR ANYONE PROPOSING A CLINICAL TRIAL WITH A SMALL MOLECULE OR A BIOLOGIC.

SO MOVING, THEN, TO REMIND YOU OF THE

TIERS, WHICH J.T. MENTIONED IN HIS INTRODUCTION, THESE ARE THE THREE TIERS, AS A REMINDER, THAT WERE APPROVED BY THIS BOARD AND HAVE ALREADY BEEN IN USE. TIER I IS DEFINED AS ANY APPLICATION SCORING BETWEEN 75 AND 100 AND IS DEFINED AS RECOMMENDED FOR FUNDING. TIER II ARE THOSE APPLICATIONS SCORING BETWEEN A 65 AND A 74. THOSE WOULD BE THEN SUITABLE FOR PROGRAMMATIC CONSIDERATION, AS MR. SHEEHY MENTIONED IN HIS COMMENTS. AND TIER III IS DEFINED AS THOSE SCORING UP TO A 64, AND THOSE ARE NOT RECOMMENDED FOR FUNDING.

THIS TABLE, I DON'T EXPECT YOU TO BE ABLE TO READ THIS, BUT YOU HAVE A COPY OF THIS IN YOUR BINDER. ESSENTIALLY YOU'RE SEEING HERE THE TIERS AS DEFINED BY THE PREVIOUS SLIDE. THERE ARE FOUR APPLICATIONS WHICH HAVE FALLEN IN TIER I WITH A COMBINED BUDGET OF 42.7 MILLION. THERE ARE FOUR APPLICATIONS IN TIER II WITH A COMBINED BUDGET OF 47.8 MILLION. AND FIVE APPLICATIONS THEN FALL IN TIER III.

SO IF THERE ARE ANY QUESTIONS ABOUT THE RFA IN GENERAL, I'D BE HAPPY TO TAKE THOSE. OTHERWISE I'M GOING TO THEN TURN IT OVER TO DR. BETTINA STEFFEN, WHO WILL WALK YOU THROUGH THE STAFF RECOMMENDATIONS.

CHAIRMAN THOMAS: THANK YOU, KEVIN, FOR THAT VERY THOROUGH INTRODUCTORY SET OF REMARKS. ANY QUESTIONS, COMMENTS, MEMBERS OF THE BOARD?

DR. STEWARD: IT MIGHT BE WORTH POINTING OUT NOW ONE ASPECT OF THIS NEW PROCESS THAT YOU MAY RECALL FROM LAST TIME, BUT PERHAPS NOT. THESE CUTOFFS ARE DETERMINED ENTIRELY BY THE SCORES. THERE WAS NO PROCEDURE AT THE END WHERE THE GRANTS WORKING GROUP LOOKED AT THESE AND SAID, WELL, I WANT TO MOVE THE CUTOFF LINE UP AND DOWN ONE GRANT. I JUST WANTED TO SAY THAT BECAUSE THAT DIFFERS FROM WHAT WE'VE DONE IN THE PAST.

CHAIRMAN THOMAS: THAT IS CORRECT, ALTHOUGH I WOULD SAY THAT THEY'RE FULLY AWARE OF THE MEANING OF WHERE THEY VOTE. SO THEY KNOW BY IN SO DOING, THAT'S THEIR SENSE OF WHERE IT SHOULD GO.

DR. STEWARD: YES AND NO. YES, INDIVIDUALLY. NO, ACCORDING TO THE MEAN. SO YOU MIGHT PERSONALLY VOTE A SCORE THAT WOULD PUT IT IN A PARTICULAR TIER. BUT AFTER EVERYBODY VOTES, THE MEAN TAKES IT SOMEWHERE ELSE. JUST TO SAY.

CHAIRMAN THOMAS: FAIR ENOUGH. OKAY. GIL.

DR. SAMBRANO: I WOULD AGREE WITH THAT, BUT I THINK ALSO THE AVERAGE REPRESENTS THE GROUP'S

FEELING ON THE APPLICATION. SO IN MANY CASES YOU WILL SEE THAT WE PROVIDE THE AVERAGE, THE MEDIAN, THE RANGE. SO IT IS THE OPINION OF THE BROADER GROUP WHERE IT ENDS UP.

DR. STEFFEN: THANK YOU. MR. CHAIRMAN, BOARD MEMBERS, STAFF, MEMBERS OF THE AUDIENCE, AND GUESTS, I'LL BE PRESENTING THE STAFF RECOMMENDATIONS FOR THE DISEASE TEAM III AWARD. FOR THOSE OF YOU WHO HAVEN'T MET ME, MY NAME IS BETTINA STEFFEN, AND I'VE BEEN WORKING WITH THE DISEASE TEAM PROGRAM SINCE ITS INCEPTION IN 2007.

THIS AGENDA ITEM IS IN YOUR BINDER. I WILL BE WORKING OFF THE SLIDES, BUT WANTED TO POINT OUT TO YOU THAT THERE IS A MEMO IN YOUR BINDER, THE VERY FIRST DOCUMENT, THAT HAS ALL THE DETAIL OF THE STAFF RECOMMENDATIONS.

A NOTE ON THE PROCESS THAT WE USE. THE SCIENCE OFFICERS OF THE DEVELOPMENT TEAM AND THE EARLY TRANSLATIONAL TEAM, OF WHICH NUMBER NOW ELEVEN IN TOTAL, AND MANY OF THEM ARE HERE TODAY, CONVENED FOLLOWING THE GRANTS WORKING GROUP IN SEPTEMBER ON SEVERAL OCCASIONS TO REVIEW AND DISCUSS THE APPLICATIONS AND CONSIDER OUR STAFF RECOMMENDATIONS. IN SEVERAL CASES WE FELT THAT THERE WAS ADDITIONAL INFORMATION THAT WE NEEDED TO GATHER AND DISCUSS.

IN SOME CASES IT INCLUDED FOLLOW-UP TELECONFERENCES WITH THE APPLICANT, THE TEAMS, AND ALSO EXPERTS IN AREAS WHERE WE NEEDED CLARIFICATION OF ISSUES. SO I WANT YOU TO KNOW THAT WE FEEL VERY CONFIDENT IN OUR STAFF RECOMMENDATIONS AND THE APPLICATIONS.

THIS TABLE HERE PRESENTS THE SUMMARY OF OUR RECOMMENDATIONS, AND I WILL WALK YOU THROUGH THE DETAIL AND RATIONALE FOR EACH OF THE RECOMMENDATIONS ON SUBSEQUENT SLIDES. THERE IS A CIRM SCIENCE OFFICER HERE TODAY WHO IS PREPARED TO WALK YOU THROUGH THE SUMMARY OF THE GRANTS WORKING GROUP RECOMMENDATIONS SHOULD YOU WANT MORE INFORMATION ABOUT THE FINDINGS IN THE SCIENTIFIC REVIEW.

SO IN SUMMARY, WE ARE GOING TO BE RECOMMENDING ONE APPLICATION FOR FUNDING WITH A CONDITION, TWO APPLICATIONS FOR FUNDING, AND ONE APPLICATION THE STAFF RECOMMENDS THAT YOU DO NOT FUND. FOR THE THREE RECOMMENDATIONS, I WANT TO POINT OUT THAT THESE ARE ALL CELL THERAPIES WHERE THE STEM CELL CONNECTION IS VERY STRONG AND CLEAR. THEY HAVE THE POTENTIAL FOR IMPACT IN THE PATIENT POPULATIONS THAT THEY'RE ADDRESSING. AND TWO OF THESE FALL INTO A PRIORITY AREA FOR THE RFA, WHICH ARE CONTINUATIONS OF EXISTING CIRM DISEASE TEAM OR TRANSLATIONAL AWARDS.

THE FIRST APPLICATION I'D LIKE TO PRESENT TO YOU -- SORRY -- THE RECOMMENDATION ON APPLICATION 7281, ENTITLED "A TISSUE ENGINEERED RECELLULARIZED LARYNGOTRACHEAL IMPLANT." THIS APPLICATION IS TARGETING DISEASED AND DAMAGED TRACHEAS, AND THE APPROACH THE APPLICANT IS USING IS AN AUTOLOGOUS STEM OR PROGENITOR CELL SEATED ONTO A BIOLOGIC SCAFFOLD.

I WANTED TO GIVE YOU SOME BACKGROUND OF WHAT IS GOING ON IN THIS EXCITING AREA OF TISSUE ENGINEERING SO THAT YOU CAN UNDERSTAND THE CONTEXT OF OUR RECOMMENDATION. IN 2008 THE FIRST PATIENT WAS ACTUALLY TRANSPLANTED WITH SUCH A BIOLOGIC DEVICE. AND SHE WAS A YOUNG WOMAN WITH SEVERE TUBERCULOSIS DISEASE. AND DESPITE NEEDING MULTIPLE STINTING PROCEDURES OVER THE COURSE OF THE FIVE YEARS, SHE IS ALIVE AND HER QUALITY OF LIFE HAS IMPROVED. SINCE THEN, 14 OTHER PATIENTS HAVE RECEIVED TRANSPLANTS, MOST DONE UNDER A COMPASSIONATE USE RULE, WHICH IS ALLOWED IN SERIOUSLY ILL PATIENTS WHERE CONVENTIONAL THERAPY WON'T WORK.

THE CHALLENGE -- SO THAT IS A COMPLETELY LEGITIMATE WAY TO PUT A NEW THERAPY INTO A PATIENT, BUT THE CHALLENGE IS THAT THE OUTCOMES ARE VERY

DIFFICULT TO INTERPRET. SO WE CAN'T REALLY AT THIS TIME SAY WHETHER THIS IS A TERRIFIC SUCCESS FOR TISSUE ENGINEERING AND REGENERATIVE MEDICINE OR IT'S WORRISOME BECAUSE IN SOME CASES A COUPLE OF THOSE PATIENTS WHO HAVE DIED, ACKNOWLEDGING THAT THEY HAVE GONE INTO VERY SERIOUSLY ILL PATIENTS, MAY OR MAY NOT BE ATTRIBUTED TO THE ACTUAL TRANSPLANT.

SO THAT YOU WILL ASK WHY SHOULD WE GO BACKWARDS. OUR RECOMMENDATION IS TO FUND THE PRECLINICAL ASPECT OF THIS PROJECT. AND THE REASON WE BELIEVE THAT THIS IS, AND WE ARE IN AGREEMENT WITH THE APPLICANT, IS THAT THERE ARE KEY QUESTIONS THAT CAN ONLY BE ANSWERED IN THE PRECLINICAL MODELS AT THIS TIME. AND THAT IS WITH RESPECT TO WHETHER THE TRACHEAL TRANSPLANTS WILL BE SAFE OVER THE LONG TERM AND TO ANSWER SOME QUESTIONS ABOUT BIOLOGIC MECHANISM AND HOW THEY ACTUALLY WORK. THE OPPORTUNITY IN THE PRECLINICAL MODELS IS TO RECOVER THE GRAFT, LOOK AT WHETHER THEY WERE REVASCULARIZED, AND HOW THE CELLS BEHAVE IN CONJUNCTION WITH THE TISSUE. WE AND OTHERS IN THE FIELD AGREE THAT THIS IS IMPORTANT WORK.

THAT IS THE BACKGROUND TO OUR PROGRAMMATIC RECOMMENDATION. AND OUR PROGRAMMATIC REASONS, WHICH ARE NOW DETAILED ON THE SLIDE, IS THE PROJECT

FOCUSES ON DEVELOPING TISSUE-ENGINEERED REPLACEMENTS FOR A LARGE AIRWAY DISEASE WHICH WE BELIEVE AND OTHERS THAT IS POTENTIALLY A TRANSFORMATIVE AREA OF REGENERATIVE MEDICINE. THIS IS A FIRST STEP IN A WAY TO BRING ENGINEERED TISSUES TO THE FIELD.

THE PROJECT BRINGS THIS TECHNOLOGY TO CALIFORNIA. IT'S A NOVEL TECHNIQUE AND LEVERAGES THE MORE ADVANCED WORK THAT'S BEEN DONE IN THE UK THROUGH A SPECIFIC COLLABORATION WITH THIS TEAM. THE PROJECT WOULD CREATE AN OPPORTUNITY TO MODEL THE TECHNOLOGY TRANSFER IN THESE COMPLEX ENGINEERED PRODUCTS. SO THEY KNOW HOW TO MAKE IT IN THE UK, AND WE WANT TO BRING THAT TO CALIFORNIA AND SHOW THAT YOU CAN TRANSFER A COMPLEX PROCESS AND DO IT IN ANOTHER LOCATION, MAKING IT AVAILABLE TO PATIENTS IN CALIFORNIA.

IF THE POTENTIAL THERAPEUTIC WOULD BE TESTED AND DEVELOPED, IT PROVIDES ADVANCES IN CLINICAL DEVELOPMENT, AND EARLY ACCESS WOULD BE AVAILABLE TO PATIENTS IN CALIFORNIA.

NOTABLY, THIS FILLS A GAP IN THE CIRM PORTFOLIO AS WE HAVE NO OTHER KIND OF HOLLOW TUBE CONDUITS FOR TISSUE ENGINEERING APPROACHES, AND THIS IS FELT BY THE FIELD TO BE A VERY LOGICAL ENTRY POINT FOR SOME OF THESE FASCINATING 3D TISSUE AND

ORGAN REGENERATIONS.

SO OUR STAFF RECOMMENDATION IS TO FUND IT WITH A CONDITION. WE RECOMMEND THAT YOU APPROVE LIMITED FUNDS NOT TO EXCEED $4.4 MILLION IN TOTAL COST FOR TWO YEARS IN THE PRECLINICAL ACTIVITIES. AND WE'VE DETAILED THOSE OUT IN THE RECOMMENDATION.

OUR NEXT GRANT TO DISCUSS --

CHAIRMAN THOMAS: DR. STEFFEN, I WANT TO ASK MR. HARRISON. WITH RESPECT TO THESE, SHOULD WE WAIT TO HEAR ALL FOUR, OR DO WE ACT --

MR. SHEEHY: I THINK, HONESTLY, IF I HAD BEEN ORDERING THIS, I PROBABLY WOULD HAVE HAD THOSE PRESENTATIONS IN LINE WHEN WE WENT THROUGH THEM THROUGH THE APPROVAL PROCESS. IF YOU WANT TO GO THROUGH THEM ALL --

DR. STEFFEN: YOU MAY ASK FOR THE INDIVIDUAL SCIENTIFIC PRESENTATION IF YOU'D LIKE.

MR. SHEEHY: I DON'T WANT -- I REALLY APPRECIATE THE WORK YOU GUYS HAVE DONE, DR. STEFFEN, AND I DON'T WANT TO HIJACK YOU. BUT IF YOU PRESENT AND THEN WE DISCUSS, AND THEN WE HAVE TO GO TAKE A MOTION AND DISCUSS AGAIN, IT GETS FAIRLY CHAOTIC. IT'S ALMOST EASIER BECAUSE MY INTENTION HAD BEEN TO TAKE ALL OF YOUR RECOMMENDATIONS TO FUND AS VIRTUAL MOTIONS AND HAVE YOU GUYS PRESENT, THEN HAVE A

DISCUSSION, AND THEN MOVE FROM THERE. IF YOU GUYS ARE COMFORTABLE, THAT MIGHT BE EASIER.

DR. STEFFEN: SURE. WE WERE PREPARED FOR THAT POSSIBILITY.

MR. SHEEHY: OKAY. DOES THAT SOUND FAIR? COMFORTABLE WITH THAT?

CHAIRMAN THOMAS: SOUNDS GOOD.

MR. SHEEHY: MR. JUELSGAARD, WE'RE JUST GOING TO THEM AS MOTIONS WHEN THEY COME UP, AND THEN WE CAN HAVE A DISCUSSION.

DR. JUELSGAARD: DISCUSSION ON THIS ONE NOW?

MR. SHEEHY: NO. WE'LL HAVE THE DISCUSSION AS ACTUAL MOTIONS TO FUND SO THAT WE CAN HAVE VOTES AND THEN DISPOSE OF THEM. EITHER WAY.

DR. JUELSGAARD: WELL, THE QUESTIONS ARE FRESH IN YOUR MIND AND THIS DISCUSSION IS FRESH IN YOUR MIND.

MR. SHEEHY: I THINK WE'LL HAVE THE PRESENTATION. WE WON'T GO THROUGH EACH OF THESE ONE BY ONE. WE WILL START THE DISCUSSION OF EACH STAFF RECOMMENDATION IN THE CONTEXT OF THE DISCUSSION OF TIER II. EITHER THE CHAIR OR A MEMBER WILL MAKE THE MOTION TO ACCEPT THE STAFF RECOMMENDATION. WE'LL HAVE THE PRESENTATION, WE'LL HAVE A DISCUSSION,

WE'LL HAVE A VOTE. DOES THAT MAKE SENSE? I THINK THAT WILL BE CLEARER THAN HAVING A FULL DISCUSSION OF ALL THESE RIGHT NOW AND THEN GOING BACK AND TRYING TO VOTE ON THEM AFTER. WE NEED TO HAVE SOME SORT OF ORDER. IS THAT OKAY, DR. STEFFEN?

DR. STEFFEN: I JUST NEED CLARIFICATION WHAT WE WANT TO DO NEXT.

DR. FEIGAL: YEAH. I THINK WE'RE STILL A LITTLE UNCLEAR ABOUT THE PROCESS IF YOU COULD JUST CLARIFY IT FOR US.

MR. SHEEHY: WELL, I THINK DR. SAMBRANO HAS SOMETHING HE WANTS TO OFFER, AND THEN I WOULD GO INTO MOVING THINGS AROUND TIERS, STARTING WITH TIER I AND ASKING THE QUESTION WHETHER ANYONE WOULD LIKE TO MOVE A PROJECT OUT OF TIER I.

CHAIRMAN THOMAS: THE NET EFFECT OF THIS IS WE WILL RAPIDLY GET TO DISCUSSION OF THIS. JUST IT PUTS A PROCEDURAL FRAMEWORK.

MR. SHEEHY: WE'LL TAKE THEM ONE BY ONE AT THAT POINT AS OPPOSED TO TAKING THEM OMNIBUS.

CHAIRMAN THOMAS: CAN I JUST ASK DR. STEFFEN ONE OTHER THING? IN EACH OF YOUR DISCUSSIONS OF TIER II PROJECTS, THERE WERE SOME RESERVATIONS OF THE GRANTS WORKING GROUP THAT RESULTED IN THE PROJECTS BEING IN TIER II TO BEGIN

WITH. IF YOU COULD JUST PERHAPS ALLUDE TO THOSE AND HOW IN YOUR ANALYSIS OF ALL THE RELEVANT FACTORS YOU CONCLUDED THAT YOU'VE OVERCOME THOSE CONCERNS.

DR. FEIGAL: DR. STEFFEN, MAYBE WHAT WE COULD DO, EACH SCIENCE OFFICER -- WE'RE DOING THIS ALL AD HOC, AS YOU CAN SEE. WHAT I WOULD SUGGEST IS EACH SCIENCE OFFICER IS PREPARED TO TALK ABOUT THE ISSUES THAT WERE RAISED AT GRANT REVIEW GROUP. I THINK THAT WOULD BE MAYBE EASIER TO HAVE THE SCIENCE OFFICER AS OPPOSED TO DR. STEFFEN GO OVER EACH INDIVIDUAL ONE.

CHAIRMAN THOMAS: THAT WORKS TOO.

DR. STEFFEN: AND WE'RE GOING TO WAIT TO DO THAT. WE'RE GOING --

CHAIRMAN THOMAS: CORRECT. DR. SAMBRANO.

DR. SAMBRANO: I THINK WE'RE ALL ON THE SAME PAGE. SO WHAT I WANT TO JUST HIGHLIGHT ARE A COUPLE OF THINGS. ONE WE'RE SHOWING ON THE SCREEN, WHICH IS VERY DIFFICULT TO READ, BUT IS IN YOUR BOOKS AS WELL, WHICH IS A TABLE THAT SHOWS EACH OF THE APPLICATIONS IN RANK ORDER. IT PROVIDES THE AVERAGE, MEDIAN, AND STANDARD DEVIATION RANGE OF SCORES, THE BUDGET THAT WAS REQUESTED FOR EACH APPLICATION. IN THE CASES WHERE THERE WERE ANY ADJUSTMENTS, THOSE ARE REFLECTED IN WHAT IS

PRESENTED. SO YOU CAN ALSO SEE WHAT THE TOTAL FOR TIER I AND TIER II WOULD BE IN TERMS OF DOLLARS.

YOU ALSO HAVE -- WE DISTRIBUTED A SECOND TABLE WHICH PARALLELS THE ONE I'M SHOWING YOU THAT PROVIDES A SUMMARY OF REQUESTS FOR APPEAL OR RECONSIDERATION AND THE ACTION THAT CIRM TOOK ON THOSE REQUESTS. SO FROM THAT TABLE, WHICH LOOKS LIKE THIS, YOU CAN SEE THAT THERE WERE FOUR APPLICANTS THAT CONSULTED WITH THE REVIEW OFFICE THAT CHOSE TO SUBMIT AN APPEAL OR RECONSIDERATION REQUEST. AND THE STAFF FINDINGS ARE PROVIDED IN EACH OF THOSE INSTANCES.

AND I ALSO WANT TO ADD THAT APPLICATION DR-37201, WHICH IS THE ONE SHOWN AT THE BOTTOM OF THE TABLE, A NEW REQUEST HAS ARISEN. AND SO IN ORDER FOR US TO PROCEDURALLY ADDRESS AND GO THROUGH THAT REQUEST AND MAKE A DETERMINATION, WE'RE GOING TO DEFER CONSIDERATION OF THAT APPLICATION UNTIL THE NEXT BOARD MEETING. SO THAT ONE WILL NOT BE THE SUBJECT OF A VOTE TODAY.

CHAIRMAN THOMAS: THANK YOU.

DR. JUELSGAARD: SO JUST A QUESTION OF DR. SAMBRANO. SO IN LOOKING AT THE, NOT THIS SLIDE, BUT THE ONE THAT SHOWS THE APPEALS, AM I CORRECT IN NOTING THAT OF THE THREE STAFF RECOMMENDATIONS, THE

FIRST OF WHICH WE JUST WENT THROUGH, THE OTHER TWO YET TO COME, THAT THERE WAS NO APPEAL MADE OF ANY OF THOSE APPLICANTS OR AT LEAST NONE IS NOTED ON THIS SHEET?

DR. SAMBRANO: THAT'S CORRECT.

DR. JUELSGAARD: THE APPEAL THAT WAS MADE IS ON THE ONE FOR WHICH THERE IS A RECOMMENDATION IN TIER II FOR NO FUNDING. SO DOES THAT MEAN THAT AB INITIO THE STAFF DECIDED TO RE-REVIEW THIS IN LIGHT OF THE CDAP RECOMMENDATION AND COME UP WITH A DIFFERENT RECOMMENDATION?

DR. SAMBRANO: I'M NOT SURE I'M CLEAR ON YOUR QUESTION. SO IN TIER II 7061 IS ONE THAT STAFF DID NOT RECOMMEND.

DR. JUELSGAARD: SO IF YOU LOOK AT 7281, THAT'S THE ONE WE JUST DISCUSSED, RIGHT?

DR. FEIGAL: CAN I ANSWER THAT QUESTION BECAUSE I'M VERY FAMILIAR WITH THAT? THERE WAS NO -- THAT'S NOT A PREVIOUSLY FUNDED PROJECT. SO WHETHER OR NOT THERE'S A CDAP IS IRRELEVANT TO THAT ONE.

CHAIRMAN THOMAS: MR. HARRISON HAS A COMMENT AS WELL.

MR. HARRISON: STEVE, IF I UNDERSTAND YOUR QUESTION CORRECTLY, YOU'RE WONDERING WHETHER

EFFECTIVELY STAFF TREATED THOSE APPLICATIONS IN TIER II AS IF THEY WERE THE SUBJECT OF AN APPEAL AND CONDUCTED --

DR. JUELSGAARD: RIGHT. IN OTHER WORDS, WHAT I UNDERSTAND, TAKING 7281 AS AN EXAMPLE, I DON'T SEE ANY APPEAL FROM THE APPLICANT, RIGHT? WHAT I UNDERSTOOD THE PROCESS WAS IS THAT PEOPLE COULD APPEAL ON THE BASIS OF NEW INFORMATION OR A MISTAKE OR SOMETHING LIKE THAT. THE STAFF WOULD REVIEW AND DECIDE WHETHER THAT WAS TRUE OR NOT. THAT DOES NOT APPEAR TO BE WHAT'S HAPPENED HERE. SO, INSTEAD, WHAT I'M LEFT, AND THIS IS MY QUESTION, IS THE STAFF SIMPLY ITSELF DECIDED TO RE-REVIEW THE SUBMISSION AND THEN COME UP WITH A RECOMMENDATION THAT WAS NOT THE SAME RECOMMENDATION AS THE GROUP THAT REVIEWED THIS.

DR. SAMBRANO: SO IT'S NOT A RE-REVIEW. SO LET ME JUST CLARIFY. SO WHAT I'M PRESENTING IN THE APPEALS TABLE, THOSE ARE REQUESTS THAT COME FROM THE APPLICANT BASED ON THE RECOMMENDATIONS THAT WE PROVIDED TO THEM FROM THE GRANTS WORKING GROUP AS WELL AS FROM STAFF. PRIOR TO US PRESENTING THE RECOMMENDATIONS TO THE APPLICANTS, THE STAFF PREPARED, KNOWING THAT THESE ARE IN TIER II, A RECOMMENDATION THAT WOULD INFORM YOUR PROGRAMMATIC

REVIEW ON THESE APPLICATIONS. SO THOSE TWO ARE INDEPENDENT.

DR. JUELSGAARD: JUST TO BE CLEAR, THERE WAS NO OBJECTION FROM THE GROUP THAT SUBMITTED 7281 TO THE OUTCOME THAT THEY WERE IN TIER II. THEY DIDN'T SAY TO YOU, OH, MY GOSH, WHY IS THIS?

DR. SAMBRANO: NO. NO. NO.

DR. JUELSGAARD: JUST SO I'M CLEAR. SO IT WAS PURELY ON YOUR OWN AS STAFF THAT YOU DECIDED?

MR. SHEEHY: CAN I CLARIFY?

DR. SAMBRANO: NO. IT WAS BY VIRTUE OF THE FACT IT WAS IN TIER II.

CHAIRMAN THOMAS: ONE AT A TIME. LET'S START WITH MR. HARRISON, PLEASE.

MR. HARRISON: JUST TO BE CLEAR, PART OF THE POLICY CHANGES THE BOARD MADE IN RESPONSE TO THE IOM REPORT AND ACTUALLY EVEN PRIOR TO THAT WAS TO ASK STAFF, AFTER THE RECOMMENDATIONS WERE MADE BY THE GRANTS WORKING GROUP, TO EVALUATE THOSE RECOMMENDATIONS AND TO OFFER ANY ADVICE TO THE BOARD THAT THEY HAVE. AND TIER II WAS A PARTICULAR AREA OF FOCUS BECAUSE THOSE APPLICATIONS FALL WITHIN A CATEGORY WHERE REALLY THE BOARD HAS AN OPPORTUNITY TO FUND THEM IF IT THINKS THERE ARE PROGRAMMATIC REASONS TO DO SO.

SO WHAT STAFF HAS DONE HERE IS PART OF THE PROCESS THAT IS EMBODIED IN THE BYLAWS AND WAS DONE AS PART OF THE AMENDMENTS MADE IN RESPONSE TO THE IOM REPORT.

MR. SHEEHY: AND I WOULD JUST REPEAT. I JUST WANT TO SUPPORT WHAT JAMES HAS SAID. THIS IS A CHANGE WE MADE, AND IT'S KIND OF BITTERSWEET. THIS IS SOMETHING THAT DUANE ROTH WAS VERY, VERY ENTHUSIASTIC ABOUT HAVING US IMPLEMENT, WHICH WAS WE GET THESE ONES IN THE MIDDLE AREA, WE HAVE TO MAKE DECISIONS, AND IT WOULD BE HELPFUL TO HAVE A MORE EXHAUSTIVE STAFF LOOK AT THESE. AND I THINK THE SUPPOSITION THAT PEOPLE DIDN'T APPEAL, WELL, THESE WERE BEING MANAGED BY STAFF. IF STAFF HAD COME BACK AND SAID DO NOT FUND, I THINK THEY MIGHT HAVE APPEALED. BUT MOST SMART PEOPLE DON'T STOP A PROCESS THAT'S GOING IN THEIR FAVOR AND INTERFERE IN IT.

SO I THINK THAT THEY PROBABLY -- THEY WOULD HAVE TAKEN THE APPROACH THAT WE'RE GOING TO WAIT FOR THE OUTCOME OF WHAT STAFF IS DOING WITH THIS. THEY WOULD HAVE APPEALED, I WOULD SUSPECT, OR WOULD HAVE CONSIDERED APPEALING IF THEY HAD GOT A DO NOT FUND RECOMMENDATION. BUT IF WHAT THEY HEAR FROM STAFF IS THAT STAFF HAS LOOKED AT THIS, IN FACT, AS

I SAID, STAFF MAY HAVE EVEN CONTACTED THEM FOR SOME ADDITIONAL INFORMATION, AND THE RECOMMENDATION IS TO FUND, WHY WOULD YOU GET IN THE WAY OF THAT?

DR. JUELSGAARD: JUST SO I UNDERSTAND, THEN, THE PROCESS. SO THEN THERE IS INTERNAL DELIBERATION BY STAFF AND A DETERMINATION OF DO NOT FUND OR WE RECOMMEND FOR FUNDING, AND THEN THEY'RE TOLD THAT OUTCOME, AND THEN THEY CAN DECIDE WHETHER TO APPEAL. I MISSED THAT MIDDLE PART OF THE PROCESS. I DIDN'T REALIZE THAT'S WHAT WENT ON.

DR. FEIGAL: WHAT WOULD YOU LIKE US TO DO NEXT?

MR. SHEEHY: I ACTUALLY WAS PREPARED TO START REVIEW UNLESS DR. SAMBRANO HAD ANYTHING ELSE, AND WE'LL GO -- LIKE I SAID, WHEN WE COME TO TIER II, WE'LL GO THROUGH EACH INDIVIDUAL PROJECT AS WE DO THAT. DOES THAT MAKE SENSE?

SO THE VERY FIRST MOTIONS I WILL TAKE IS I WILL TAKE ANY MOTION TO MOVE ANY APPLICATION IN TIER I OUT OF TIER I. OTHERWISE IT'S IN A TO FUND CATEGORY. IF NO ONE HAS A MOTION TO THAT EFFECT, THEN THE VERY FIRST IN TIER II, WE'LL JUST GO THROUGH THE STAFF FUND RECOMMENDATIONS. I DON'T THINK IT'S NECESSARY TO GO THROUGH THE STAFF DO NOT FUND RECOMMENDATION.

SINCE THE VERY FIRST ONE WHICH WAS JUST BROUGHT UP, THAT IS ONE WITH WHICH I HAVE A CONFLICT, I WILL PASS THE CHAIR TO DR. STEWARD FOR HIM TO CONDUCT THAT. I THINK THE PROCESS IS PROBABLY TO ASK FOR A MOTION ON THAT AT THAT POINT, DR. STEWARD, FROM SOMEBODY. THANK YOU.

DR. STEWARD: SO DO WE HAVE ANY MOTIONS RELEVANT TO THIS PROJECT? YOU JUST HEARD IT DESCRIBED.

CHAIRMAN THOMAS: MOVE WE FUND, PUT IN TIER I.

DR. STEWARD: OKAY. IS THERE A SECOND?

DR. DULIEGE: SECOND.

DR. STEWARD: SO IT IS OPEN FOR DISCUSSION THEN. SO WE HAVE HEARD THE BASIS OF IT.

MR. HARRISON: CAN I JUST ASK FOR A CLARIFICATION? IS THAT TO FUND WITH THE CONDITION RECOMMENDED BY STAFF WITH A BUDGET OF 4.4?

DR. STEWARD: RIGHT.

DR. KRONTIRIS: QUESTION. I WAS A LITTLE CONFUSED THAT WOULD THIS -- IS THERE ANY EXPECTATION THAT THIS GRANT WILL FINISH A CLINICAL TRIAL BY THE END OF THE FULL PERIOD? AND IF NOT, WHY WOULDN'T YOU MOVE THIS TO AN EARLY TRANSLATION -- BACK INTO AN EARLY TRANSLATION CATEGORY?

DR. STEFFEN: THAT IS EFFECTIVELY WHAT WE HAVE DONE BY ASKING FOR TWO YEARS OF FUNDING AT A REDUCED RATE THAT'S CONSISTENT WITH EARLY TRANSLATION WITH THE PRECLINICAL TYPE ACTIVITIES. WITHOUT THAT DATA PACKAGE IN HAND, WE THINK IT IS VERY DIFFICULT FOR A GRANTS WORKING GROUP, AND THEY AGREED, TO ASSESS THE FEASIBILITY, DESIGN, AND SO FORTH OF A CLINICAL TRIAL.

DR. KRONTIRIS: SO I GUESS THE QUESTION, THEN, EVOLVES TO WHY ARE YOU TAKING MONEY FROM THIS POT WHICH IS SUPPOSED TO GET TO A CLINICAL TRIAL TO FUND SOMETHING WHICH ISN'T READY FOR A CLINICAL TRIAL?

DR. FEIGAL: BECAUSE WE'RE TRYING NOT TO BE BUREAUCRATIC. WE ACTUALLY DO HAVE A PATHWAY CALLED THE ET ALLOWANCE PATHWAY THAT DID ALLOW PROJECTS THAT WERE MEETING THEIR MILESTONES TO GET TO THE POINT WHERE THEY COULD DO AN IND FILING. WE'RE TAKING A PROJECT THAT DID COME INTO THE CLINICAL TRIAL PATHWAY; BUT WHERE WE FEEL THAT IT'S A VERY UNIQUE OPPORTUNITY, IT WOULD ADD VALUE TO CALIFORNIA, THEY HAVE A VERY CLEAR PLAN THAT'S IMPORTANT, AND THEY HAVE A COLLABORATION WITH THE INNOVATORS FOR THIS IN THE UK TO LET THEM COME IN AND WE'LL CONVERT IT INTO THIS ET-TYPE ALLOWANCE

PATHWAY WHERE THE END GOAL IS FILING OF AN IND.

SO THAT'S THE WAY WE THOUGHT OF IT. WE HAVE THE FLEXIBILITY AND THE DISCRETION TO DO THAT, WHETHER OR NOT YOU THINK THAT'S A WISE CHOICE OR A COMPELLING ARGUMENT, BUT THAT WAS OUR MIND-SET IN THINKING THROUGH IT.

ALSO, I DO WANT TO ADD IF YOU DO WANT TO HEAR MORE ABOUT THE GRANT WORKING GROUP ISSUES, WE DO HAVE DR. WHITTLESEA, WHO CAN GO OVER THAT FOR YOU. DR. STEFFEN WAS GIVING YOU THE PROGRAMMATIC RECOMMENDATION.

DR. STEWARD: I'D LIKE TO ACTUALLY SUGGEST THAT WE HEAR THAT BRIEF SUMMARY OF STRENGTHS AND WEAKNESSES OF THE PROJECT.

DR. WHITTLESEA: SURE. MEMBERS OF THE BOARD, I'D BE HAPPY TO GIVE YOU A SUMMARY OF APPLICATION 7221. SO AS DR. STEFFEN MENTIONED IN HER BRIEF INTRODUCTION ON THE STAFF RECOMMENDATIONS, SO IN THIS CASE THE APPLICANT HAS PROPOSED TO USE AN ENGINEERED REPLACEMENT TRACHEA TO TREAT LARGE AIRWAY STENOSIS. SO THIS IS A CONDITION THAT CAUSES SEVERE AIRWAY OBSTRUCTION. AND THE INTENDED APPROACH IS ACTUALLY USING A BIOLOGICAL SCAFFOLD WHICH IS THEN POPULATED BY THE PATIENT'S OWN CELLS, SO IT'S AN AUTOLOGOUS THERAPY, TO ESSENTIALLY ENGINEER A

REPLACEMENT TRACHEA WHICH IS THEN SURGICALLY IMPLANTED.

AS WAS MENTIONED BY DR. STEFFEN, SO THE THERAPEUTIC APPROACH WAS ALREADY USED IN FIRST-IN-HUMAN STUDIES FOR INDIVIDUAL CASES. AND THE PROPOSAL BUILDS ON THAT CLINICAL EXPERIENCE TO CONDUCT THE PRECLINICAL DEVELOPMENT ACTIVITIES AND, AS PROPOSED, A CLINICAL TRIAL REQUIRED TO MAKE THIS PROCEDURE ACCESSIBLE TO MORE PATIENTS.

IN TERMS OF ISSUES RAISED BY THE GRANTS WORKING GROUP WITHIN THE AREA OF SIGNIFICANCE AND IMPACT, GRANTS WORKING GROUP NOTED THAT THE PROPOSED APPROACH ADDRESSES A CLEAR UNMET MEDICAL NEED IN THAT THERE ARE NO GOOD THERAPEUTIC OPTIONS AVAILABLE FOR REPLACEMENT OF LARGE AIRWAY SECTIONS.

AND WHILE THE NUMBER OF CASES OF THIS PARTICULAR CONDITION IS SMALL, THIS APPROACH COULD OFFER UNIQUE AND LIFESAVING THERAPY FOR THOSE PATIENTS AFFECTED. AND REVIEWERS DID AGREE THAT THIS WAS HIGHLY RESPONSIVE TO THE RFA IN THAT IT REPRESENTS A UNIQUE OPPORTUNITY TO BRING A WORLD LEADING REGENERATIVE MEDICINE TECHNOLOGY TO CALIFORNIA. AND THEY DID NOTE THAT THIS PROJECT WAS VERY UNLIKELY TO RECEIVE FUNDING BY OTHER AGENCIES.

WITHIN THE AREA OF SCIENTIFIC RATIONALE

AND RISK BENEFIT, A KEY POINT WAS THAT ENGINEERED TRACHEAS, SIMILAR TO THE PROPOSED DEVELOPMENT CANDIDATE, HAVE ALREADY BEEN USED IN HUMANS AS WELL AS IN ANIMAL MODELS. SO THERE IS SOME PRELIMINARY SAFETY DATA FOR SIMILAR TYPE OF APPROACHES.

WITHIN THE AREA OF THERAPEUTIC DEVELOPMENT READINESS, REVIEWERS AGAIN NOTED THAT HAVING TREATED PATIENTS ALREADY IS VERY STRONG PROOF OF CONCEPT. HOWEVER, THEY DID NOTE THAT A SIGNIFICANT AMOUNT OF IND-ENABLING PRECLINICAL WORK REMAINS TO BE CONDUCTED.

AND MOREOVER, COMPARABILITY, SINCE DR. STEFFEN MENTIONED THIS, HAD BEEN USED ON A COMPASSIONATE USE BASIS WITH MORE THAN A DOZEN PATIENTS, AN OUTSTANDING QUESTION IS COMPARABILITY OF THE CONSTRUCT BEING DEVELOPED UNDER THIS PROPOSAL VERSUS THOSE WHICH HAD BEEN USED IN PREVIOUS HUMAN STUDIES. AND THE MANUFACTURING TEST METHODS WERE NOT WELL DESCRIBED IN THE PROPOSAL. THE UK COLLABORATORS WOULD CLEARLY PLAY AN IMPORTANT ROLE IN TERMS OF TECHNOLOGY TRANSFER AND HELPING THESE INVESTIGATORS DEVELOP THAT PROCESS IN CALIFORNIA.

WITHIN THE AREA OF DESIGN AND FEASIBILITY, GRANTS WORKING GROUP FELT THAT THE STUDIES WERE WELL DESIGNED WITH APPROPRIATE MILESTONES AND GO/NO-GO

DECISION POINTS. HOWEVER, THERE WAS CONCERN ABOUT THE FEASIBILITY OF THE TIMELINE TO COMPLETE BOTH THE REMAINING PRECLINICAL WORK AND THE PROPOSED CLINICAL STUDY.

IN THE AREA OF THE TEAM, THE PI AND TEAM WERE VIEWED AS WORLD LEADING IN THIS FUNCTIONAL TISSUE ENGINEERING APPROACH.

IN THE AREA OF BUDGET, REVIEWERS WERE CONCERNED THAT THE BUDGET PROPOSED MAY BE INADEQUATE TO COMPLETE ALL OF THE REMAINING PRECLINICAL STUDIES AND THAT SOME ADDITIONAL ACTIVITIES THAT MIGHT BE NECESSARY WERE NOT BUDGETED FOR.

AND LASTLY, REVIEWERS WERE SOMEWHAT UNCLEAR ON THE RELATIONSHIP BETWEEN THE CALIFORNIA AND THE UK-BASED TEAMS IN TERMS OF WHAT THAT COLLABORATION IS GOING TO LOOK LIKE. AND AS WAS MENTIONED, THAT WAS SOMETHING THAT WE INTERACTED WITH THE TEAM DURING THE STAFF RECOMMENDATION PROCESS AND CLARIFIED WHAT THAT RELATIONSHIP IS GOING TO LOOK LIKE.

SO BASED ON THOSE RECOMMENDATIONS, THE GRANTS WORKING GROUP ARRIVED AT A SCORE OF 70, WHICH PLACE IT IN TIER II. YOU HEARD A NUMBER OF POINTS WITHIN THE GRANTS WORKING GROUP RECOMMENDATION WHICH WERE INCORPORATED INTO THE STAFF RECOMMENDATION TO

ADDRESS SOME OF THOSE CONCERNS. HAPPY TO TAKE ANY QUESTIONS.

DR. STEWARD: THANK YOU. ACTUALLY JUST ONE ADDITIONAL POINT. I'M PROBABLY GOING TO ASK THIS OF THE OTHERS THAT COME UP, SO I'LL JUST WARN EVERYBODY NOW. I'M SAYING THIS BECAUSE AT THE SCIENTIFIC WORKING GROUP LEVEL, A LOT OF THEM THINK THAT WE ACTUALLY TALK ABOUT PORTFOLIO ISSUES HERE. THAT'S WHAT THEY THINK PROGRAMMATIC REVIEW ACTUALLY IS. SO COULD YOU SAY A WORD ABOUT THE DEGREE TO WHICH THIS IS REPRESENTED IN OUR PORTFOLIO NOW? I ACTUALLY KIND OF KNOW THE ANSWER, BUT JUST FOR THE RECORD.

DR. WHITTLESEA: SURE. SO DR. STEFFEN MENTIONED THAT, THAT IT'S A HOLE IN OUR PORTFOLIO. THERE'S NOTHING LIKE THIS IN TERMS OF A TISSUE-ENGINEERED CONDUIT. AS DR. STEFFEN MENTIONED, IN THE TISSUE ENGINEERING FIELD THIS IS VIEWED AS A REALLY GOOD STEPPING STONE OF FAIRLY SIMPLE STRUCTURES WITH PRIMARILY A FUNCTIONAL -- A MECHANICAL ROLE, IF YOU WILL, THAT THIS WOULD BE A REALLY GOOD FIRST STEP TO START BUILDING CAPACITY.

DR. STEWARD: THANK YOU. OTHER QUESTIONS, COMMENTS? MOTION ON THE FLOOR IS TO APPROVE FOR TWO YEARS AT A REDUCED BUDGET. NOTHING FURTHER FROM THE

BOARD. NO FURTHER DISCUSSION BY THE BOARD? PUBLIC COMMENT? COULD YOU PLEASE STATE YOUR NAME?

MR. BELAFSKY: MY NAME IS PETER BELAFSKY. I'M AN AIRWAY SURGEON AT UC DAVIS AND PI ON THE PROJECT.

THE AIRWAY STENOSIS IS A PROFOUND DISABILITY, AND I'VE DEDICATED MY PROFESSIONAL LIFE TO TAKING CARE OF THESE PATIENTS WITH COMPLEX BREATHING AND SWALLOWING PROBLEMS.

CURRENTLY WE DON'T HAVE GOOD TREATMENTS FOR THESE TYPES OF PROBLEMS. AND THIS IS A HIGHLY INNOVATIVE APPROACH IN AN AREA WHERE WE'RE EXTREMELY FRUSTRATED. AND PATIENTS WITH THIS TYPE OF BREATHING PROBLEM ARE PROFOUNDLY DISABLED. IT'S LIKE THEY'RE LIVING A LIFE LIKE A FISH OUT OF WATER, IF YOU WILL.

AND ALTHOUGH IN THE CLINICAL TRIAL THE PREVALENCE OF PROFOUND AIRWAY STENOSIS IS SMALL, THE INCIDENCE OF AIRWAY STENOSIS AFTER ENDOTRACHEAL TUBE INTUBATION IN A CRITICALLY ILL PATIENT IS AS HIGH AS 11 PERCENT. SO WE FEEL THE TRANSLATIONAL POTENTIAL FOR THIS TECHNOLOGY TO THE GENERAL GOOD OF ALL CALIFORNIANS IS EXTREMELY HIGH OR UNIQUELY POSITIONED TO TAKE THIS WORK FORWARD. AND OUR PATIENTS ARE GOING TO BE RELYING ON THIS, WHICH IS

WHY WE'VE BEEN SO DEDICATED TO THIS PROJECT.

SO THANK YOU SO MUCH FOR YOUR ATTENTION.

DR. STEWARD: THANK YOU VERY MUCH. JAMES, THAT GETS ROLL CALL ON THIS ONE?

MR. HARRISON: YES.

MS. BONNEVILLE: ANNE-MARIE DULIEGE.

DR. DULIEGE: YES.

MS. BONNEVILLE: MICHAEL GOLDBERG.

MR. GOLDBERG: YES.

MS. BONNEVILLE: STEPHEN JUELSGAARD.

DR. JUELSGAARD: YES.

MS. BONNEVILLE: ROBERT QUINT.

DR. QUINT: YES.

MS. BONNEVILLE: OSWALD STEWARD.

DR. STEWARD: YES.

MS. BONNEVILLE: JONATHAN THOMAS.

CHAIRMAN THOMAS: YES.

MS. BONNEVILLE: ART TORRES.

MR. TORRES: AYE.

MS. BONNEVILLE: DIANE WINOKUR.

MS. WINOKUR: YES.

MR. HARRISON: MOTION CARRIES.

MR. SHEEHY: OKAY. NOW, I THINK WE'LL PROCEED TO THE SECOND STAFF RECOMMENDATION. SO COULD WE GET A PRESENTATION ON PROJECT 7061, AND

THEN I'LL TAKE A MOTION TO EITHER ACCEPT OR NOT ACCEPT THE STAFF RECOMMENDATION.

DR. STEFFEN: THAT IS GOING TO BE DR. CATHERINE PRIEST.

MR. SHEEHY: THANK YOU, DR. STEFFEN.

DR. PRIEST: I'M SORRY. DID YOU ASK FOR THE SUMMARY OR THE STAFF RECOMMENDATION?

MR. SHEEHY: STAFF RECOMMENDATION.

DR. PRIEST: THIS IS APPLICATION 7061. DO YOU WANT THE WORDS ON THE COMPUTER ON THE SCREEN? APPLICATION 7061 ENTITLED "SUBRETINAL DELIVERY OF HUMAN NEUROPROGENITOR CELLS FOR THE TREATMENT OF RETINITIS PIGMENTOSA."

THE DISEASE IS RETINITIS PIGMENTOSA, AN EARLY BLINDING DISEASE IN YOUNG ADULTS. AND THE APPROACH THE APPLICANT IS USING AS AN ALLOGENEIC HUMAN NEURAL PROGENITOR CELL.

THE POINTS FOR CONSIDERATION, THE PROGRAMMATIC POINTS FOR CONSIDERATION ON THIS APPLICATION IS THAT CIRM IS FUNDING TWO OTHER DISEASE TEAMS AND ONE EARLY TRANSLATIONAL PROJECT AIMED AT RETINAL RESCUE OR RESTORATION. IN THOSE THREE PROJECTS, DIFFERENT CELL SOURCES AND TARGET REPLACEMENT CELLS ARE EMPLOYED BY THE PROJECTS. THE DETAILS OF THOSE PROJECTS ARE A DISEASE TEAM

NUMBERED 5739, DEVELOPING A CELLULAR THERAPY FOR THE SAME INDICATION, RETINITIS PIGMENTOSA.

THERE'S ANOTHER DISEASE TEAM USING A FUNCTIONALLY POLARIZED, SO THAT MEANS THE CELL HAS A TOP AND BOTTOM THAT IT RECOGNIZES ON SYNTHETIC SUBSTRATE JUST THE WAY IT WOULD BE ORGANIZED IN YOUR EYE, EMBRYONIC STEM CELL-DERIVED CELLS IN AGE-RELATED MACULAR DEGENERATION. THE FOLLOW-ON PROJECT TO THAT DISEASE TEAM IS BEING CONSIDERED TODAY AS A TIER I RECOMMENDED FOR FUNDING APPLICATION. THAT'S 7438.

AND THE THIRD APPLICATION IN OUR CURRENT TRANSLATIONAL PORTFOLIO IS A RECENTLY AWARDED EARLY TRANSLATIONAL AWARD TO DEVELOP HUMAN EMBRYONIC STEM CELL-DERIVED SHEETS OF RETINAL PROGENITOR CELLS AND RETINAL PIGMENTED EPITHELIAL CELLS, SO TWO DIFFERENT CELL TYPES, IN A SHEET. AND THAT'S RECENTLY BEEN AWARDED.

SO THAT'S THE SUMMARY OF THE STAFF RECOMMENDATION. I HAVE A SCIENCE OFFICER IF YOU WANT TO HEAR THE GRANTS WORKING GROUP.

MR. SHEEHY: IF WE NEED FURTHER DISCUSSION. SO DO I HAVE A RECOMMENDATION? DO I HAVE A MOTION TO ACCEPT THE STAFF RECOMMENDATION WHICH IS, TO BE CLEAR, NOT FUND THIS APPLICATION.

DR. JUELSGAARD: SO MOVED.

MR. SHEEHY: SECOND?

DR. PRIETO: SECOND.

MR. SHEEHY: DO WE HAVE FURTHER DISCUSSION? DO WE NEED TO HEAR ANYTHING ELSE FROM STAFF? IT'S TOTALLY TO YOUR DISCRETION IF PEOPLE WANT TO HEAR MORE.

DR. DULIEGE: QUESTION. I UNDERSTAND SOME OF THE RESERVATIONS OF YOUR RESERVATION OR THE TEAM ABSOLUTELY. AND ALSO REALIZE THAT THERE WERE SOME LIMITATIONS IN THIS PROJECT ITSELF. I'M CONFLICTED? THANK YOU FOR YOUR CAREFULNESS IN REMINDING US.

MR. SHEEHY: IS THERE ANY OTHER DISCUSSION? DO WE HAVE PUBLIC COMMENT ON THIS GRANT?

PLEASE IDENTIFY YOURSELF AND SPEAK INTO THE MIC FOR THE TRANSCRIPTIONIST. AND WE HAVE THREE MINUTES PER COMMENT.

DR. SMALL: THANK YOU FOR TAKING THIS TIME AND ENERGY AND EFFORT IN REVIEWING THIS GRANT. I'M KENT SMALL. I'M THE PRINCIPAL INVESTIGATOR ON THIS DISEASE TEAM. I'M A PRACTICING OPHTHALMOLOGIST AND RETINAL SURGEON, AND I SEE RETINITIS PIGMENTATION PATIENTS ON A DAILY BASIS. THIS HAS DRIVEN ME TO FIND NEW THERAPEUTIC APPROACHES TO TREAT DEVASTATING

DISEASES THAT AFFECT THE VISION.

OF THESE, RETINITIS PIGMENTOSA IS ONE OF THE WORST. STARTING WITH THE LOSS OF NIGHT VISION, IT PROGRESSES TO COMPLETE LOSS OF VISION OVER THE YEARS WITH FEW THERAPEUTIC OPTIONS.

IN ADDITION TO RUNNING AN ACTIVE CLINIC, I ALSO HAVE A STRONG BACKGROUND IN CLINICAL AND BASIC RESEARCH AND HAVE BEEN INVOLVED IN OVER 50 ACADEMIC AND INDUSTRY CLINICAL TRIALS OVER THE LAST 28 YEARS.

OUR DISEASE TEAM APPLICATION HAS EXTENSIVE PRECLINICAL DATA DEMONSTRATING THAT THE HUMAN NEUROPROGENITOR CELLS, CNS 10 AS WE CALL THEM, PRODUCED BY DR. STIMSON, SHOWS REMARKABLE SURVIVAL AND MIGRATION FOLLOWING TRANSPLANTATION INTO THE EYE. IT WAS SHOWN TO STABILIZE AND PRESERVE RETINAL FUNCTION IN RODENT MODELS OF RETINITIS PIGMENTOSA, A REMARKABLE FINDING THAT WAS PUBLISHED IN A LEADING JOURNAL.

IN ADDITION, THE SAME HUMAN CELLS WERE SHOWN TO SURVIVE AND BE SAFE FOLLOWING SUBRETINAL INJECTION INTO THE PRIMATE EYE. AGAIN, THIS WAS PUBLISHED IN A LEADING JOURNAL AND REPRESENTS ONE OF THE FEW, VERY FEW, STUDIES WHERE HUMAN STEM CELLS HAVE BEEN SHOWN TO SURVIVE IN THE PRIMATE EYE.

OVER MANY YEARS DR. WHANG AND HER

COLLEAGUES HAVE ALSO COMPARED THE THREE STEM CELL TYPES CURRENTLY BEING PROPOSED FOR CLINICAL TRIALS IN THE EYE AND HAVE SHOWN THAT THE CNS 10 CELLS OFFERED THE BEST PRESERVATION OF VISION.

OUR APPLICATION ALSO INCLUDED AN FDA INTERACTION. THE FDA AGREED ON OUR EXPERIMENTAL PLAN AND TO MOVE TOWARDS THE CLINIC WITH NO MORE EFFICACY DATA REQUIRED AND NO MAJOR REVISIONS. IN OTHER WORDS, THE TRANSLATIONAL STUDIES SUPPORTING THE IND CAN BEGIN IMMEDIATELY.

THIS IS IN CONTRAST TO THE EXISTING CIRM-SUPPORTED STUDY ON FETAL RETINAL PROGENITOR CELLS WHERE EFFICACY DATA HAS NOT YET BEEN PRESENTED.

THE REVIEWERS WERE GENERALLY FAVORABLE; BUT, AS YOU HAVE HEARD, HAVE A FEW CONCERNS. FIRST, THEY CLAIM THE RATIONALE FOR USING THESE CELLS WAS NOT STRONG. BUT WE COUNTERED THAT THESE CELLS SHOW A SIGNIFICANT EFFECT IN PUBLISHED REPORTS USING AN ESTABLISHED RODENT MODEL OF RETINITIS PIGMENTOSA.

THEY SUGGEST THE INCLUSION CRITERIA ARE NOT APPROPRIATE, BUT WE ARE WILLING TO DISCUSS THIS AND MODIFY BASED ON FURTHER INTERACTIONS WITH THE FDA.

THEY ARE CONCERNED WITH AN INTERRUPTION IN

MANUFACTURING THE CELLS. BUT AT THE CITY OF HOPE GMP FACILITY, WE HAVE JUST FROZEN DOWN 1,300 VIALS OF SIMILAR CELLS FOR CIRM-FUNDED ALS TRIALS USING IDENTICAL METHODS.

THEY WERE WORRIED ABOUT THE CHARACTERIZATION OF THE CELLS, BUT DR. SVENDSEN HAS BEEN WORKING WITH THESE CELLS IN THE RETINA FOR OVER TEN YEARS, AND WE KNOW MORE ABOUT THESE THAN ANY OTHER CELL THAT IS BEING CONSIDERED FOR STEM CELL THERAPY IN THE EYE OR ANY ORGAN SYSTEM.

THEY WERE WORRIED ABOUT THE FOUR-YEAR TIMELINE, BUT THE CELLS ARE READY FOR THE CLINIC, AND NOW WE HAVE AN 18-MONTH TIMELINE FOR FILING AN IND, WHICH IS VERY RAPID.

THEY WORRIED ABOUT OUR EXPERIENCE IN REGULATORY AFFAIRS, BUT WE HAVE AN OUTSTANDING EXPERT IN REGULATORY AFFAIRS, DR. NEIL HACKETT, WITH US, WHO HAS WORKED IN TRANSLATIONAL STUDIES FOR GENE THERAPY IN THE EYE AND MORE RECENTLY STEM CELL THERAPIES OVER 15 YEARS.

THIS IS A HIGH QUALITY PROPOSAL, HAS A GREAT SCORE WITHIN THE FUNDABLE RANGE, AND A GREAT TEAM. FURTHERMORE, CEDARS-SINAI IS A LEADING MEDICAL CENTER THAT HAS GAINED MUCH EXPERIENCE IN STEM CELL THERAPIES FOR THE HEART AND ALS. THE EYE

IS IDEALLY SUITED FOR CELL-BASED THERAPY. AS IT HAS IMMUNE PRIVILEGE, IT CAN BE EASILY INJECTED IN THE EYES, DIRECTLY OBSERVE THEM, AND RELIABLY MEASURES ANY EFFECTS THEY HAVE.

ONLY PROBLEM SEEMS TO BE THAT THERE ARE OTHER GRANTS FUNDING THE EYE, FOCUSING ON THE EYE. WELL, OF COURSE. THIS IS BECAUSE THE EYE IS THE MOST LIKELY AREA OF IMMEDIATE SUCCESS IN THE STEM CELL TRANSPLANT FIELD. I STAND READY TO GET TO WORK AND MOVE THESE PROMISING CELLS INTO THE CLINIC FOR BLINDNESS.

DR. SVENDSEN: CLIVE SVENDSEN, CEDARS-SINAI. WELL, HERE I AM AGAIN. I'M GOING TO BE SUPPORTING THIS PROPOSAL. FIRST, I'D LIKE TO POINT OUT IT IS AN OUTSTANDING APPLICATION FROM A VERY EXPERIENCED INVESTIGATOR. YOU JUST HEARD FROM DR. SMALL. IT'S NOT A NEW PROJECT FOR ME. I'VE BEEN COORDINATING EYE PROJECTS, ALTHOUGH I'M BETTER KNOWN FOR ALS, FOR THE LAST TEN YEARS IN THE RETINA, WORKING WITH DR. GAM AND DR. LUND AND DR. WHANG, WHO'S IN THIS PROJECT.

WE'VE HAD FOUR PAPERS PUBLISHED IN THIS AREA. AND THESE CELLS, CNS 10, CAN MIGRATE. THAT'S FROM THE CORTEX. THEY ACTUALLY MIGRATE WITHIN THE EYE AND PULL THE WHOLE OF THE BACK OF THE EYE UP AND

PROVIDE FANTASTIC RESULTS IN THESE PRECLINICAL ANIMAL STUDIES, BOTH IN MACULAR DEGENERATION AND RETINITIS PIGMENTOSA.

LOOK AT THE LIST OF GRANTS UP ON THE SCREEN JUST NOW. WE SCORED WELL BY THE REVIEWERS. IN FACT, WE'RE THE SAME LEVEL OR HIGHER THAN TWO OTHERS THAT WERE RECOMMENDED FOR FUNDING BY STAFF, AS YOU JUST HEARD. THE ONLY REASON WE'RE NOT BEING RECOMMENDED IS THERE WERE TOO MANY EYE GRANTS APPARENTLY.

RATHER THAN DESCRIBING OUR TRIAL FEATURES, THEY SIMPLY LISTED OTHER GRANTS FOCUSED ON THE EYE. I'D LIKE TO ADDRESS THIS DIRECTLY. FIRST, THREE OF THE FUNDED DISEASE TEAM AWARDS TO DATE FOCUS ON CANCER. SIX PREVIOUS CIRM GRANTS HAVE BEEN AWARDED JUST FOR BRAIN CANCER, 11 FOR LEUKEMIA, 31 FOR CANCER OVERALL. LIST GOES ON. TEN FOR AUTISM, 20 FOR PARKINSON'S DISEASE, AND 45 FOR HEART. HOW MANY HAVE BEEN FUNDED FOR THE EYE? NINE. NINE GRANTS FOR AN ORGAN THAT'S CLEARLY SUITED TO STEM CELL THERAPY. WHY SHOULD WELL-SCORED GRANTS USING STEM CELLS TO TREAT THE EYE AND BLINDNESS SUDDENLY BE TREATED DIFFERENTLY BY CIRM TO ALL THE OTHER DISEASES? IT MAKES NO SENSE TO ME, AND I DON'T THINK IT'S FAIR.

IT'S EXACTLY BECAUSE THE EYE IS IDEALLY SUITED TO TESTING THESE THERAPIES, THAT THERE ARE SO MANY APPLICATIONS USING STEM CELLS IN THIS AREA. INDEED, THE FIRST WORLD'S AUTOLOGOUS IPS TRANSPLANT IS GOING TO BE IN THE EYE, AS YOU HEARD FROM DR. TROUNSON EARLIER.

IN ADDITION, THE ONLY HUMAN EMBRYONIC STEM CELL TRIALS CURRENTLY GOING ON IN THE U.S.A. ARE IN THE EYE, AND MANY MORE ARE PLANNED AROUND THE WORLD. WHY? THE EYE IS UNIQUE. IT'S IMMUNE PRIVILEGED. YOU CAN SEE EASILY THE EFFECTS WITH THIS FANTASTIC MODERN EQUIPMENT. SURGICAL APPROACH TO PUT CELLS IN THE EYE ARE WELL DEVELOPED AND SAFE. OUR TEAM IN THIS PROPOSAL, WE HAVE EXTREMELY STRONG PRECLINICAL DATA, SUGGESTING THAT THESE MIGRATE -- THESE CELLS CAN MIGRATE AND RESTORE FUNCTION IN MODELS. EYE DISEASES ARE DEVASTATING CONDITIONS FOR ANY PERSON TO LIVE WITH, AS YOU WILL HEAR IN A MOMENT. IT ROBS YOU OF SEEING THOSE YOU LOVE, ROBS YOU OF MOTILITY.

IN MY HUMBLE OPINION, LAST COMMENT, IF CIRM WANTS A HOME RUN AS A RESULT OF SPENDING $3 BILLION ON STEM CELLS, A FOCUS ON THE EYE MAY BE THE BEST CHANCE OF SUCCESS. AS MENTIONED PREVIOUSLY BY MANY OF MY FRIENDS AT CIRM, WE SHOULD BE MAKING MULTIPLE STRIKES AT THE GOAL WHEREVER POSSIBLE, NOT

JUST FOCUSING ON A SINGLE APPROACH. BUT THE CANCER PROPOSAL IS STRONG, HAS A GREAT CHANCE OF SCORING AN IMPORTANT GOAL FOR THE STATE. MAKING A BLIND PERSON SEE AGAIN OR REDUCING VISION LOSS FOR SOMEONE WHO'S TOLD THEY'LL GO BLIND COULD BE THE GREATEST LEGACY LEFT BY CIRM. NOW IS THE TIME TO INVEST IN THE PROPOSAL. THE SCIENCE IS GOOD AND SUPPORTED BY THE REVIEW PROCESS. WE HAVE THE CELLS. WE HAVE THE FDA ON BOARD. WE HAVE THE SURGEONS AND PATIENTS READY AND NOW WE NEED THE FUNDING.

MS. APPLEGREN: HELLO. GOOD MORNING. I THINK IT'S MORNING. MY NAME IS CARMEN APPLEGREN. I HAVE HAD RETINITIS PIGMENTOSA SINCE I WAS SEVEN YEARS OLD. IT'S A VERY DEBILITATING DISEASE. IT STARTS OFF AS PARTIAL SIGHT, AND THEN IT GETS WORSE AND WORSE AND WORSE. AND AS YOU GET OLDER, I AM 65 NOW, IT CHANGES DAILY. MY SIGHT IS WORSE TODAY THAN IT WAS YESTERDAY. I WORKED FOR 21 YEARS AT BRAILLE INSTITUTE AND WAS PART OF THE RP COMMUNITY FOR ALL OF THAT TIME. I KNOW MANY, MANY PEOPLE WITH THIS DISEASE.

THERE ARE 15,000 PEOPLE IN CALIFORNIA WITH RETINITIS PIGMENTOSA. LOSING YOUR SIGHT IS JUST -- IT'S A TERRIBLE THING. IT TAKES AWAY, IT IMPAIRS YOUR HUMAN ABILITIES, IT MAKES LIFE VERY DIFFICULT,

SOMETIMES MISERABLE, AND AT THIS POINT VERY SCARY. VERY SCARY.

WHAT KENT SMALL IS DOING WITH HIS TEAM IS PROGRESS. WE NEED THIS CURE NOW. THERE ARE SO MANY OF US OUT THERE, THAT WE NEED THIS CURE NOW. PLEASE FUND THIS STUDY. FROM BOTTOM OF MY HEART, I REPRESENT ALL THE PEOPLE WITH RETINITIS PIGMENTOSA. PLEASE HELP US NOW SO WE CAN LIVE A GOOD LIFE ONCE AGAIN.

MR. SHEEHY: ANY ADDITIONAL PUBLIC COMMENT? SO DO WE HAVE ANY ADDITIONAL BOARD COMMENT?

MS. WINOKUR: IT SEEMS THAT THERE IS SYNERGY WITH THE PROCESSES INVOLVED IN THIS PROPOSAL WITH ALS. IT'S NEURAL STEM CELLS THAT ARE GOING TO BE USED. AND THERE IS A CIRM-FUNDED ALS PROJECT AT CEDARS-SINAI DR. SVENDSEN HEADS. SO COULD YOU ANSWER MY QUESTION ABOUT THE SYNERGY BETWEEN THE TWO?

DR. SVENDSEN: CLEARLY THERE'S A LOT OF SYNERGY. THE CELLS THAT WE'RE USING ARE FAIRLY -- PRETTY MUCH THE SAME CELL. WE JUST DON'T ENGINEER THEM TO MAKE GDNF AS WE DID WITH THE LINE. BUT THE GMP MANUFACTURING PROCESS IS IDENTICAL. IT'S ALREADY BEING CARRIED OUT AT CITY OF HOPE. SO I

THINK THERE'S A LOT -- THERE WOULD BE A LOT OF INTERACTIONS BETWEEN DR. SMALL AND BETWEEN MY GROUP. AND I THINK WE'VE BEEN THROUGH A LOT OF REGULATORY PROCESS HERE WITH CIRM, SO WE'RE VERY FAMILIAR WITH THE TECHNIQUES, AND WE WOULD BE APPLYING THIS TO THIS GRANT.

AGAIN, IT WAS SCORED IN THAT ZONE. IN FACT, WE'RE NO. 6. AND SO TWO GRANTS BELOW US ARE GOING TO GET FUNDED IF WE CARRY ON, IF THE VOTES GO THE WAY THEY DO. WE WERE SCORED BETTER THAN ONE OF THOSE GRANTS THAT WERE RECOMMENDED FOR FUNDING BY THE STAFF.

NOW, I UNDERSTAND THERE ARE FOUR OR FIVE OTHER GRANTS IN THIS AREA, BUT WHY DO WE SUDDENLY START PICKING THE EYE AS AN AREA WE'RE NOT GOING TO FUND MANY GRANTS IN? IT JUST DOESN'T MAKE SENSE TO ME.

MS. WINOKUR: IT SEEMS THAT A MAJOR OBJECTION IS THE CONCATENATION RIGHT NOW OF PROPOSALS HAVING TO DO WITH RETINITIS PIGMENTOSA. I AM INTERESTED IN ALS, AND I THINK THAT ALS DOES NOT HAVE VERY MANY PROJECTS DONE UNDER CIRM. AND IF THIS WOULD HELP MOVE FORWARD THE DEVELOPMENT OF THE SAME NEURAL STEM CELLS THAT COULD BE DIVERTED TO HELPING WITH ALS, I THINK THAT'S ANOTHER THING IN

FAVOR OF THE PROPOSAL.

MR. SHEEHY: MR. THOMAS HAD A COMMENT, AND THEN MAYBE WE COULD HEAR FROM STAFF ABOUT SOME OF THE QUESTIONS THAT MS. WINOKUR OFFERED.

CHAIRMAN THOMAS: SO THE STAFF RECOMMENDATION, INDEED, IS BASED ON MULTIPLE PROJECTS. BUT, AGAIN, THIS WAS PLACED IN TIER II BECAUSE OF A VARIETY OF CONCERNS WITHOUT WHICH IT WOULD HAVE BEEN POTENTIALLY IN TIER I. SO I'D LIKE TO HEAR FROM DR. PRIEST ABOUT WHAT THOSE CONCERNS WERE AND AN ANALYSIS OF THOSE.

DR. PRIEST: THANK YOU, J.T. GOOD MORNING, MEMBERS OF THE PUBLIC AND MEMBERS OF THE BOARD. MY NAME IS CATHERINE PRIEST, AND I'M PREPARED TO GIVE YOU A SUMMARY OF THE GRANTS WORKING GROUP'S ASSESSMENT OF THIS APPLICATION.

THIS APPLICATION DESCRIBES DEVELOPMENT OF AN ALLOGENEIC HUMAN NEURAL PROGENITOR CELL OR HNPC THAT WOULD BE ADMINISTERED TO SLOW OR HALT PROGRESSION OF RETINITIS PIGMENTOSA AS WE'VE HEARD. THE APPLICANTS PRESENT DATA FROM PRECLINICAL STUDIES SHOWING LONG-TERM ENGRAFTMENT OF THE CELLS AND MAINTENANCE OF VISUAL FUNCTION IN PRECLINICAL MODELS OF PROGRESSIVE RETINAL DISEASE.

THE PROPOSAL INCLUDES MANUFACTURING

CLINICAL GRADE HNPC, EXAMINING THE ACTIVITY AND SAFETY OF THE CELLS IN PRECLINICAL MODELS, SUBMITTING THE SUPPORTING DATA TO THE FDA, AND IF APPROVED, CONDUCTING A PHASE I-II A CLINICAL TRIAL TO ASSESS THE SAFETY AND EFFICACY OF THE CELLS IN PATIENTS WITH RETINITIS PIGMENTOSA.

THE KEY STRENGTHS OF THIS APPLICATION WERE IDENTIFIED UNDER THE SIGNIFICANCE AND IMPACT CRITERIA. THE APPLICATION PROPOSES TO DEVELOP A STANDARDIZED CELLULAR THERAPEUTIC PRODUCT FOR USE IN PATIENTS WITH RETINITIS PIGMENTOSA, WHICH IS A COMMON FORM OF PROGRESSIVE BLINDNESS FOR WHICH THERE IS CURRENTLY NO CURE.

AND THE PRINCIPAL INVESTIGATOR WAS RECOGNIZED AS AN ACTIVE, EXPERIENCED CLINICAL RESEARCHER WHO HAS ASSEMBLED A CALIFORNIA-BASED TEAM WHO HAS EXPERTISE WORKING WITH HNPC AND RETINAL DISEASES. HOWEVER, THE GRANTS WORKING GROUP DID FIND WEAKNESSES IN THE APPLICATION THAT LED TO THE REVIEW SCORE AND A RECOMMENDATION TO PLACE THIS APPLICATION IN TIER II.

THE FIRST SET OF POINTS CONCERNED THE SCIENTIFIC RATIONALE AND FEASIBILITY OF DEVELOPING THE HNPC AS A CELLULAR THERAPEUTIC FOR THE TREATMENT OF RETINITIS PIGMENTOSA UNDER THE CURRENT RFA.

REVIEWERS THOUGHT THAT THE SCIENTIFIC RATIONALE IS NOT VERY STRONG TO SUPPORT THE MECHANISM THROUGH WHICH THE APPLICANTS PROPOSE THE HNPC COULD BE AFFECTING CLINICAL PROGRESSION OF RETINITIS PIGMENTOSA. THERE ARE, AS WE'VE HEARD, CELL THERAPIES CURRENTLY UNDER DEVELOPMENT FOR TREATMENT OF RETINITIS PIGMENTOSA.

FROM THE FEASIBILITY CRITERION, REVIEWERS NOTED THAT THE APPLICATION DID NOT PRESENT A VERY COMPREHENSIVE CHARACTERIZATION OF THE HNPC POPULATION THAT WOULD BE DELIVERED, AND THIS WOULD BE NECESSARY FOR DEMONSTRATION THAT THE CELLS REMAIN COMPARABLE OVER THE DEVELOPMENT PROGRAM.

IT DID NOT APPEAR POSSIBLE TO CONDUCT THE PROPOSED STUDY DESIGNS WITHIN THE FOUR-YEAR PROJECT TIMELINE OF THE RFA. AND THE APPLICATION DESCRIBES RETINITIS PIGMENTOSA AS, QUOTE, A SLOWLY PROGRESSING DISEASE, UNQUOTE, WHICH THE REVIEWERS NOTED COULD REQUIRE A PROLONGED PATIENT OBSERVATION PERIOD TO IDENTIFY CLINICAL EFFECTS OF THIS TREATMENT.

THE SECOND SET OF CONCERNS CENTER ON THE RISK BENEFIT CONSIDERATIONS OF SUPPORTING A DEVELOPMENT PROGRAM USING THESE NPC'S AS A TREATMENT FOR RETINITIS PIGMENTOSA. SOME REVIEWERS THOUGHT THAT THE INCLUSION CRITERIA PROPOSED FOR THE PHASE

I-IIA CLINICAL TRIAL WOULD SELECT AN INAPPROPRIATE PATIENT POPULATION FOR A FIRST-IN-HUMAN INDICATION. AND GETTING REGULATORY APPROVAL FOR THE DEVELOPMENT OF THESE CELLS AS A POTENTIAL THERAPEUTIC FOR PATIENTS WITH RETINITIS PIGMENTOSA MAY BE CHALLENGING. AND WITHOUT HAVING CERTAIN REGULATORY AGREEMENTS IN PLACE, REVIEWERS THOUGHT THEY COULD NOT FULLY ASSESS THE POTENTIAL FOR SUCCESSFUL TRANSLATION OF THE PROGRAM.

THIS CONCLUDES THE SUMMARY. I'D BE HAPPY TO TAKE ANY QUESTIONS.

MR. SHEEHY: DR. STEWARD.

DR. STEWARD: COULD YOU REMIND US WHERE WE ARE IN TERMS OF BUDGET? ASSUMING, FOR EXAMPLE, THAT WE FUNDED THE TOP TIER AND WE JUST APPROVED ONE, WHERE DO WE STAND IN TERMS OF THE APPROVED BUDGET FOR THIS VERSUS -- I'M ASKING THIS QUESTION BECAUSE I THINK, AS WE'VE HEARD MANY TIMES AT THIS MEETING, WE NEED TO LOOK VERY CAREFULLY AT ISSUES OF OUR ECONOMY AS WE LOOK TOWARD THE FUTURE.

MR. SHEEHY: TIER I IS 47 MILLION AND THEN WE JUST ADDED FOUR MILLION.

DR. STEWARD: AND THE AMOUNT APPROVED?

MR. SHEEHY: GLOBAL IS 100 MILLION FOR THIS ROUND.

DR. SAMBRANO: I JUST ADDED THE ONE THAT WAS VOTED ON INTO TIER I. SO THE 47,192 INCLUDES APPLICATION 7281.

MR. SHEEHY: SO IT'S 47. I WAS WONDERING. I HAD A NOTE DOWN THAT IT WAS 42.7 AND I WONDERED. I THOUGHT MAYBE I WAS GETTING A LITTLE TOUCHED IN THE HEAD.

ANY OTHER COMMENTS? ANY OTHER QUESTIONS, COMMENTS FROM MEMBERS OF THE BOARD? I THINK WE ARE READY FOR ROLL CALL.

CHAIRMAN THOMAS: CAN I JUST ASK ONE OTHER QUESTION? PUTTING ASIDE THE ISSUE OF MULTIPLE OTHER FUNDED PROJECTS, AS WE'VE DISCUSSED, FROM A SCIENTIFIC ANALYTICAL POINT OF VIEW, WHAT IS YOUR OPINION AS TO WHETHER OR NOT THIS WOULD DESERVE FUNDING?

DR. STEFFEN: SO THAT QUESTION WAS DISCUSSED WITH THE TEAM. AND THERE ARE SOME KEY ACTIVITIES THAT CAN BE DONE IN THE INTERIM TO ASSURE A REGULATORY PATHWAY FOR THE USE OF THESE CELLS IN THE TRIAL AND FOR COMMERCIALIZATION. SO WE WOULD RECOMMEND THAT THE APPLICANT ADDRESS THOSE ISSUES, AND WE WOULD WELCOME THE APPLICATION TO COME BACK. WE WILL STILL FACE THE SAME CONUNDRUM OF OTHER APPLICATIONS IN THE AREA, BUT THERE WAS AT LEAST ONE

KEY ISSUE THAT NEEDS TO BE ADDRESSED WITH THE REGULATORY AUTHORITIES.

CHAIRMAN THOMAS: THANK YOU.

DR. SVENDSEN: CAN I JUST RESPOND TO THAT VERY BRIEFLY BECAUSE WE HAVE BEEN IN COMMUNICATION WITH CIRM. IS THAT OKAY?

MR. SHEEHY: GO AHEAD, PLEASE.

DR. SVENDSEN: THANK YOU. THOSE PROBLEMS WE HAVE ADDRESSED SPECIFICALLY. ONE WITH THE FDA, WHO ACTUALLY SENT US A NOTE SAYING THAT WE COULD GET TISSUE EXEMPTION FOR USE IN RETINITIS PIGMENTOSA BY SENDING THEM A LETTER. THEY WERE VERY LIKELY TO GIVE US THE EXEMPTION. SO THAT WASN'T AN ISSUE.

THE MANUFACTURING ISSUES ARE ALL RESOLVED. WE'VE HAD THOSE -- ALREADY THE CELLS FROZEN IN THE BANK. SO I DON'T UNDERSTAND EXACTLY WHAT THE MANUFACTURING OR REGULATORY ISSUES WERE THAT WERE NOT IN PLACE BECAUSE, FROM MY UNDERSTANDING OF THE PROPOSAL, EVERYTHING IS IN PLACE.

DR. STEFFEN: SO WE'RE -- IN AN ATTEMPT TO KEEP YOUR PROJECT INFORMATION CONFIDENTIAL, OUR READ OF THE REGULATORY DOCUMENTATION, THE EMAIL THAT WAS SENT RECENTLY AS PART OF THE APPEAL, IS THE SAME MESSAGE THAT WAS IN THE MIDDLE OF JULY 2012, WHICH IS SUBMIT YOUR PACKAGE, WE WILL REVIEW IT, AND WE

WILL CONSIDER IT FOR AN EXEMPTION. SO WE WERE LOOKING FOR THAT ACTIVITY TO OCCUR AND HAPPEN TO GIVE US ASSURANCE THAT THIS CELL SOURCE HAS A PATHWAY FORWARD, NOT ONLY INTO THE PHASE I, BUT TO BE FULLY COMMERCIALIZED. IT HAS TO DO WITH DONOR --

DR. FEIGAL: I THINK THERE'S CONFIDENTIAL INFORMATION THAT STILL RAISES SOME ISSUES THAT HAVE NOT YET BEEN RESOLVED TO OUR SATISFACTION THAT WOULD REQUIRE SOME ADDITIONAL INPUT. SO IF YOU WANT TO GO INTO CONFIDENTIAL, WE COULD GO INTO THAT.

MR. SHEEHY: UNLESS A MEMBER REQUESTS IT, I THINK WE'RE AT A POINT OF ROLL CALL. AGAIN, IT'S TO THE DISCRETION.

MR. HARRISON: TO RESTATE THE MOTION, IT'S TO ACCEPT THE STAFF RECOMMENDATION NOT TO FUND APPLICATION 7061.

MS. BONNEVILLE: MARCY FEIT.

MS. FEIT: YES.

MS. BONNEVILLE: MICHAEL GOLDBERG.

MR. GOLDBERG: NO.

MS. BONNEVILLE: STEPHEN JUELSGAARD.

DR. JUELSGAARD: YES.

MS. BONNEVILLE: FRANCISCO PRIETO.

DR. PRIETO: AYE.

MS. BONNEVILLE: ROBERT QUINT.

DR. QUINT: NO.
MS. BONNEVILLE: AL ROWLETT.
MR. ROWLETT: YES.
MS. BONNEVILLE: JOAN SAMUELSON. JEFF SHEEHY.
MR. SHEEHY: YES.
MS. BONNEVILLE: OSWALD STEWARD.
DR. STEWARD: NO.
MS. BONNEVILLE: JONATHAN THOMAS.
CHAIRMAN THOMAS: YES.
MS. BONNEVILLE: ART TORRES.
MR. TORRES: AYE.
MS. BONNEVILLE: DIANE WINOKUR.
MS. WINOKUR: NO.
MR. HARRISON: THAT MOTION CARRIES.
MS. WINOKUR: IS IT APPROPRIATE TO MAKE A MOTION TO FOLLOW UP ON THE STAFF RECOMMENDATION, THAT THE TEAM DISCUSS PRIVATELY WITH THEM THE REGULATION ISSUES THAT WERE RAISED?
DR. FEIGAL: I CAN TELL YOU WITHOUT YOU EVEN MAKING A MOTION THAT WE WILL DO THAT.
MS. WINOKUR: OKAY.
MR. SHEEHY: SO JUST AS A QUESTION, DO WE WANT TO KEEP PLOWING THROUGH, OR DO PEOPLE WANT TO TAKE A BREAK? YOU KNOW WHOSE MEMORY IS IN MY MIND

IS LEEZA YESTERDAY. BUT IF YOU GUYS WANT TO KEEP GOING, WE CAN, BUT I JUST WANTED TO OFFER THAT UP, JUST LIKE A SHORT BREAK IF ANYBODY NEEDS A BREAK. WE JUST KIND OF PLOW THROUGH THIS STUFF. IF NOBODY WANTS TO, I'LL GO -- A BREAK. LET'S TRY TO GET THROUGH THESE. JUST A SHORT FIVE- OR TEN-MINUTE BREAK JUST SO WE CAN GET SOME -- WE DON'T HAVE TO MAKE THIS A MARATHON. FIVE-MINUTE BREAK.

(A RECESS WAS TAKEN.)

MR. SHEEHY: IF WE COULD GO AHEAD AND QUEUE UP THE NEXT APPLICATION, WHICH WOULD BE THE STAFF RECOMMENDATION FOR 6945.

MS. WINOKUR: COULD I MAKE A MOTION THAT APPLIES TO THE PROJECT WE JUST REVIEWED? WE DIDN'T QUITE FINISH.

MR. HARRISON: I GUESS IT DEPENDS WHAT THE MOTION IS. THE DETERMINATION NOT TO FUND HAS BEEN MADE, SO THAT MOTION IS FINAL. IF IT'S A DIFFERENT TOPIC --

MS. WINOKUR: NO. IT RELATES TO THAT.

MR. HARRISON: WELL, UNLESS IT'S A MOTION TO RECONSIDER THE PRIOR VOTE, I GUESS I'M NOT SURE WHAT -- MAYBE YOU SHOULD EXPLAIN THE MOTION YOU'D LIKE TO MAKE.

MS. WINOKUR: LET ME MAKE THE MOTION AND

THEN YOU CAN TELL ME.

MR. HARRISON: SURE. PERFECT.

MS. WINOKUR: I WOULD LIKE TO MOVE THAT WE GIVE PARTIAL FUNDING TO THE PROPOSAL JUST AS WE DID WITH THE PRIOR ONE, AND MAYBE FOR TWO YEARS, AND THAT WE SHOULD HAVE A MILESTONE THAT THE REGULATORY ASPECTS THAT WERE LACKING BE FULFILLED IN THAT TIME.

MR. SHEEHY: I HAVE TO SAY THAT THAT WOULD NOT BE IN ORDER AT THIS POINT UNFORTUNATELY. I THINK THAT IT PRESENTS A LEVEL OF COMPLEXITY. THAT'S REALLY A RECOMMENDATION. YOU'RE KIND OF REWRITING THE GRANT AT THIS POINT AFTER IT'S BEEN SCIENTIFICALLY REVIEWED. WE'VE TAKEN A VOTE HERE, AND SO IT WOULD TAKE BASICALLY A TWO-THIRDS MAJORITY OF THE PEOPLE WHO VOTED TO RECONSIDER THE ITEM. IF YOU WANTED TO MAKE A MOTION TO RECONSIDER THE ITEM, I WOULD ACCEPT THAT MOTION. I THINK JAMES WOULD AGREE THAT WOULD BE THE APPROPRIATE MOTION.

AND THEN YOU COULD INTRODUCE THAT MOTION IF YOU WANTED TO DO THAT. JAMES, AM I CORRECT IN THAT THAT WOULD BE THE APPROPRIATE PROCESS?

MR. HARRISON: YES. I'M JUST CHECKING ROBERT'S RULES OF ORDER ON THE THRESHOLD.

MR. SHEEHY: BECAUSE WE'VE ALREADY ACTED, SO IT TAKES A SUPER MAJORITY TO ACT AGAIN. SO DO

YOU WANT -- JAMES, DO WE NEED A RULING, OR SHOULD I -- I ALWAYS UNDERSTOOD IT WAS A SUPER MAJORITY TO RECONSIDER.

MR. HARRISON: MAY I MAY A SUGGESTION, THAT YOU PROCEED ON TO THE NEXT APPLICATION WHILE WE CONFER AND VERIFY OUR FRIENDS, ROBERT'S RULES OF ORDER? THANK YOU.

MR. SHEEHY: PLEASE.

DR. STEFFEN: YOU'D LIKE THE STAFF RECOMMENDATION ON THE NEXT APPLICATION, WHICH IS 6945. THE TITLE OF THE APPLICATION IS "A CLINICAL TRIAL OF STEM CELL GENE THERAPY FOR SICKLE CELL DISEASE." THE APPLICANT IS TARGETING SICKLE CELL DISEASE, AND THE APPROACH IS TO USE AUTOLOGOUS HEMATOPOIETIC STEM CELLS, SO BONE MARROW TRANSPLANT, AND THESE CELLS WILL BE GENETICALLY CORRECTED BY THE ADDITION OF A HEMOGLOBIN GENE THAT BLOCKS SICKLING.

AND THE APPLICANT IS TACKLING SICKLE CELL DISEASE, A DISEASE THAT DISPROPORTIONATELY AFFECTS AFRICAN-AMERICANS AND HISPANIC AMERICANS.

THE PROGRAMMATIC POINTS FOR OUR CONSIDERATION AND RECOMMENDATION TO FUND THIS APPLICATION IS THAT THIS PROJECT LEVERAGES A TEAM AND THE KNOW-HOW GAINED IN A DISEASE TEAM I PROJECT, WHICH IS A PRIORITY AREA FOR THIS RFA. THE TEAM AND

THE PI, NOT ONLY ARE THEY RECOGNIZED AS LEADERS WITHIN CALIFORNIA, CERTAINLY WITHIN THE UNITED STATES AND THE WORLD. THIS INVESTIGATOR HAS DEDICATED HIS CAREER TO THIS DISEASE.

THE PROJECT IS AT THE MOST ADVANCED DEVELOPMENT STAGE OF THE PROJECTS IN THE CIRM PORTFOLIO TARGETING BLOOD DISEASES. AS THE DISEASE TEAM I WRAPS UP AND THIS GRANT WOULD START, WE WOULD SEE THE IND FILING AND THE START OF THE TRIAL IN THE FIRST HALF OF NEXT YEAR, 2014.

SICKLE CELL DISEASE HAS A HIGH UNMET MEDICAL NEED, AND THE APPROACH ALLOWS FOR A CHANCE TO DETECT THAT EARLY EVIDENCE OF BIOLOGIC ACTIVITY EARLY IN THE TRIAL IN SUPPORT OF CIRM'S KEY STRATEGIC GOAL TO DEMONSTRATE CLINICAL PROOF OF CONCEPT.

SO WHAT WE MEAN BY THAT IS THEY'RE REPLACING BLOOD WITH A NEW GENE SO THAT THE CELLS WON'T SICKLE. AND 120 DAYS AFTER THOSE PATIENTS, THOSE FIRST COHORT, GETS THAT TREATMENT, THERE WOULD BE A CHANCE TO SAMPLE AND UNDERSTAND WHETHER THERE'S BIOLOGIC ACTIVITY. THESE ARE SOME OF THE PRINCIPLES WE TALK ABOUT WITH EARLY PROOF OF CONCEPT.

MR. SHEEHY: THANK YOU, DR. STEFFEN. SO DO I HAVE A MOTION TO ACCEPT STAFF RECOMMENDATION?

DR. PRIETO: SO MOVED.

MR. SHEEHY: DO I HAVE A SECOND?

MS. WINOKUR: SECOND.

MR. TORRES: SECOND.

MR. SHEEHY: MULTIPLE SECONDS. DO WE HAVE ANY BOARD DISCUSSION? CHAIRMAN THOMAS.

CHAIRMAN THOMAS: DR. STEFFEN, AS I UNDERSTAND IT, ANOTHER INTERESTING ASPECT OF THIS IS THAT IT DOES COMBINE STEM CELL AND GENE THERAPY TECHNOLOGIES. AND THAT IS SOMETHING THAT WE'RE INTERESTED IN ADVANCING AS SORT OF FROM A PLATFORM TECHNOLOGICAL POINT OF VIEW, AND WE CAN LEARN THINGS FROM THAT THAT COULD BE APPLICABLE IN THAT JOINING IN OTHER AREAS; IS THAT CORRECT?

DR. STEFFEN: CORRECT. THIS IS A GENE MODIFIED-STEM CELL THERAPY. AND MANY OF THE TECHNIQUES AND APPROACHES AND SAFETY DEMONSTRATION ARE APPLICABLE BROADLY ACROSS CELL TYPES AND OTHER INDICATIONS. SO WE WILL LEARN A LOT FROM THIS.

DR. STEWARD: I MAY HAVE HAD A TRANSIENT ISCHEMIC ATTACK, BUT DID YOU SAY ANYTHING ABOUT PORTFOLIO?

DR. STEFFEN: I DID SAY THIS IS THE MOST ADVANCED PROJECT IN THE BLOOD DISEASES, AND I CAN COUNT UP PROJECTS IF YOU NEED ME TO.

DR. STEWARD: ACTUALLY IT WOULD BE HELPFUL TO KNOW THAT. THANKS.

MR. SHEEHY: I THINK SPECIFICALLY FOR SICKLE WE HAVE ONE OTHER.

DR. FEIGAL: THAT'S CORRECT.

MR. SHEEHY: ONE OTHER IN SICKLE CELL, AND THEN WE HAVE ONE OTHER IN BETA THALASSEMIA.

DR. FEIGAL: BUT IN SICKLE CELL THERE'S REALLY JUST ONE OTHER PROGRAM.

MR. SHEEHY: THERE'S JUST ONE OTHER. I THINK BLOOD DISORDER IS A LITTLE BIT BROAD TO LOOK AT AS PORTFOLIO. I THINK IF YOU WANT TO REALLY -- THE TWIN DISEASES ARE BETA THALASSEMIA AND SICKLE CELL, I THINK, THAT PEOPLE TYPICALLY USE TO MAKE A PORTFOLIO ANALYSIS.

DR. STEWARD: I AGREE. AND IF THE ANSWER IS ONE, THAT'S ACTUALLY FINE.

MR. SHEEHY: DO WE HAVE ADDITIONAL BOARD DISCUSSION?

DR. JUELSGAARD: MR. SHEEHY, WELL, CONSISTENT WITH THE OTHERS THAT WE'VE HAD TODAY, CAN WE HAVE A REVIEW OF WHAT CDAP THOUGHT ABOUT THIS PROPOSAL?

DR. FEIGAL: ACTUALLY WHAT I SUGGEST IS WE HAVE A SCIENCE OFFICER WHO CAN GIVE YOU AN

ASSESSMENT OF WHAT THE GRANTS WORKING GROUP THOUGHT ABOUT IT. IS THAT WHAT YOU ARE ASKING, CONSISTENT WITH THE OTHER PROJECTS?

DR. JUELSGAARD: YES. AT THE MEETING IN OAKLAND AT THE CLAREMONT WHERE THIS WAS DISCUSSED.

DR. FEIGAL: THE GRANTS WORKING GROUP.

DR. JUELSGAARD: SO THAT WASN'T CDAP.

DR. FEIGAL: WELL, I'M JUST SAYING IF YOU WANT TO ALIGN IT WITH WHAT WE'VE DONE WITH OTHER PROJECTS, WE'VE BEEN GIVING YOU SUMMARIES FROM THE GRANTS WORKING GROUP AS OPPOSED TO THIS SEPARATE ASSESSMENT GROUP. SO THAT'S HOW I'M RESPONDING. BUT IF YOU'RE ASKING FOR SOMETHING ELSE.

DR. JUELSGAARD: I'M JUST CONFUSED, THEN, ON WHAT WE'RE TALKING ABOUT.

DR. FEIGAL: WELL, THE GRANTS WORKING GROUP IS A GROUP THAT REVIEWED ALL OF THESE PROPOSALS. IN ADDITION, FOR THE DISEASE TEAM PROJECTS, WE HAVE A SEPARATE PROCESS CALLED CDAP THAT YOU'RE FAMILIAR WITH. AND SO ARE YOU ASKING FOR BOTH? YOU WANT TO HEAR WHAT'S THE GRANTS WORKING GROUP THOUGHT AS WELL AS CDAP?

DR. JUELSGAARD: WELL, JUST SO I'M CLEAR. SO DOES CDAP DISCUSSIONS FROM LAST SUMMER, WHENEVER IT WAS, WHATEVER MONTH THAT WAS, ARE THEY INCLUDED

IN THE COMMENTS THAT WERE DISTRIBUTED TO US OR NOT?

DR. FEIGAL: THE COMMENTS THAT WERE DISTRIBUTED AS PART OF THE SUMMARY ARE REFLECTIVE OF THE GRANTS WORKING GROUP RECOMMENDATIONS.

LET ME HAVE THE LAWYER DISCUSS IT BECAUSE I MAY BE MISSING SOMETHING.

MR. SWEEDLER: IT GETS CONFUSING BECAUSE THIS PROJECT IS TWO SEPARATE GRANTS. THE ORIGINAL DISEASE TEAM, AS AN EXISTING AWARD, WAS REVIEWED ON AN ONGOING BASIS WITH CDAP. THAT'S WHAT THEY DO. THEY REVIEW OUR FUNDED AWARDS. AS A FORWARD-LOOKING PROPOSAL FOR THE NEW ONE, THAT WENT TO THE GRANTS WORKING GROUP. SO THE SCIENCE IS CONTINUOUS, BUT IT'S A SEPARATE PROCEEDING IN A WAY. IT'S A GRANTS WORKING GROUP PROCEEDING.

MR. SHEEHY: DO YOU WANT TO HEAR THE GRANTS WORKING GROUP REVIEW?

DR. JUELSGAARD: YES.

DR. STEFFEN: SO DR. SOHIL TALIB, THE SCIENCE OFFICER ON THE PROJECT, IS GOING TO DO THAT.

DR. TALIB: THANK YOU, DR. STEFFEN. MY NAME IS SOHIL TALIB, AND I'M THE SCIENCE OFFICER. AND I'LL JUST GIVE YOU A BRIEF SUMMARY OF THE PROJECT WHICH WAS REVIEWED BY THE GRANTS WORKING GROUP. AND AS DR. STEFFEN POINTED OUT, THIS IS

ACTUALLY A STEM CELL GENE THERAPY PROJECT IN WHICH THE GOAL OF THE PROJECT IS TO INITIATE AND COMPLETE A PHASE I CLINICAL TRIAL. THIS HAS BEEN A DISEASE TEAM I GRANT. SO THIS HAS COMPLETED ALMOST FOUR YEARS OF THE GRANT WHILE ALL THE MILESTONES HAVE BEEN MET. AND THAT DISEASE TEAM HAS ALREADY COMPLETED A REVIEW BY THE PRE-IND, AS WELL AS BY THE RECOMBINANT ADVISORY COMMITTEE BECAUSE IT'S A STEM CELL GENE THERAPY PROJECT, AND ALSO HAD COMPLETED A REVIEW BY THE INSTITUTION IRB.

SO THIS TEAM HAS COMPLETED ALL THE MILESTONES SO FAR AND IS READY TO INITIATE -- SUBMIT AN IND IN Q1 OF 2014 AND THEN START A PHASE I CLINICAL TRIAL.

SO IN TERMS OF THE STRENGTH AND THE WEAKNESSES, LET ME POINT OUT, WHICH WAS POINTED OUT DURING THE GRANTS WORKING GROUP. SO IN TERMS OF THE STRENGTH, THIS IS AN UNMET MEDICAL NEED. IF SUCCESSFUL, IT WILL HAVE A SIGNIFICANT IMPACT ON THIS PARTICULAR DISEASE WHICH DISPROPORTIONATELY AFFECT THE MINORITY POPULATIONS IN CALIFORNIA. AND ALSO AT THE MOMENT THERE IS NO CURATIVE TREATMENT FOR THIS DISEASE. WORLDWIDE THERE ARE MILLIONS OF PEOPLE WHICH ARE AFFECTED BY THIS DISEASE.

AND THE ONLY CURATIVE TREATMENT FOR THIS

DISEASE IS AN ALLOGENEIC BONE MARROW TRANSPLANT, BUT THAT CANNOT BE PERFORMED BECAUSE OF THE IMMUNOLOGICAL REQUIREMENT WHICH IS NEEDED. SO ONLY 20 TO 30 PERCENT OF THE PATIENTS WHICH COULD BENEFIT FROM THIS CURATIVE TREATMENT ARE NOT TREATED BECAUSE OF THE IMMUNOLOGICAL COMPLICATIONS.

WHAT THIS PARTICULAR TEAM IS DOING IS TO MAKE AN AUTOLOGOUS BONE MARROW TRANSPLANT, TAKING PATIENT'S OWN BLOOD FORMING STEM CELLS, GENE MODIFY THEM, AND GIVE IT BACK TO THE PATIENT. SO IN A WAY THIS WILL BE APPLICABLE TO LARGE NUMBER OF POPULATIONS.

THE STRENGTH OF THIS PARTICULAR TEAM, AS WAS POINTED OUT BY THE GRANTS WORKING GROUP, IS THE SCIENTIFIC RATIONALE FOR STEM CELL GENE THERAPY. CURRENTLY THERE HAVE BEEN COUPLE OF STEM CELL GENE THERAPY TRIALS WHICH ARE GOING ON IN EUROPE AND WHICH ARE SHOWING A CLINICAL BENEFIT AND SHOWS THAT IT'S SCIENTIFICALLY POSSIBLE THAT YOU COULD MODIFY THE STEM CELL WITH A GENE AND THEN GIVE IT TO THE PATIENTS. SO THE CLINICAL PROOF OF CONCEPT IS VALID AND IS APPRECIATED BY THE GRANTS WORKING GROUP.

AS DR. STEFFEN POINTED OUT, THE PI OF THE TEAM IS VERY WELL ESTABLISHED. THEY HAVE DONE CLINICAL TRIALS, EXTENSIVE GENE THERAPY TRIALS

PREVIOUSLY FOR OTHER DISEASES.

AND AS I POINTED OUT, THIS TEAM HAS ALREADY COMPLETED THE PRE-IND RECOMBINANT ADVISORY COMMITTEE MEETINGS AS WELL AS INSTITUTIONAL IRB'S.

NOW, IN TERMS OF THE WEAKNESS, WHICH WAS THE REASON THIS PARTICULAR TEAM -- THIS PARTICULAR APPLICATION WAS NOT PUT IN THE TIER I WAS THERE WAS SOME CONCERN ABOUT THE TIMING OF THE FILING OF THE IND. ORIGINALLY, WHEN THIS PARTICULAR APPLICATION WAS SUBMITTED TO THE DISEASE TEAM III, THE TEAM HAS PROPOSED THAT THEY WILL FILE AN IND AT THE END OF Q4 OF 2013 BEFORE SOME OF THE ONGOING TREATMENT STUDIES WILL BE COMPLETED. AND THE GRANTS WORKING GROUP THOUGHT THAT THIS WOULD BE A WEAKNESS. THIS MAY BE RISKY TO SUBMIT AN IND BEFORE THE RESULTS OF THE ONGOING PRECLINICAL STUDIES ARE COMPLETELY AVAILABLE.

SINCE THEN, SINCE THE DISEASE TEAM I, AND WE ARE IN CONTACT WITH THE DISEASE TEAM, THEY HAVE REVISED THEIR MILESTONES. AND THEY ARE ACTUALLY SUBMITTING IND IN Q1 OF 2014 WHEN ALL THE ONGOING PRECLINICAL STUDIES WILL BE COMPLETED. SO THEY WILL BE COMPLETELY READY TO FILE THE IND AND START A CLINICAL TRIAL. SO THAT PARTICULAR WEAKNESS HAS ALREADY BEEN ADDRESSED.

ALSO THERE WAS SOME CONCERN ABOUT THE MANUFACTURING ASPECT OF THIS PARTICULAR PRODUCT. AND THAT ALSO HAS BEEN ADDRESSED BY THE DISEASE TEAM. THEY HAVE OPTIMIZED THE MANUFACTURING PROCESS SUCH THAT THEY WILL BE ABLE TO PRODUCE A PRODUCT WHICH WILL HAVE A STRENGTH OR THE POTENTIAL TO MAKE A DIFFERENCE IN A CLINICAL TRIAL.

SO BOTH OF THE CONCERNS WHICH THE GRANTS WORKING GROUP HAD HAS ALREADY BEEN ADDRESSED BY THE DISEASE TEAM.

I THINK FROM OUR POINT OF VIEW THIS DISEASE TEAM IS READY TO START THE CLINICAL TRIAL. AND AS DR. STEFFEN POINTED OUT, THIS IS THE MOST ADVANCED TEAM TO GET THIS PARTICULAR APPLICATION OR THIS TYPE OF TREATMENT IN CALIFORNIA FOR THE PATIENTS WITH BOTH SICKLE CELL DISEASE.

IN TERMS OF THE PORTFOLIO, I THINK THERE WAS QUESTION. CURRENTLY WE HAVE IN THE SICKLE CELL DISEASE WE HAVE ONLY ONE EARLY TRANSLATION GRANT WHICH, IN FACT, IS WITH THE SAME DISEASE TEAM WHICH ARE USING, IT'S EARLY TRANSLATION, WHICH WILL BE STARTING ACTUALLY THIS YEAR. SO THEY ARE REALLY BEHIND. IN FACT, THEIR APPROACH IS VERY DIFFERENT. IT'S A GEN TWO APPROACH TO DO A DIFFERENT APPROACH FOR SICKLE CELL DISEASE.

WE ALSO HAVE A DISEASE TEAM WHICH IS LOOKING AT BETA THALASSEMIA. IT'S HEMOGLOBIN. IT'S THE SAME KIND OF DISEASE, AND THAT DISEASE TEAM IS ALSO JUST STARTING. SO THEY ARE REALLY BEHIND IN TERMS OF COMPLETING WITH THIS TYPE OF APPROACH.

SO THIS IS PROBABLY THE MOST ADVANCED DISEASE TEAM TO GET THIS PARTICULAR TREATMENT TO THE PATIENTS.

MR. SHEEHY: ANY OTHER QUESTIONS OR COMMENTS FROM THE BOARD? THANK YOU, DR. TALIB. ANY PUBLIC COMMENT? ARE WE READY TO CALL THE ROLL? THE MOTION IS TO ACCEPT STAFF'S RECOMMENDATION THAT THIS BE MOVED INTO THE TIER I.

DR. DULIEGE: I SECOND.

MR. SHEEHY: WE ALREADY HAD THE MOTION. I'M JUST REPEATING THE MOTION.

MR. HARRISON: AND THIS IS APPLICATION 6945.

MS. BONNEVILLE: ANNE-MARIE DULIEGE.

DR. DULIEGE: YES.

MS. BONNEVILLE: MICHAEL GOLDBERG.

MR. GOLDBERG: YES.

MS. BONNEVILLE: STEPHEN JUELSGAARD.

DR. JUELSGAARD: NO.

MS. BONNEVILLE: FRANCISCO PRIETO.

DR. PRIETO: AYE.
MS. BONNEVILLE: ROBERT QUINT. AL ROWLETT.
MR. ROWLETT: YES.
MS. BONNEVILLE: JEFF SHEEHY.
MR. SHEEHY: YES.
MS. BONNEVILLE: OS STEWARD.
DR. STEWARD: YES.
MS. BONNEVILLE: JONATHAN THOMAS.
CHAIRMAN THOMAS: YES.
MS. BONNEVILLE: ART TORRES.
MR. TORRES: AYE.
MS. BONNEVILLE: DIANE WINOKUR.
MS. WINOKUR: YES.
MR. SHEEHY: I THINK THE MOTION CARRIES. DO WE NEED TO WAIT FOR DR. QUINT TO CAST A VOTE?
MR. HARRISON: THE MOTION CARRIES.
MR. SHEEHY: NOW, TO GO BACK TO MS. WINOKUR'S QUESTION -- DR. QUINT, WOULD YOU LIKE TO CAST A VOTE ON THE PREVIOUS MOTION TO APPROVE THIS APPLICATION FOR STEM CELL THERAPY?
DR. QUINT: I THINK I BETTER ABSTAIN.
MR. SHEEHY: DR. QUINT IS ABSTENTION.
MS. WINOKUR HAD A QUESTION WHETHER OR NOT -- SHE WISHED TO MAKE ANOTHER MOTION -- DID YOU

WANT TO MAKE A PUBLIC COMMENT?

MS. SHAPIRO: I'D LIKE TO MAKE A PUBLIC COMMENT.

MR. SHEEHY: PLEASE BE MY GUEST, AND PLEASE IDENTIFY YOURSELF. ARE YOU SPEAKING ABOUT THE PREVIOUS APPLICATION?

MS. SHAPIRO: YES.

MR. SHEEHY: JUST TO LET YOU KNOW, THAT HAS BEEN RECOMMENDED FOR FUNDING.

MS. SHAPIRO: OH, YES. BELIEVE ME. THAT'S WHY I'M STANDING HERE.

MY NAME IS ADRIENNE SHAPIRO. I STAND BEFORE YOU. I AM A FOURTH GENERATION OF MOTHERS -- I THOUGHT I WAS THE THIRD, BUT ACTUALLY I'M THE FOURTH MOTHER TO HAVE A FIRST CHILD BORN WITH SICKLE DISEASE. AND SO FAR, I'M THE ONLY ONE THAT HASN'T BURIED THAT CHILD. AND I HAVE BEEN THROWING MYSELF OVER THAT CHILD'S BODY FOR MANY YEARS KEEPING HER SAFE AND ALIVE AND WAITING FOR THIS MOMENT. AND I JUST WANT TO THANK YOU.

THE SIGNIFICANCE OF THIS RESEARCH AT THIS TIME, I MADE A LIST OF WHAT MY LIFE WOULD HAVE BEEN LIKE IF SICKLE CELL RESEARCH HADN'T BEEN STOPPED IN THE '80S. AND I MADE A LIST OF ALL THOSE THINGS, AND I WAS ALL PREPARED TO COME AND TELL YOU THAT IF

YOU DIDN'T DO THIS, ALL THE MOTHERS WHO WOULD HAVE TO GO THROUGH WHAT I DID. AND I'M SO THANKFUL THAT I DON'T. AND I WANTED TO SAY TO YOU THANK YOU. AND FOR THOSE MOTHERS WHO ARE NOW ANGELS AND WITH THOSE FIRST-BORN CHILDREN WHO WERE BEAUTIFUL AND BRIGHT AND BOLD AND LEFT TOO SOON, I WANT TO SAY THANK YOU. AND TO THE STEM CELL COMMUNITY, NOT ONLY MY CHILD, BUT SO MANY OTHERS, WE THANK YOU.

MR. SHEEHY: THANK YOU. AND, YOU KNOW, I DO THINK THIS IS AN IMPORTANT GRANT. I REALLY WANT TO GIVE A LOT OF CREDIT TO DR. KOHN FOR HIS PERSISTENCE. I MEAN THAT'S BEEN EVIDENT IN ALL THE REVIEWS. THIS IS A GRANT THAT WE FIRST APPROVED, WHAT, BACK IN 2009, AND I HOPE WE CAN MAKE A DIFFERENCE HERE.

DR. KOHN: I JUST WANT TO SAY THANK YOU FOR THE SUPPORT. THE STAFF HAS REALLY HELPED US GET TO WHERE WE DID. SO THE STAFF FROM CIRM, AS PERSISTENT AS THEY ARE, HAVE BEEN VERY HELPFUL IN GETTING THE PROJECT MOVING FORWARD.

CHAIRMAN THOMAS: DON, YOU MIGHT IDENTIFY YOURSELF FOR THOSE WHO DON'T KNOW YOU.

DR. KOHN: I'M DONALD KOHN FROM UCLA, THE PI OF THE GRANT FOR SICKLE CELL.

(APPLAUSE.)

MR. SHEEHY: MS. WINOKUR WOULD LIKE TO MAKE A NEW MOTION RELATIVE TO THE RETINITIS PIGMENTOSA GRANT. IN ORDER TO DO THAT, WE NEED A MOTION TO RECONSIDER. A MOTION TO RECONSIDER CAN ONLY BE MADE BY ONE WHO IS ON THE OPPOSING SIDE OF MS. WINOKUR'S MOTION.

DR. QUINT: I'LL MAKE THE MOTION TO RECONSIDER.

MR. SHEEHY: YOU'D LIKE TO MAKE A MOTION TO RECONSIDER? DO WE NEED A SECOND ON THAT?

MR. ROWLETT: I'LL SECOND THE MOTION TO RECONSIDER.

MR. HARRISON: I'M SORRY. MR. QUINT IS NOT ELIGIBLE TO MAKE THE MOTION.

MR. ROWLETT: I'LL MAKE THE MOTION TO RECONSIDER.

MR. SHEEHY: DO WE HAVE A SECOND FOR THAT MOTION?

CHAIRMAN THOMAS: I'LL SECOND.

MR. SHEEHY: OKAY. CAN WE HAVE A VOTE ON THE MOTION TO RECONSIDER?

MS. BONNEVILLE: MARCY FEIT. MICHAEL GOLDBERG.

MR. GOLDBERG: YES.

MS. BONNEVILLE: STEPHEN JUELSGAARD.

DR. JUELSGAARD: NO.
MS. BONNEVILLE: FRANCISCO PRIETO.
DR. PRIETO: AYE.
MS. BONNEVILLE: ROBERT QUINT.
DR. QUINT: YES.
MS. BONNEVILLE: AL ROWLETT.
MR. ROWLETT: YES.
MS. BONNEVILLE: JEFF SHEEHY.
MR. SHEEHY: NO.
MS. BONNEVILLE: OS STEWARD.
DR. STEWARD: YES.
MS. BONNEVILLE: JONATHAN THOMAS.
CHAIRMAN THOMAS: YES. I'D LIKE TO HEAR WHAT THE MOTION IS.
MS. BONNEVILLE: ART TORRES.
MR. TORRES: AYE.
MS. BONNEVILLE: DIANE WINOKUR.
MS. WINOKUR: YES.
MR. HARRISON: SO THE MOTION TO RECONSIDER CARRIES.
MR. SHEEHY: MS. WINOKUR, YOU ARE FREE TO MAKE YOUR MOTION.
MS. WINOKUR: I WOULD LIKE TO MOVE THAT WE RECONSIDER OUR DECISION ON PROPOSAL 7061 AND GRANT PARTIAL FUNDING TO THE PROPOSAL JUST AS WE DID WITH

THE 7281 THAT WE VOTED ON JUST BEFORE THIS. AND IN THAT TIME FRAME, SAY, TWO YEARS, THAT THE PI, ETC., WORK ON SATISFYING THE REGULATORY QUESTIONS THAT WERE RAISED.

MR. SHEEHY: SO YOUR MOTION IS TO FUND THE FIRST TWO YEARS OF THE AWARD, CUTTING THE AWARD IN HALF?

MS. WINOKUR: NO. NOT ONLY THAT, BUT THAT THAT BE DONE.

MR. SHEEHY: DO WE HAVE A SECOND?

DR. QUINT: I'LL SECOND THE MOTION.

DR. STEWARD: SO I'M IN GENERAL IN FAVOR OF THE CONCEPT OF FLEXIBILITY. I'M A LITTLE CONCERNED ABOUT THE SPECIFICS HERE OF JUST SAYING CUT IT IN HALF AND GO FOR TWO YEARS. I'D BE VERY CURIOUS TO HEAR SCIENCE STAFF COMMENTS AND RECOMMENDATIONS IN THAT REGARD.

MR. ROWLETT: I'D LIKE TO DITTO THAT. IN ADDITION, IF YOU COULD TELL US IF YOU CONSIDERED THAT IN MAKING YOUR RECOMMENDATION INITIALLY NOT TO FUND. IT WOULD BE VERY HELPFUL.

DR. JUELSGAARD: ONE MORE QUESTION. SO IN THIS CUTTING IT IN HALF, CONSISTENT WITH THAT, IS THAT CUTTING THE DOLLARS IN HALF?

MR. SHEEHY: YES.

DR. JUELSGAARD: SO THE QUESTION IS IS WHEN THE SPEND WAS LAID OUT, THE BUDGET THAT WAS PROPOSED, WAS THE SPEND LAID OUT IN AN EVENHANDED YEAR-BY-YEAR FASHION, OR DID IT RAMP UP AS USUALLY IS THE CASE OVER TIME?

MR. SHEEHY: I THINK MAYBE WE SHOULD HEAR FROM STAFF. I DON'T KNOW WHO WOULD BE -- DR. FEIGAL WOULD BE APPROPRIATE TO KIND OF ADDRESS THE WISDOM AND FEASIBILITY OF THIS PROPOSAL.

DR. FEIGAL: I THINK IF WHAT YOU REALLY MEANT TO SAY IS YOU WANT US TO FUND TO AN IND-ENABLING STAGE, IF THAT'S WHAT YOU MEANT TO SAY, THAT'S A DIFFERENT ISSUE THAN THE REGULATORY BECAUSE THERE'S SCIENTIFIC -- THERE WERE CLINICAL TRIAL DESIGN AND, IN ADDITION, THERE WERE REGULATORY ISSUES. SO IF THAT'S WHAT YOU MEANT TO SAY, THAT'S MORE UNDERSTANDABLE THAN JUST -- THE REGULATORY ISSUE MIGHT BE VERY LIMITED FUNDING TO ADDRESS THAT ISSUE. SO I DON'T KNOW WHAT YOU MEANT.

SO, ANYWAY, THAT'S A CLARIFICATION I DEFINITELY WOULD NEED. AND IF THAT IS SOMETHING YOU MEANT, THEN THAT WOULD TAKE QUITE A BIT OF LOOKING INTO THE APPLICATION TO FIGURE OUT THE BUDGET AMOUNT.

MR. SHEEHY: CAN I ASK THE MAKER OF THE

MOTION A QUESTION? ARE YOU RECOMMENDING THIS FUNDING BECAUSE YOU BELIEVE IT MIGHT -- CAN I ASK YOU A QUESTION ABOUT YOUR MOTION?

MS. WINOKUR: OKAY.

MR. SHEEHY: DO YOU THINK THAT FUNDING THIS MOTION WILL HAVE SOME IMPACT ON ALS, OR IS THIS JUST --

MS. WINOKUR: I THINK THIS PROJECT WILL.

MR. SHEEHY: COULD DR. SVENDSEN PLEASE EXPLAIN THE RELATIONSHIP OF THIS PROJECT TO ALS?

DR. FEIGAL: AND WE ARE ALSO FUNDING A PROJECT IN ALS WITH THESE CELLS, AS YOU KNOW.

DR. SVENDSEN: I THINK THERE IS A RELATIONSHIP BETWEEN THIS PROCESS. THE CELLS --

MR. SHEEHY: I MEAN COULD YOU REALLY GIVE SOME GRANULARITY IN THAT HOW, IF WE FUND THIS ON TOP OF THE PROJECT WE'RE ALREADY FUNDING YOU IN ALS, THAT WILL MAKE A DIFFERENCE IN ALS?

DR. SVENDSEN: ANY CELLS THAT GO INTO THE CLINIC USING THIS TECHNIQUE OF TRANSPLANTATION INTO THE EYE OR INTO THE SPINAL CORD IS GOING TO BE SYNERGISTIC. AND THE PROCESSES THAT WE USE IN BOTH CASES WILL BENEFIT EACH OTHER. SO THERE'S A RELATIONSHIP BETWEEN THESE CELLS WHETHER THEY GO INTO ALS PATIENTS OR THE EYE.

THE REAL QUESTION IS STILL RELATED TO THE CELLS THAT WE'RE PRODUCING AND THEIR EFFICACY IN MODELS THAT WE'VE SHOWN EFFICACY IN SPILLING OUT BETWEEN THE TWO DISEASE. SO, YEAH, THERE IS A RELATIONSHIP, AND THERE IS A BENEFIT TO THE ALS PROJECT. IF WE HAVE THIS GOING ALONG BESIDE IT, WE'LL INCREASE THE SAFETY PROFILE OF THE CELLS IN THE DISORDER FROM OUR PRECLINICAL STUDIES, AND WE'LL LEARN A LOT MORE ABOUT THE PROCESS OF TAKING THESE CELLS THROUGH THE REGULATORY SYSTEM. WE'RE NOT THERE YET IN ALS. WE'RE IN THE MIDDLE OF IT.

MR. SHEEHY: SO IF WE FUND YOU FOR THOSE, ARE YOU WILLING TO REDUCE YOUR ALS BUDGET TO CAPTURE THOSE SYNERGIES?

DR. SVENDSEN: LOOK, WHEN I FIRST PUT IN A DISEASE TEAM GRANT THREE YEARS AGO, I SAID WE SHOULD BE DOING THREE DISEASES. WE SHOULD BE DOING STROKE, ALS, AND RETINITIS PIGMENTOSA. CIRM REGULATIONS WERE WE HAD TO DO ONE DISEASE PER DISEASE TEAM. I REALLY FEEL THERE'S AN ENORMOUS SYNERGY IN EACH DISEASE TEAM GRANT TO HELP OTHER DISEASES. THEY'RE NOT INDEPENDENT. SO, YES, I WOULD BE WILLING TO TAKE A SLIGHT REDUCTION IN THE ALS FUNDING TO GET THE SYNERGY GOING AND HAVE THE TWO GRANTS RUNNING BESIDE EACH OTHER.

MR. SHEEHY: I LEAVE THIS TO STAFF TO PROVIDE SOME SORT OF FEEDBACK. AND THEN, OF COURSE, EACH MEMBER WILL HAVE TO MAKE THEIR OWN DECISION ON HOW THEY FEEL ABOUT MOVING THIS FORWARD.

DR. FEIGAL: CAN I MAKE A COMMENT?

DR. TROUNSON: WELL, I'VE BEEN LISTENING THROUGH ALL OF THIS. I THINK YOU COULD MAKE THESE ARGUMENTS FOR A LOT OF CASES, TO BE HONEST. I THINK YOU NEED TO BE CAREFUL THAT WE ARE SORT OF STICKING WITH THE PROJECT. IT IS REALLY ABOUT A CORRECTION OF BLINDNESS, AND IT'S NOT ABOUT ALS. AND THE PROBABILITIES THAT THIS WILL IMPACT ALS, YOU COULDN'T REALLY COMPUTE THAT, TO BE HONEST.

SO IT SHOULD BE REALLY ABOUT THE EYE PROJECT AND HOW THESE CELLS MIGHT HELP THE EYE PROJECT. AND I THINK YOU'VE HEARD THE EVIDENCE. IT JUST SEEMS THAT IF YOU SPREAD THE ARGUMENT TOO FAR OUT, IT MAKES A CASE FOR THESE ARGUMENTS TO GO ON FOR A LOT OF OTHER CONDITIONS. AND I'D BE A LITTLE -- I WOULD BE VERY CONCERNED ACTUALLY ABOUT THAT BEING SOMETHING THAT WE WOULD HAVE TO CONSIDER IN THE FUTURE.

MR. SHEEHY: DR. FEIGAL.

DR. FEIGAL: MS. WINOKUR, AS YOU MENTIONED EARLIER, WILL WE WORK WITH THE TEAM, I'VE ALREADY AT

THIS CONFERENCE CONTACTED THE PI, DR. KENT SMALL. HE HAS A WAY TO GET BACK. WE'RE GOING TO ARRANGE A FOLLOW-UP NEXT WEEK TO TALK ABOUT THE ISSUES FROM THIS REVIEW THAT HE COULD POTENTIALLY ADDRESS, INCLUDING THE SCIENTIFIC, THE CLINICAL TRIAL DESIGN, IN ADDITION TO THE REGULATORY. AND WE'RE VERY RECEPTIVE TO WORKING WITH THEM TO SEE IF WE CAN ADDRESS THOSE ISSUES SO THAT SUBSEQUENTLY HE CAN REVISE IT, ADDRESS THE ISSUES. AND WE WILL HAVE ANOTHER WINDOW TO COME BACK IN.

SO I JUST WANT TO LET YOU KNOW THAT, THAT WE ARE IMMEDIATELY FOLLOWING UP WITH THE TEAM IN RESPONSE TO THE ISSUE THAT YOU RAISED.

MS. WINOKUR: AND WILL YOU TAKE INTO ACCOUNT THE POSSIBILITY OF THERE BEING SOME HELP FOR ALS AS A RESULT OF DEVELOPING THE NEURAL STEM CELL TRANSFER?

DR. FEIGAL: THAT'S A MORE COMPLICATED QUESTION. WE DO HAVE A FULL PROJECT WITH HIM ON ALS WHERE IT'S GENE MODIFIED, AND YOU'RE VERY FAMILIAR. BUT CERTAINLY WE CAN HAVE A DISCUSSION ABOUT HOW THIS COULD HELP ALS. OKAY.

MS. WINOKUR: THEN SHALL I WITHDRAW THE MOTION?

MR. SHEEHY: YOU WOULD HAVE TO GET THE

CONCURRENCE OF YOUR SECOND, WHICH IS DR. QUINT, I BELIEVE.

DR. QUINT: I AGREE.

MR. SHEEHY: SO THE MOTION IS WITHDRAWN. OKAY. THERE YOU GO.

SO CAN WE GO TO THE NEXT RECOMMENDATION? AND I THINK --

MR. ROWLETT: JUST ONE QUICK COMMENT TO STAFF. THIS CONVERSATION, WHILE IT WAS A BIT TIME INTENSIVE, IS VERY HELPFUL IN UNDERSTANDING THE PROCESS. AND WHILE I VOTED YES TO SUPPORT THE STAFF RECOMMENDATION, I ALSO, AS A MEMBER OF THE PATIENT ADVOCATE COMMUNITY, APPRECIATE DIANE'S APPROACH TO THIS. AND, AGAIN, IT IS A HELP TO ME TO APPRECIATE WHAT COULD HAPPEN WHEN YOU SEE A POTENTIAL FOR, I.E., I'LL SPEAK VERY GLOBALLY, PARTIALLY FUNDING A PROJECT. AND SO THANK YOU.

MR. SHEEHY: WE HAVE DONE SO IN THE PAST, BUT USUALLY WE'RE ABLE TO TEASE OUT A VERY DISCRETE SET OF ACTIVITIES. AND SINCE WE'VE INTRODUCED THIS NEW PROCESS WITH STAFF, STAFF HAS HAD THE ABILITY TO REALLY TO DO THAT AND ADDRESS MAYBE THOSE ONE OR TWO FATAL FLAWS. AND WE'VE ALSO ENCOURAGED THE WORKING GROUP TO TAKE THAT ON AS WELL. SO WE ARE TRYING TO BE NIMBLE.

SO, AGAIN, WE'RE GOING TO THE NEXT PROJECT. I'M GOING TO PASS THE CHAIR TO DR. STEWARD FOR THIS ONE BECAUSE I WOULD LIKE TO MAKE THE MOTION ON THIS ONE. DR. STEFFEN. SO THIS IS SEVEN OH --

DR. STEFFEN: 7078. AND THE TITLE OF THE APPLICATION IS "EMBRYONIC STEM CELL-DERIVED CHRONDROPROGENITOR CELLS TO REPAIR OSTEOCHONDRAL DEFECTS."

THE DISEASE TARGET THAT THE APPLICANT IS ADDRESSING IS DEFECTS IN THE CARTILAGE, OSTEOCHRONDRAL DEFECT. AND THEIR APPROACH IS TO USE ALLOGENEIC HESC, HUMAN EMBRYONIC STEM CELL-DERIVED, CHONDROCYTE PROGENITORS ALONG WITH A BIOLOGIC SCAFFOLD.

AND THE PROGRAMMATIC POINTS FOR CONSIDERATION, WE DID LOOK AT OUR TRANSLATIONAL PORTFOLIO TABLE TO ANSWER YOUR QUESTION IN THE CONTEXT OF NUMBERS. THERE ARE TWO EXISTING TRANSLATIONAL AWARDS. I'LL DETAIL THEM IN THE RECOMMENDATION. AND THIS WOULD ADD THE THIRD. SO THERE WOULD BE THREE TOTAL.

THE PROJECT, AGAIN, LEVERAGES A TEAM AND THE KNOW-HOW GAINED IN A COMPLETED EARLY TRANSLATIONAL PROJECT, A PRIORITY AREA FOR THE RFA. AND WITH RESPECT TO THE PORTFOLIO, THIS PROJECT IS

AT THE MOST ADVANCED DEVELOPMENT STAGE OF THESE PROJECTS IN THE CIRM PORTFOLIO TARGETING CARTILAGE DISORDERS. IT UNIQUELY FOCUSES ON A PLURIPOTENT DERIVED PROGENITOR CELL.

DR. ABO IS GOING TO ADDRESS, IF YOU WOULD LIKE HIM TO, IN HIS SCIENTIFIC PRESENTATION WHY THE PLURIPOTENT CELL IS IMPORTANT IN THIS PARTICULAR CASE.

THE OTHER TWO AWARDS, AN EARLY TRANSLATIONAL DEVELOPMENT CANDIDATE FEASIBILITY AWARD -- LET ME REMIND YOU THAT IS A VERY EARLY AWARD TO DEMONSTRATE THAT THERE MIGHT BE BIOLOGIC ACTIVITY. IT'S PROOF OF CONCEPT IN A PRECLINICAL MODEL -- WAS RECENTLY FUNDED TO DEVELOP AN AUTOLOGOUS SKIN-ISOLATED STEM CELL-DERIVED TISSUE-ENGINEERED PRODUCT FOR FOCAL CARTILAGE DEFECTS, JUST BEGUN. AND ANOTHER EARLY TRANSLATIONAL AWARD IS A SMALL MOLECULE DESIGNED TO INDUCE CHONDROCYTE DIFFERENTIATION IN MESENCHYMAL STEM CELLS THAT ARE RESIDENT IN THE HOST FOR THE TREATMENT OF OSTEOARTHRITIS. SO DIFFERENT PROJECTS.

THERE ARE NO FUNDED DISEASE TEAM AWARDS OR STRATEGIC PARTNER AWARDS IN THE CIRM PORTFOLIO IN CARTILAGE DISORDERS.

THAT CONCLUDES THE STAFF RECOMMENDATION.

DR. STEWARD: THANK YOU. OPEN TO MOTIONS.

MR. SHEEHY: I WOULD LIKE TO MOVE TO REJECT STAFF RECOMMENDATION NOT TO FUND IT, AND I WILL EXPLAIN AND HOPEFULLY I WILL GET A SECOND.

DR. JUELSGAARD: I SECOND.

MR. SHEEHY: OH, GREAT. THANKS. THAT'S FASTER.

THE PROBLEM IS -- AND I'M ACTUALLY INDICATED FOR THIS PARTICULAR PRODUCT. I'M DUE FOR A KNEE REPLACEMENT, SUPPOSED TO HAVE IT LAST YEAR ABOUT THIS TIME, AND A SERIES OF UNFORTUNATE EVENTS PREVENTED THAT FROM HAPPENING. THE PROBLEM WITH THIS IS THAT THIS IS A PLURIPOTENT CELL SOURCE. AND SO AT MINIMUM THIS IS FIVE YEARS FOR A PHASE I, AND THERE ARE A HOST OF OTHER TREATMENTS AVAILABLE FOR THIS. AND AS ONE OF THE REVIEWERS SAID, YOU KNOW, THERE'S A CELL THERAPY AVAILABLE FOR THIS FROM GENZYME CALLED CARDICELL. IT WAS APPROVED IN 1997, AND THAT'S NOT WIDELY TAKEN UP BECAUSE THERE'S A TREATMENT THAT PEOPLE USE, A MICROFRACTURE, THAT OFFERS OUTCOME FOR A VAST MAJORITY OF PATIENTS.

AND THE REVIEWER, WHO ALSO, BY THE WAY, SUFFERS FROM OSTEOARTHRITIS, MADE A POINT OF THAT AND IS VERY FOND OF SAYING, YOU KNOW, I WISH WE'D BE FOCUSING ON TREATING REALLY SERIOUS INCURABLE

DISEASE AND NOT MAKING IT POSSIBLE FOR MIDDLE-AGED WEEKEND ATHLETES TO GET BACK OUT THERE ON THE TENNIS COURT.

THIS IS 15 OR 20 YEARS FROM GOING INTO A PATIENT. AND, AGAIN, WITHIN THIS WHOLE FRAMEWORK OF TRYING TO MAKE A DIFFERENCE IN SERIOUS DISEASES TO FULFILL THE MANDATE OF PROP 71 AND TO BE GOOD SHEPHERDS OF THE FUNDS THAT WE'VE BEEN GIVEN, I THINK THIS IS ONE WE SHOULD PASS ON. IT'S VERY HARD TO, FRANKLY, BECAUSE EMOTIONALLY I WANTED TO DO THE APPLICATION THAT MS. WINOKUR WAS PUSHING FOR. AND I AGREE. I HAVE TO TAKE THE ADVICE OF STAFF AND THE REVIEWERS ON THAT, BUT AT LEAST I'M TRYING TO MAKE A DIFFERENCE IN A SERIOUS CONDITION IN SOMEBODY'S LIFE IF I MAKE THAT BET.

HERE, I'M PUTTING DOWN A LOT OF MONEY TO START A PROCESS THAT'S GOING TO LAST A VERY LONG TIME. AND EVEN WHEN IT GETS THERE, IT'S NOT GOING TO MAKE A DRAMATIC DIFFERENCE IN PEOPLE'S LIVES. IT'S PROBABLY GOING TO BE A VERY EXPENSIVE PROCEDURE FOR WHICH THERE'S ALREADY A LOT OF TREATMENTS AVAILABLE. AND, AGAIN, WE DON'T HAVE AN INFINITE AMOUNT OF MONEY. THIS IS WHAT I MEAN BY PRIORITIZATION, THAT SOME THINGS DON'T NEED TO GO FORWARD. LET'S SAVE OUR MONEY FOR THINGS -- THINK

ABOUT WHAT HAPPENS IF WE RUN OUT OF MONEY BEFORE THIS SICKLE CELL PROJECT IS IN PHASE III. THAT WOULD BREAK MY HEART. SO LET'S SAVE OUR POWDER ON THIS ONE. THAT'S MY ARGUMENT. PURELY PROGRAMMATIC, BY THE WAY.

DR. STEWARD: THANK YOU. OTHER COMMENTS?

CHAIRMAN THOMAS: I'D LIKE TO HEAR STAFF'S RESPONSE TO THAT.

DR. STEFFEN: DR. ARI ABO IS GOING TO GIVE THE SUMMARY OF THE GRANTS WORKING GROUP RECOMMENDATION.

DR. ABO: HI. MY NAME IS ARI ABO. I'M SCIENCE OFFICER ON THE TRANSLATIONAL TEAM, AND I HAVE SOME PROJECTS IN DISEASE TEAM. SO JUST TO PUT THIS IN CONTEXT, THIS PROJECT, WE SUPPORTED IT FOR THE LAST THREE YEARS UNDER THE EARLY TRANSLATION INITIATIVE. AND I WAS THE PROGRAM OFFICER WORKING WITH THE PI ON THIS INDICATION. SO THEY WORKED VERY CLOSELY WITH US TO REALLY MOVE TO DEVELOP A DEVELOPMENT CANDIDATE, A DC CANDIDATE, THAT POTENTIALLY COULD MOVE TO CLINICAL DEVELOPMENT.

AND THROUGH THE PROCESS, WE STARTED WITH VARIOUS CELLS AND THEN DID PROOF OF CONCEPT AND REALLY SHOWED DISEASE MODIFYING ACTIVITY WITH THIS PARTICULAR DEVELOPMENT CANDIDATE. AND THEN WE

RECOMMENDED THE APPLICANTS TO APPLY FOR THE DISEASE TEAM UNDER THE EARLY TRANSLATION PATH.

SO HAVING SAID THAT, I WILL GO THROUGH SOME OF THE ISSUES THAT THE REVIEW RAISED, SOME CAPTURED BY MR. SHEEHY. AND THERE WAS UNANIMOUS AGREEMENT BY REVIEWERS THAT THE DATA, THE PRECLINICAL DATA, WAS IMPRESSIVE. AND THE REASON WE GOT EXCITED ABOUT SOME OF THIS PRECLINICAL DATA AND THE DATA THAT WAS SUPPORTED BY THE APPLICANT IS THIS IS THE FIRST EXAMPLE OF USING EMBRYONIC STEM CELL-DERIVED CHRONDROPROGENITOR CELL THAT MAKES A VERY HIGH QUALITY OF CARTILAGE. AND THIS IS BASED ON THE APPLICATIONS.

IF YOU GO BACK TO THE APPLICATION, THERE IS DATA THERE COMPARING THE ACTIVITY OF THESE CELLS DERIVED TO EXISTING CELLS THAT'S USED FOR SIMILAR THERAPIES, SUCH AS MSC'S AND EVEN HUMAN CHONDROCYTES. SO IT SEEMS THAT THE CELLS THAT WERE THE EMBRYONIC STEM CELL-DERIVED THAT WAS SELECTED TO BECOME A CARTILAGE PRECURSOR CELL SEEMS TO BE MAKING THE RIGHT CARTILAGE, WHICH IS ARTICULAR CARTILAGE, AND THEY HAVE THE RIGHT STIFFNESS THAT IS REQUIRED FOR THIS KIND OF INDICATION, TO REPAIR FOCAL CARTILAGE LESIONS.

SO THAT'S VERY EXCITING. THE REVIEWERS --

NEVERTHELESS, REVIEWERS WERE RAISING THIS ISSUE ABOUT COMPETITIVENESS OF THIS APPROACH, ASSUMING, AS MR. SHEEHY SAID, THAT THERE ARE SEVERAL PRODUCTS IN THE MARKET THAT ARE ACTUALLY USED FOR THESE KIND OF INDICATIONS. AND THIS IS TRUE. THERE ARE SEVERAL PRODUCTS IN THE MARKET AND SEVERAL IN DEVELOPMENT TO TREAT FOCAL CARTILAGE DEFECTS. HOWEVER, THE MAIN ISSUE, AS ADDRESSED BY THE APPLICANTS, ARE THAT THE CURRENT APPROACH TYPICALLY GENERATES A THERAPY. THE DURABILITY OF THE APPROACH IS NOT VERY LONG AND REQUIRES ADDITIONAL THERAPIES FOR THIS. OKAY.

SO THAT'S ESSENTIALLY WHAT THE MAIN ISSUE THAT WAS RAISED BY THE REVIEWERS, THE COMPETITIVENESS OF THIS MOLECULE ASSUMING THERE'S OTHER PRODUCTS.

ANOTHER CONCERN THE REVIEWERS RAISED IS THE ISSUE ASSOCIATED WITH TREATING PATIENTS FOR NONLIFE-THREATENING DISEASES WITH PLURIPOTENT STEM CELLS. AND JUST A REMINDER, THIS APPLICATION IS REQUIRED TO FUND PRECLINICAL STUDIES ALL THE WAY TO IND, NOT TO GO TO CLINICAL DEVELOPMENT. PART OF THE PROPOSAL WAS TO CONDUCT TOXICITY AND SAFETY STUDIES.

OVERALL THERE WAS ENTHUSIASM FOR THE APPLICATION, AND THE SCIENCE SOUNDS -- VERY EXCITING PRELIMINARY DATA. THE TEAM SEEMS TO BE VERY STRONG

AND THE COLLABORATIVE AND THE INSTITUTION SEEMS TO BE THE RIGHT PLACE TO THIS SUPPORT THIS STUDY.

DR. STEWARD: THANK YOU. OTHER BOARD COMMENTS?

MR. TORRES: YES.

DR. STEWARD: I THINK THAT'S ART.

MR. TORRES: YES. YES, IT IS. I WANT TO ASSOCIATE MYSELF HALFWAY WITH JEFF SHEEHY'S REMARKS, BUT ALSO I KNOW THE IMPETUS FOR THE PASSAGE OF PROPOSITION 71 BY THE VOTERS WAS TO LOOK FOR CURES FOR INCURABLE DISEASES. BUT WE ALSO HAVE TO KEEP IN MIND THAT THERE'S SUCH A LARGE POPULATION OF THOSE OF US WHO ARE CHRONOLOGICALLY GIFTED WHO MAY NEED THIS KIND OF TREATMENT IN THE FUTURE TO CONTINUE TO LEAD PRODUCTIVE LIVES. AND A LOT OF THOSE PEOPLE WERE ALSO VOTERS FOR PROPOSITION 71 AND MIGHT BE ABLE TO BENEFIT IN THEIR OWN LIVES AS I HEAR SO MANY ANECDOTAL RESPONSES TO PEOPLE WHO ARE LOSING THEIR ABILITY TO WALK, LOSING THEIR ABILITY TO FUNCTION THAT MIGHT SOMEDAY BENEFIT FROM THIS TYPE OF TREATMENT.

AND THAT'S WHY I WOULD SUPPORT THE STAFF RECOMMENDATION TO FUND, WITH ALL DUE RESPECT.

DR. STEWARD: THANK YOU.

DR. JUELSGAARD: SO I ACTUALLY AM VERY

SUPPORTIVE OF WHAT JEFF WAS TALKING ABOUT EARLIER. SO I HARKEN BACK TO YESTERDAY'S DISCUSSION WHICH WE HAD IN QUITE SOME DETAIL ABOUT PRIORITIZATION, WHICH HAS BEEN INFORMING MY DECISION-MAKING THIS MORNING, INCLUDING VOTING AGAINST THE PREVIOUS PROJECT THAT WAS APPROVED IN SICKLE CELL ANEMIA, NOT BECAUSE I DON'T THINK IT'S A WORTHY CAUSE, BUT BECAUSE, FROM MY POINT OF VIEW IN THE PRIORITIZATION DISCUSSION, IT SUFFERS FROM SOME PROBLEMS.

AND IT'S ONE OF THOSE THINGS WE'RE GOING TO HAVE TO START WRESTLING WITH SOONER RATHER THAN LATER. SO ONE OF THE PROBLEMS WE'RE GOING TO RUN INTO WITH LIMITED AMOUNT OF RESOURCES IS WE'RE GOING TO AT SOME POINT NOT HAVE THE FUNDS TO CONTINUE PROJECTS THAT MAY WELL VERY MUCH DESERVE CONTINUATION, BUT WE WON'T HAVE THE FUNDS FOR IT AND IT WILL BE VERY DIFFICULT FOR THEM TO FIND FUNDS ANYWHERE ELSE BECAUSE OF THE NATURE OF THE PROBLEM, THE SIZE OF THE DISEASE POPULATION, ETC. AND IT'S A LITTLE HARD TO PREDICT WHAT THOSE MIGHT BE. BUT IN ANY EVENT, THAT'S A PARTICULAR PROBLEM.

SO I'M IN THIS CASE EVEN MORE TO ONE SIDE IN TERMS OF THE CONDITION THAT IT'S AIMED AT, AND IN PARTICULAR IN THE FACT THAT THERE ARE ALTERNATIVE THERAPIES, AS JEFF HAS POINTED OUT, PARTICULARLY IN

THE DEVICE AREA, FOR SOME OF THESE PROBLEMS. SO I VERY MUCH AM A STRONG BELIEVER THAT WE NEED TO START EXERCISING BUDGET RESTRAINT, AND WE NEED TO START EXERCISING IT NOW. THAT'S MY POINT OF VIEW, AND THAT'S WHY I'M OPPOSED TO THIS ONE AND WHY I WAS OPPOSED TO THE PREVIOUS ONE. AND I FROM HERE ON OUT VERY MUCH WILL BE VIEWING ALL OF THESE PROPOSALS AS MUCH FROM AN OVERALL BUDGET CONSIDERATION AS SORT OF INDIVIDUAL MERIT.

DR. STEWARD: THANK YOU. DR. FINE.

DR. FINE: I DON'T HAVE ANY PROBLEMS WITH EITHER OF MY KNEES TO DECLARE. THE ECONOMIC BURDEN OF THIS PROBLEM IS ASTRONOMICAL. AND I THINK IT'S HIGHLY LIKELY THAT IF APPROACH, THIS THERAPEUTIC APPROACH, DOES EVOLVE, THAT IT WILL BE EMPLOYED NOT WHEN PEOPLE NEED KNEE REPLACEMENTS OR MICROFRACTURES, BUT WELL IN ADVANCE OF THAT WHEN THE EARLY SIGNS OF OSTEOARTHRITIS ARE EVIDENT. AND THESE CAN NOW BE PICKED UP BY ALL SORTS OF NONINVASIVE IMAGING TECHNIQUES.

SO THE BENEFIT TO SOCIETY COULD BE SUBSTANTIAL, AND I THINK THAT, ON THE BASIS OF THE ECONOMIC ARGUMENT, I WOULD JUST WISH TO POINT THAT OUT.

DR. STEWARD: THANK YOU. JEFF.

MR. SHEEHY: I THINK DR. FINE JUST MADE MY ARGUMENT FOR ME IN PART. I HAD A TWO-PART ARGUMENT. YOU'RE NOT GOING TO PUT A PLURIPOTENT SOURCE INTO THOSE PATIENTS. YOU'RE JUST NOT, NOT FOR 20 YEARS. WHY WOULD YOU GET SOMEBODY WHO HAD VERY LITTLE RESTRICTION IN THEIR ABILITY TO DO ANYTHING, WHY YOU WOULD YOU GO IN THERE WITH SOMETHING THAT COULD CAUSE HORRENDOUS CANCERS? THE PROBLEM HERE IS THAT IT'S A PLURIPOTENT SOURCE. AND THOSE ARE ONLY -- THE DEVELOPMENT PATHWAY FOR THAT IS GOING TO NEED TO GO DOWN, I THINK, A MORE SERIOUS DISEASE CONDITION ROUTE BEFORE WE START DOING IT.

I AGREE WITH YOU. THIS MIGHT BE A GREAT PROJECT DOWN THE ROAD. BUT FOR US WITHIN OUR TIME FRAME THIS PROJECT IS NOT, I THINK, GOING TO BE REALIZED CERTAINLY WITHIN THE LIFE OF OUR CURRENT FUNDING AND HIGHLY UNLIKELY, 15 TO 20 YEARS. YOUR INDICATION FOR THIS DISEASE SOUNDS GREAT, BUT YOU WOULD NEVER PUT IN PLURIPOTENT DERIVED CELLS IN THE NEXT FIVE TO TEN YEARS IN SOMEBODY IN THAT STATE.

MY SECOND POINT GOES TO THE ACTUAL REVIEW AND THE REVIEWERS. IF YOU LOOK AT THE DISTRIBUTION OF SCORES, THE HIGHEST SCORE WAS A 75. AND THIS, AGAIN, GOES TO MR. JUELSGAARD'S ARGUMENT. THERE WAS NOBODY WHO WAS DOING HANDSTANDS ON THIS GRANT. THE

HIGHEST SCORE WAS AT THE VERY BOTTOM OF THE FUNDABLE CATEGORY. AND PEOPLE WERE VERY CLEAR. IF YOU THINK THIS SHOULD BE FUNDED, FUND IT 75 AND ABOVE. SO ONE PERSON KIND OF WENT, ANH, 75. SO THE LEVEL OF ENTHUSIASM, EVEN IF WE TAKE ALL THE OTHER ARGUMENTS, THIS IS JUST NOT NECESSARILY THE GREATEST PROJECT. AND GIVEN ALL THOSE ISSUES AND THE LIMITATIONS ON OUR FUNDING AND THE THINGS THAT WE'RE GOING TO HAVE TO TALK ABOUT, I THINK, IN THE NEXT YEAR AND A HALF TO TWO YEARS NOT DOING, I THINK THIS IS SOMETHING WE CAN PASS ON.

IF THEY DO INDEED HAVE GREAT CELLS, THEN THEY SHOULD COME BACK WITH A PROJECT IN A SERIOUS DISEASE THAT THEY CAN MAKE A BIG IMPACT ON. I THINK THAT WAS BROUGHT UP BY THE REVIEWERS. THEY COULD HAVE TARGETED SOMETHING ELSE. THIS IS JUST THE MOST LUCRATIVE PLACE THEY COULD IMAGINE TO TARGET. WE'RE NOT REALLY HERE TO DO THAT. WE'RE HERE TO REALLY MAKE A DIFFERENCE IN SERIOUS DISEASES AND CONDITIONS.

DR. STEWARD: I'M JUST GOING TO TAKE THE TEMPORARY CHAIR'S PREROGATIVE AND ADD TO THAT. I ACTUALLY ALREADY HAVE HAD MY HIP REPLACEMENT. THANK YOU VERY MUCH. PLANNING TO GO SNOWBOARDING NEXT WEEK. DOING FINE. ALSO, SPINE SURGERY AND SHOULDER

SURGERY TOO. I TOTALLY AGREE. THERE'S REALLY GOOD TREATMENTS OUT THERE RIGHT NOW.

ONE OF THE POINTS THAT'S MADE, AGAIN, THIS IS GOING TO BE SOMETHING THAT'S INJECTED INTO PEOPLE WHO ARE REALLY ALREADY PRETTY HEALTHY, AND THE BAR IS GOING TO BE REALLY HIGH TO DO THAT IN OTHERWISE PRETTY HEALTHY PEOPLE. SO I'M SUPPORTING EVERYTHING THAT YOU'VE ALREADY SAID ON THAT.

I DO THINK, ALSO, JUST TO MENTION, THAT THERE IS A LUCRATIVE MARKET OUT THERE. PEOPLE WHO WOULD BE INTERESTED IN THIS ARE ABLE TO PAY. I THINK THIS IS SOMETHING THAT COMPANIES COULD DEVELOP PRETTY EASILY IF THAT REALLY LOOKED LIKE THE WAY TO GO. I'M SORRY TO TAKE CHAIR'S PREROGATIVE, BUT ANY OTHER COMMENTS BY THE BOARD? J.T.

CHAIRMAN THOMAS: I THINK THIS ISSUE OF COMPETITIVE LANDSCAPE IS A BIG ISSUE. ONE OF THE THINGS THAT CAUSED ME TO BE TORN ON THE RETINITIS PIGMENTOSA GRANT IS THERE ARE OTHER TECHNOLOGIES GOING FORWARD, BUT THERE AREN'T COMPETITIVE PRODUCTS OUT THERE. AND THE QUESTION OF HAVING A BUNCH OF DIFFERENT SHOTS ON GOAL IS VERY DIFFERENT FROM HAVING A TECHNOLOGY THAT'S COMPETING AGAINST WAYS TO DEAL WITH THINGS THAT ARE ALREADY ESTABLISHED, WHICH IS WHAT WE HAVE HERE.

SO I THINK THAT THIS IS AN INSTANCE WHERE WE HAVE TO PAY ATTENTION TO THE COMPETITIVE LANDSCAPE ASPECT, PARTICULARLY GIVEN THE NONLIFE THREATENING, THOUGH DEBILITATING, AND I APPRECIATE ALL WHAT ART HAD TO SAY AND WHAT LEON HAD TO SAY AS WELL, BUT HERE AT THE TIME OF PRIORITIZATION, I THINK THAT THE COMPETITIVE LANDSCAPE ISSUE, IN MY OPINION, IS A VERY MATERIAL THING TO CONSIDER.

DR. STEWARD: THANK YOU. OTHER BOARD COMMENTS? PUBLIC COMMENT?

DR. OLSON: I'D JUST LIKE TO MAKE ONE COMMENT ABOUT THE COMPETITIVE LANDSCAPE. CARDICELL, WHICH HAS BEEN CITED BY SOME PEOPLE, IS NOT VERY WELL TAKEN UP BECAUSE IT'S NOT A VERY GOOD PRODUCT. IT MAKES FIBROUS CARTILAGE, AND IT DOESN'T DO A VERY GOOD JOB. THE CARTILAGE GRAFTS, WHICH IS THE OTHER OPTION, AGAIN, IT'S A FIBROUS CARTILAGE THAT USUALLY NEEDS TO BE REPLACED WITHIN A FEW YEARS.

THIS IS THE ONLY CELL TYPE THAT BASICALLY HAS BEEN ABLE TO GENERATE AN ARTICULAR CARTILAGE CHONDROCYTE IN COMPARATIVE STUDIES WITH OTHER CELLS. I APPRECIATE THE ISSUE THAT IT IS A PLURIPOTENT CELL, BUT PART OF WHY WE WERE PUT HERE WAS ESSENTIALLY TO FIGURE OUT HOW TO USE EMBRYONIC STEM CELLS. AND PART OF WHAT -- AS PEOPLE -- I WILL

AGREE THAT THE FDA WILL OBVIOUSLY SET A BAR FOR SAFETY AND WHAT HAVE YOU, BUT WE ARE SEEING NOW THAT PEOPLE ARE USING -- TALKING ABOUT USING EMBRYONIC-DERIVED CELLS IN NONLIFE THREATENING INDICATIONS WITH MORBIDITIES AND SUCH.

SO I WOULD RESPECTFULLY DISAGREE WITH THE 15 TO 20 YEARS BEFORE IT WILL EVER GET INTO THE CLINIC. BUT I JUST AM POINTING OUT THAT IT'S THE UNIQUE INSTANCE OF A CELL THAT'S BEEN ABLE TO GENERATE THE CELL THAT IS UNIQUE IS NEEDED. SO THAT'S ALL I WANTED TO SAY.

MR. SHEEHY: CAN I RESPOND? SO ARE YOU WILLING TO GIVE UP SOMETHING ELSE IN THE PORTFOLIO THAT YOU CAN CONTROL TO FUND THIS? ARE YOU WILLING TO GIVE UP ONE OF THE BASIC BIOLOGY ROUNDS TO FUND THIS?

DR. OLSON: I DON'T THINK I REALLY NEED TO DO THAT. I DON'T KNOW THAT THIS IS THAT DRAMATIC A TRADE-OFF. I THINK IT IS A -- WHERE DO YOU THINK WE CAN MAKE A DIFFERENCE?

MR. SHEEHY: THESE ALL ARE TRADE-OFFS, AND THAT'S WHAT WE'RE TRYING TO DO. IT'S EASY TO COME UP AND ARGUE THAT THESE ARE GREAT CELLS, BUT THEY'RE GOING INTO PEOPLE'S KNEES. IF YOU ARE GOING TO ARGUE FOR THIS, I WOULD LOVE TO DO THE HAPLOTYPE

BANK. I THINK THAT'S A GREAT PROJECT. WE'RE GOING TO HAVE TO START MAKING THESE CHOICES, AND I THINK IT'S HARD IF YOU ARE GOING TO ARGUE FOR THE INDIVIDUAL PROJECT IF YOU'RE NOT GOING TO PUT SOMETHING ON THE TABLE THAT YOU'RE NOT WILLING TO DO TO ARGUE FOR AN INDIVIDUAL PROJECT.

DR. FEIGAL: CAN I JUST MAKE ONE COMMENT AND THEN I'LL DEFER? I THINK THE MAIN POINT OF DR. OLSON'S COMMENT WAS THE UNIQUE ABILITY OF THIS CELL TYPE TO MAKE THE TYPE OF CARTILAGE, AND THE QUALITY OF CARTILAGE WAS IMPORTANT, WHICH IS AN IMPORTANT ADVANCE. THAT'S ALL I'M GOING TO SAY.

DR. STEWARD: OKAY. I THINK WE'VE EXHAUSTED BOARD COMMENT. WE DO HAVE PUBLIC COMMENT. BOB KLEIN.

MR. KLEIN: I HAD NO INTENT OF COMMENTING TODAY, BUT I THINK ON A PORTFOLIO BASIS I'D LIKE TO ADDRESS THIS ISSUE BECAUSE I'VE NOT STUDIED THIS INDIVIDUAL GRANT. AND ON A PORTFOLIO BASIS, I'D MUCH RATHER HAVE MY SON HAVE A CELL TYPE FOR TYPE 1 DIABETES DERIVED FROM HUMAN EMBRYONIC STEM CELLS, FROM IPS CELLS, WHICH I THINK THERE'S SOME SUBSTANTIAL DOCUMENTATION ON REAL DIFFERENCES FROM THOSE DERIVED CELL TYPES AS COMPARED TO BEING DERIVED FROM EMBRYONIC STEM CELLS.

IN ADDITION, I THINK THERE'S GOING TO BE A PUBLICATION, AN SCNT PUBLICATION, IN A VERY PRESTIGIOUS MAGAZINE SHORTLY THAT COMPARES SCNT-DERIVED CELL TYPES WITH CELLS DERIVED FROM IPS CELLS WHICH IS GOING TO SHOW SOME SUBSTANTIAL DIFFERENCES. I THINK IT'S VERY IMPORTANT IN TERMS OF OUR SPECIFIC CHARTER TO BE ABLE TO BE PROVING OUT CELL TYPES THAT QUALITATIVELY IMPROVE MEDICINE THAT ARE DERIVED FROM HUMAN EMBRYONIC STEM CELLS.

THE READINESS OF THIS, AS I LISTEN TO THIS PRESENTATION, IS VERY IMPORTANT. THE QUALITATIVE IMPROVEMENT ON THE THERAPY IS VERY IMPORTANT. MY MOTHER HAD, BEFORE SHE DIED, A KNEE REPLACEMENT. AND I WILL TELL YOU THAT IN THE AGED POPULATION THIS IS A MASSIVE PROBLEM WITH HUGE, HUGE COSTS. THE FACT THAT WE HAVE A READINESS HERE, I THINK, IS VERY IMPORTANT. AND FROM WHAT I'VE READ, WHICH IS PERSONAL TO MY READING, THE SCIENTIFIC STAFF, I THINK, HAS A BETTER HANDLE ON THIS THAN I WOULD, BUT FROM WHAT I'VE TALKED TO THE SCIENTIFIC STAFF ABOUT AND LISTENED TO THIS PRESENTATION, I DON'T THINK BECAUSE IT'S DERIVED FROM A HUMAN EMBRYONIC STEM CELL IT'S 15 YEARS OUT.

WHEN IMPERIAL COLLEGE LONDON DID THE WORK FOR AGE-RELATED MACULAR DEGENERATION AND THEIR

PRECLINICAL WORK IN PIGS WITH HUMAN CELLS, THEY FOUND THAT, IN FACT, THERE WAS AN IMMUNE RESPONSE THAT IS IN THE LITERATURE PUBLISHED FOR IPS CELLS AND NOT AN IMMUNE RESPONSE FOR THE EMBRYONIC STEM CELL-DERIVED CELLS. AND THERE IS A SIGNIFICANT AMOUNT OF LITERATURE THAT SAYS THAT THAT DERIVATION IS MORE STABLE THAN PERHAPS SOME OF THE DERIVATIONS FROM IPS CELLS.

I WOULD SAY THE JUDGE AND JURY ARE STILL OUT ON THIS ISSUE. BUT FROM THE LITERATURE THAT I'VE SEEN TODAY, I THINK EMBRYONIC STEM CELLS ARE IMPORTANT TO OUR CHARTER. SEVEN MILLION PEOPLE SAID THEY WERE IMPORTANT TO OUR CHARTER. THIS HAS GOT QUALITATIVE VALUE IN AN AREA, THE COST TO SOCIETY, AS DR. FINE SAYS, MASSIVE AMOUNTS OF MONEY. IT'S VERY PREVALENT IN THE OLDER POPULATION. AND IF THIS IS A WAY TO GET TO RESULTS EARLY WITH A BROAD SCALE PROBLEM THAT THERE'S EVIDENCE THAT CAN GO FORWARD IN INTO PHASE II, EVEN IF IT GETS JUST THROUGH -- IF THERE'S GOOD EVIDENCE IT CAN GO THROUGH A PHASE III TRIAL, EVEN IF IT JUST GETS THROUGH A PHASE II TRIAL, I THINK IT IS A VERY IMPORTANT MILESTONE THAT MAY HELP YOU GET MORE MONEY IN THE FUTURE BECAUSE THE PUBLIC WILL SEE A RESULT THAT AFFECTS A LOT OF PEOPLE.

DR. STEWARD: THANKS, BOB. AND THANKS FOR STAYING WITHIN THE THREE-MINUTE TIME WINDOW. I REALLY APPRECIATE THAT. IT WOULD HAVE HURT ME TO CUT YOU OFF, BUT I WOULD HAVE DONE IT.

DR. TROUNSON: SO I JUST WANT TO INTRODUCE A COUPLE THINGS BECAUSE I THINK IT'S IMPORTANT THAT YOU HAVE ENOUGH INFORMATION THERE. THE WAY CELLS MIGHT BE DELIVERED FOR CARTILAGE, IT MIGHT BE THROUGH MSC'S, MESENCHYMAL STEM CELLS, AN ADULT STEM CELL, OR THROUGH IPS. I THINK IT'S ABSOLUTELY AGREED. I'VE BEEN TO THE INTERNATIONAL TISSUE ENGINEERING MEETINGS RECENTLY, AND EVERYBODY IS AGREED THAT THERE'S SOMETHING ABOUT EMBRYONIC STEM CELLS THAT CAN MAKE THE ARTICULATED CARTILAGE THAT THE OTHERS CAN'T. THEY CAN'T DO IT. AND UNLESS THEY'RE GOING TO PUT GENES IN TO MAKE THEM DO WHAT THE EMBRYONIC STEM CELLS -- THE EMBRYONIC STEM CELL WILL DO, THAT WILL BE THE WAY WHICH YOU WILL GO.

AND I THINK THERE ARE TEAMS THAT ARE SET UP IN JAPAN, FOR EXAMPLE, GOING WITH EMBRYONIC STEM CELL RATHER THAN IPS CELL, WHICH IS PRETTY INTERESTING IN JAPAN. SO NO DOUBT IT'S GOING TO GO THERE. PEOPLE ARE GOING TO GO THERE WITH THOSE CELLS BECAUSE IT'S THE ONLY ONE THAT MAKES ARTICULATED CARTILAGE. IF YOU CAN INJECT IT IN, IT

WILL WORK. THAT WILL BE A LOT EASIER THAN WHAT THEY DID TO YOU, TO BE HONEST.

I THINK IN THE END IT WILL BE DEVELOPED BY SOMEBODY, AND IT DOESN'T HAVE TO BE DEVELOPED BY US. THESE CELLS DON'T MAKE CANCERS, JEFF. THESE MAKE TERATOMAS IF YOU DON'T DO IT PROPERLY, AND WE DO THINGS PROPERLY. SO NO CELLS THAT WE PUT IN THE EYE, THE PANCREAS, ANYTHING FROM EMBRYONIC STEM CELLS OR IPS WILL EVER MAKE TERATOMAS, AND THEY WON'T MAKE CANCERS EITHER BECAUSE THEY DON'T DO THAT.

SO I THINK IT'S AN OPTION FOR THE BOARD REALLY TO SAY, OKAY, WE'LL PASS ON THIS. THAT'S FAIR ENOUGH. THAT'S ABSOLUTELY FAIR ENOUGH. AND I THINK ACTUALLY SOMEONE ELSE WILL DEVELOP IT, AND THAT'S FAIR ENOUGH TOO. WE CAN'T DO EVERYTHING, ABSOLUTELY EVERYTHING IN THE FIELD, BUT I JUST WANTED TO MAKE SURE YOU UNDERSTOOD MSC'S WON'T DO IT, THE CARDICELL STUFF DOESN'T TO IT, AND THE IPS CELLS DON'T LOOK LIKE THEY'RE DOING IT EITHER. BUT THE EMBRYONIC STEM CELLS APPARENTLY WILL DO IT, WHICH IS INTERESTING.

DR. STEWARD: THANK YOU FOR THAT. SO I THINK WE'VE EXHAUSTED THIS AND READY FOR A VOTE, I THINK.

MR. HARRISON: JUST AS A REMINDER, THE MOTION IS NOT TO FUND APPLICATION 7078.

MS. BONNEVILLE: ANNE-MARIE DULIEGE.

DR. DULIEGE: I AGREE.

MS. BONNEVILLE: MARCY FEIT. MICHAEL GOLDBERG.

MR. GOLDBERG: YES.

MS. BONNEVILLE: STEPHEN JUELSGAARD.

DR. JUELSGAARD: YES.

MS. BONNEVILLE: FRANCISCO PRIETO.

DR. PRIETO: AYE.

MS. BONNEVILLE: ROBERT QUINT.

DR. QUINT: YES.

MS. BONNEVILLE: AL ROWLETT.

MR. ROWLETT: YES.

MS. BONNEVILLE: JOAN SAMUELSON. JEFF SHEEHY.

MR. SHEEHY: YES.

MS. BONNEVILLE: OS STEWARD.

DR. STEWARD: YES.

MS. BONNEVILLE: JONATHAN THOMAS.

CHAIRMAN THOMAS: YES.

MS. BONNEVILLE: ART TORRES.

MR. TORRES: NO.

MS. BONNEVILLE: DIANE WINOKUR.

MS. WINOKUR: YES.

MR. HARRISON: MOTION CARRIES.

MR. SHEEHY: OKAY. SO I THINK WE'RE DUE FOR THE OMNIBUS MOTION NEXT AND PUBLIC COMMENT AROUND THE OMNIBUS MOTION, BUT I'M TOLD BY STAFF THAT WE NEED TO BREAK FOR LUNCH. YOU WANT TO DO THE OMNIBUS MOTION FIRST? SOMEBODY TELL ME HOW WE SHOULD DO IT.

MR. HARRISON: I'D SUGGEST SO THAT THE BOARD CAN HEAR PUBLIC COMMENT WHILE YOU'RE EATING LUNCH. IF YOU MAKE THE MOTION NOW AND THEN WE CAN GET LUNCH AND CAN COME BACK AND HEAR PUBLIC COMMENT BEFORE VOTING.

MR. SHEEHY: SO I NEED A MOTION FROM SOMEONE WHO'S UNCONFLICTED TO MOVE ALL THE APPLICATIONS -- TO FUND ALL THE APPLICATIONS IN TIER I AND TO NOT FUND ANY OF THE REMAINING APPLICATIONS. AM I CORRECT?

MR. TORRES: SO MOVED.

MR. GOLDBERG: I SECOND.

MR. SHEEHY: AND THEN WE'LL TAKE LUNCH AND TAKE ANY PUBLIC COMMENT THAT'S OUT THERE. SO LET'S GO GET LUNCH AND WE'LL BE BACK SHORTLY.

(A RECESS WAS TAKEN.)

MR. SHEEHY: SO IS EVERYBODY BACK IN THEIR

PLACES READY TO GO? I NEED TO MAKE A CLARIFYING POINT. SENATOR TORRES, ARE YOU ON THE LINE? I NEED TO MAKE A CLARIFICATION TO THE MOTION WHICH I BELIEVE WAS MADE BY SENATOR TORRES AND SECONDED BY MICHAEL GOLDBERG. AND THAT IS THAT IT IS TO FUND ALL THE APPLICATIONS THAT WE RECOMMENDED FOR FUNDING AND TO NOT FUND ANY OF THE OTHER APPLICATIONS EXCEPT FOR --

MR. HARRISON: 7201.

MR. SHEEHY: -- 7201 WHICH HAS BEEN REMOVED FROM CONSIDERATION IN THIS ROUND. SO IF THAT'S OKAY WITH BOTH THE MAKER AND THE SECOND.

MR. GOLDBERG: MR. CHAIRMAN, AFTER EXTENSIVE CONSULTATION WITH MYSELF, I'VE DECIDED THAT'S ACCEPTABLE.

MR. SHEEHY: OKAY. WE'RE GOING TO NEED HIM FOR THE VOTE ANYWAY, RIGHT. SO SHOULD WE -- YEAH. IS THERE ANY PUBLIC COMMENT ON THE MOTION?

DR. JUELSGAARD: SO JUST FOR CLARIFICATION SAKE, JUST WHICH APPLICATIONS ARE SUBJECT TO THIS MOTION? WHICH ARE WE VOTING TO FUND? IF WE CAN JUST HAVE THOSE NUMBERS FOR ME, PLEASE.

DR. SAMBRANO: THE NUMBERS FOR APPLICATIONS THAT ARE IN TIER I AND THAT WERE IN THE TIER II AND WERE APPROVED, THEY START WITH 6924,

6965, 7438, 7067, 7281, 6945. AND THE TOTAL BUDGET FOR ALL OF THOSE IS 61.128 MILLION.

MR. SHEEHY: WE HAD BUDGETED FOR THIS A HUNDRED MILLION.

DR. SAMBRANO: CORRECT.

MR. SHEEHY: SO WE'RE UP TO 270, STEVE.

DR. JUELSGAARD: THANK YOU.

MR. SHEEHY: SENATOR TORRES.

MR. TORRES: YES, I'M HERE.

MR. SHEEHY: GREAT. SO WILL YOU ACCEPT AN AMENDMENT TO YOUR MOTION TO EXCLUDE FROM CONSIDERATION APPLICATION --

DR. SAMBRANO: 7201.

MR. SHEEHY: -- 7201 WHICH WAS PULLED FROM CONSIDERATION?

MR. TORRES: REMIND ME AGAIN WHAT THE NATURE AND THE SUBJECT WAS.

MR. SHEEHY: IT WAS THE CARDIOVASCULAR DISEASE GRANT THAT WAS SCORED AT THE VERY BOTTOM OF THE PILE, AND THAT'S BEEN REMOVED FROM CONSIDERATION.

MR. TORRES: YES. I SUPPORT THAT REMOVAL FOR RECONSIDERATION, AND I WILL SO AMEND MY MOTION.

MR. GOLDBERG: SECOND.

MR. SHEEHY: THE SECOND HAD. SO I THINK

WE'RE READY FOR A VOTE. AND DOES THE COUNSEL NEED TO REMIND US AS TO -- I THINK ASKED FOR PUBLIC COMMENT, BUT I'LL ASK FOR IT AGAIN. ANY PUBLIC COMMENT? SEEING NONE.

MR. HARRISON: JUST A REMINDER. IF YOU HAVE AN APPLICATION LISTED ON THE CONFLICT SHEET IN FRONT OF YOU, YOU SHOULD VOTE YES OR NO ON THE MOTION EXCEPT WITH RESPECT TO THOSE APPLICATIONS FOR WHICH YOU HAVE A CONFLICT OF INTEREST.

MR. SHEEHY: COULD WE CALL THE ROLL, PLEASE.

MS. BONNEVILLE: ANNE-MARIE DULIEGE.

DR. DULIEGE: YES, EXCEPT FOR THOSE WITH WHICH I HAVE A CONFLICT.

MS. BONNEVILLE: MARCY FEIT.

MS. BONNEVILLE: MICHAEL GOLDBERG.

MR. GOLDBERG: YES.

MS. BONNEVILLE: STEPHEN JUELSGAARD.

MR. JUELSGAARD: YES.

MS. BONNEVILLE: SHERRY LANSING.

MS. BONNEVILLE: FRANCISCO PRIETO.

DR. PRIETO: YES, EXCEPT FOR THOSE WITH WHICH I HAVE A CONFLICT.

MS. BONNEVILLE: ROBERT QUINT.

DR. QUINT: YES.

MS. BONNEVILLE: AL ROWLETT.

MR. ROWLETT: YES, EXCEPT FOR THOSE WITH WHICH I HAVE A CONFLICT.

MS. BONNEVILLE: JOAN SAMUELSON. JEFF SHEEHY.

MR. SHEEHY: YES, EXCEPT FOR THOSE WITH WHICH I HAVE A CONFLICT.

MS. BONNEVILLE: OSWALD STEWARD.

DR. STEWARD: YES.

MS. BONNEVILLE: JONATHAN THOMAS.

CHAIRMAN THOMAS: YES.

MS. BONNEVILLE: ART TORRES.

MR. TORRES: AYE.

MS. BONNEVILLE: DIANE WINOKUR.

MS. WINOKUR: YES.

MR. HARRISON: MOTION CARRIES.

MR. SHEEHY: PASS IT BACK TO CHAIRMAN THOMAS.

CHAIRMAN THOMAS: THANK YOU, MR. SHEEHY.

MR. TORRES: WELL DONE, MR. SHEEHY.

CHAIRMAN THOMAS: YES. I WOULD LIKE TO ECHO THAT. THIS WAS A MAJOR TEST OF OUR NEW PROTOCOL WHICH WE PUT IN PLACE IN JANUARY OR I SHOULD SAY MARCH OF THIS YEAR, AND I THINK THE PROCESS WENT EXTREMELY WELL. AND I'D JUST LIKE TO

THANK MR. SHEEHY AND DR. STEWARD FOR THEIR VERY ABLE STEWARDSHIP, IF YOU WILL, OF THAT PROCESS. I THINK WE GOT A VERY GOOD RESULT AFTER A ROBUST DISCUSSION AND CONSIDERATION OF ALL ISSUES. SO THANK YOU TO BOTH OF YOU GENTLEMEN.

MR. SHEEHY: COULD I MAKE A COMMENT FOR THE RECORD. JUST A CLARIFICATION ABOUT THE ROLE OF EMBRYONIC STEM CELLS. SO THESE PRODUCTS ARE VERY READY FOR TRANSLATION INTO HUMAN BEINGS AT THIS POINT. AND, FRANKLY, I THINK WE ARE ANTICIPATING IN THE NEXT YEAR MOVING INTO PHASE I TRIALS WITH AT LEAST ONE AND POSSIBLY TWO EMBRYONIC STEM CELL-DERIVED PRODUCTS.

THE POINT HERE IN THE APPLICATION WHERE THIS WAS DISCUSSED WAS THAT IN A DISEASE THAT WAS NOT LIFE THREATENING, THE CRITICAL PATHWAY FOR APPROVAL WAS LIKELY TO TAKE A MUCH LONGER TIME. AND WE WANTED TO FOCUS ON MORE DISEASES AND CONDITIONS WHERE WE COULD HAVE A MAJOR IMPACT. BUT EMBRYONIC STEM CELLS, I THINK, AS ANYONE WHO LOOKS AT OUR PORTFOLIO WOULD ACKNOWLEDGE, ARE VERY, VERY RIPE FOR TRANSLATION AT THIS POINT.

CHAIRMAN THOMAS: THANK YOU, JEFF.

OKAY. WE ARE GOING TO GO -- AT THIS POINT WE'RE WAITING ON ONE MEMBER TO GET BACK FOR A

QUORUM. SO WAS GOING TO PROPOSE THAT WE PROCEED TO THE PRESIDENT'S REPORT, BUT THE PRESIDENT APPEARS TO BE OUT OF THE ROOM AT THE MOMENT. IF YOU COULD PERHAPS SUMMONS HIM, AMY. THANK YOU VERY MUCH.

IN LIEU OF THAT AT THE MOMENT, LET'S PROCEED. WE HAVE IN THE ROOM KEVIN MCCORMACK, WHO'S NOW GOING TO GIVE US THE COMMUNICATIONS REPORT.

MR. MC CORMACK: CHAIRMAN THOMAS, MEMBERS OF THE BOARD, MEMBERS OF THE PUBLIC, COLLEAGUES, IT'S BEEN AWHILE SINCE WE TALKED. I WANTED TO GO BACK A FEW MONTHS TO TALK ABOUT AN EVENT THAT WE HELD IN OCTOBER WHICH WAS A TOWN HALL FORUM ON ALL THE RESEARCH THAT'S GOING ON INTO HIV AND AIDS AND CURING IT. AND IT WAS ORGANIZED IN PART WITH OUR COLLEAGUE JEFF SHEEHY AND BROUGHT TOGETHER PEOPLE FROM CIRM, FROM UCSF, FROM THE GLADSTONE INSTITUTES, AND VARIOUS OTHER RESEARCHERS WHO ARE DOING SOME REALLY INTERESTING WORK, INCLUDING PEOPLE FROM CALIMMUNE WHO OBVIOUSLY ARE FUNDING A CLINICAL TRIAL IN THIS WORK.

IT WAS AN EXCELLENT RECEPTION. WE HAD MORE THAN A HUNDRED PEOPLE THERE, I THINK, FROM VARIOUS DIFFERENT GROUPS, A LOT OF PATIENT ADVOCATES AND ACTIVISTS. AND IT WAS TREMENDOUSLY SUCCESSFUL. I THINK IT REPRESENTS A NEW WAY OF REACHING OUT TO

THE COMMUNITY AND GETTING OUR MESSAGE OUT DIRECTLY AND TALKING TO PEOPLE ABOUT THE WORK THAT WE'RE DOING AND THE WORK THAT WE'RE FUNDING AND IMPACT IT CAN HAVE.

IT WAS WELL RECEIVED, NOT ONLY HERE, BUT ALSO AROUND -- WE HEARD FROM A NUMBER OF OTHER PEOPLE AROUND THE STATE. SO WE'RE GOING TO BE HOLDING A SIMILAR EVENT IN LOS ANGELES IN EARLY 2014. WE ALSO SHOT A VIDEO OF THE ENTIRE THING, AND THAT'S UP ON YOUTUBE, AND THAT'S GETTING A GOOD RESPONSE AS WELL.

LAST WEEK MANY OF US WERE AT THE WORLD STEM CELL SUMMIT IN SAN DIEGO. IT WAS A GREAT EVENT. WE HAD A LOT OF INTEREST FROM DIFFERENT AREAS. THERE WERE A NUMBER OF DIFFERENT PRESENTATIONS AND PANEL DISCUSSIONS AROUND THE EVENT, INCLUDING ON THE OPENING NIGHT, IN FACT, WE HAD A PATIENT ADVOCATE SUMMIT. AND IT WAS REALLY WELL ATTENDED. IT WAS A PACKED ROOM, GREAT QUESTIONS, GREAT PANEL DISCUSSION, AND I THINK IT'S ANOTHER WAY OF REACHING OUT TO AN AUDIENCE AND TALKING TO THEM DIRECTLY. WE CAN BYPASS THE NORMAL FILTERS AND REACH OUT AND TALK TO THEM ABOUT THE THINGS THAT WE THINK ARE PARTICULARLY IMPORTANT.

AND A NUMBER OF THINGS CAME UP AT THE

MEETING. ONE WAS DISCUSSION ABOUT CREATING A PATIENT ADVOCATE NETWORK BECAUSE MANY OF THE GROUPS THAT WE WORK WITH ARE VERY PASSIONATE ABOUT WHAT THEY DO, BUT THEY'RE QUITE SMALL. SO BY CREATING A NETWORK, WE MIGHT BE ABLE TO HELP LINK THIS TOGETHER SO THAT THEY CAN SHARE RESOURCES AND SKILLS AND GET A BETTER UNDERSTANDING OF HOW THEY AS AN OVERALL GROUP CAN BE MORE EFFECTIVE IN WHAT THEY DO.

AND WE'RE ALSO COMMITTED AT THE AGENCY TO CREATING A PATIENT ADVOCATE TOOLBOX AS PART OF THAT NETWORK. AND THAT WILL BE A PLACE WHERE WE CAN PUT INFORMATION ABOUT HOW TO CONTACT OTHERS, HOW TO CREATE -- HOW TO BE A MORE EFFECTIVE ADVOCATE, INCLUDING THINGS LIKE COMMUNICATION SKILLS, PRESENTATION SKILLS, HOW TO DO MEDIA INTERVIEWS, HOW TO TALK ABOUT STEM CELLS, SOME FAIRLY BASIC THINGS. THERE WAS A GREAT DEAL OF INTEREST IN THAT, SO THAT'S SOMETHING WE'RE GOING TO BE EXPLORING AS WE MOVE INTO 2014.

ONE OF THE OTHER THINGS WE DID AT THE WORLD STEM CELL SUMMIT WAS LAUNCH A NEW ONLINE CAMPAIGN CALLED CHAMPIONS. AND IT WAS ACTUALLY FORMER COLLEAGUE LEEZA GIBBONS WHO GAVE US THE IDEA FOR THIS. WE'VE BEEN PLAYING AROUND WITH A NUMBER OF DIFFERENT PERMUTATIONS ABOUT HOW TO DO SOMETHING

SIMPLE ONLINE THAT ENGAGED PEOPLE THAT MADE THEM FEEL INVOLVED AND ALSO GAVE THEM A CHANCE TO TALK ABOUT WHAT IT IS THAT GOT THEM INVOLVED IN THIS CAUSE AND WHY THEY CARE.

SO WE CAME UP WITH THE STEM CELL CHAMPION WHERE WE'LL USE SHEETS LIKE THIS THAT SAYS I'M A STEM CELL CHAMPION BECAUSE, AND THE INDIVIDUAL THEN FILLS THAT OUT. IT GIVES PEOPLE A CHANCE TO TALK ABOUT WHY THEY GOT INVOLVED AND WHAT IT IS THAT THEY'RE PASSIONATE ABOUT. AND EVERYONE HAS A STORY, AND I THINK THIS IS A WAY OF BRINGING THOSE STORIES OUT. AND WE'RE POSTING THOSE. AMY ADAMS CREATED A SPECIAL PAGE ON OUR WEBSITE SO WE NOW HAVE A SPECIAL CHAMPIONS PAGE WHERE WE TALK ABOUT THE WORK THAT WE'RE DOING AND ALSO FEATURE THE PHOTOS OF ALL THE DIFFERENT PEOPLE.

OVER TIME WE'RE GOING TO BE CREATING A VIDEO FEATURING ALL OF THESE PEOPLE. EACH PERSON -- WE HAVE JEANNE LORING HERE. EVERYONE WAS INVOLVED HAD A DIFFERENT STORY, A DIFFERENT REASON FOR BEING THERE. THERE WAS EVEN THIS NICE LADY. I HAVE NO IDEA WHO SHE IS, BUT SHE WAS QUITE HAPPY TO BE PART OF IT AS WELL.

WE'RE GOING TO BE DOING A COUPLE MORE GOOGLE HANGOUTS. WE DID ONE ON ALS EARLIER THIS

YEAR. AND THESE ARE ONLINE, INTERACTIVE WEBINARS, KIND OF A CHANCE FOR ORDINARY PEOPLE TO CHAT WITH SOME OF THE LEADING RESEARCHERS AND CIRM STAFF AND FIND OUT WHAT'S GOING ON IN THEIR PARTICULAR DISEASE. WE'RE DOING ONE ON DECEMBER 19TH. THAT'S NEXT THURSDAY. AND IT FEATURES DR. JOSEPH WU FROM STANFORD, DR. CATHY PRIEST, ONE OF OUR SCIENCE OFFICERS, AND FRED LESIKER, WHO IS A PATIENT WHO UNDERWENT SOME STEM CELL THERAPY THROUGH DR. MARBAN. AND OBVIOUSLY THAT'S A CLINICAL TRIAL THAT WE'RE FUNDING NOW FOR THE NEXT PHASE.

SO NORMALLY THESE ARE REALLY GREAT OPPORTUNITIES, AGAIN, TO REACH OUT TO A MUCH MORE TARGETED AUDIENCE. AND PEOPLE ARE INTERESTED, SPECIFICALLY IN THIS CASE, HEART DISEASE SO THAT THEY CAN FIND ABOUT WHAT'S GOING ON, THE LATEST RESEARCH. AND THEY'RE ALWAYS VERY INTERESTING AND GET GOOD QUESTIONS. AND THE BEAUTY OF USING A GOOGLE HANGOUT IS THAT IT'S FREE FOR EVERYONE INVOLVED. ONCE IT'S FINISHED, AND THEY LAST FOR ABOUT AN HOUR, THAT THING GETS POSTED STRAIGHT AWAY TO YOUTUBE. SO IT THEN BECOMES A RESOURCE THAT YOU CAN USE OVER AND OVER AGAIN SO THAT ORGANIZATIONS OR INDIVIDUALS WHO WEREN'T PART OF IT CAN THEN USE THAT AS A RESOURCE AND A REFERENCE POINT.

AND WE'RE GOING TO BE HOLDING ANOTHER ONE IN JANUARY. THAT'S DIABETES WITH BOARD MEMBER DR. PRIETO HERE, SOMEONE FROM VIACYTE, AND CHRIS STIEHL, WHO'S A GREAT CHAMPION OF THE AGENCY, HAS BEEN HEAVILY INVOLVED IN A LOT OF WHAT WE DO, AND HAS BEEN BATTLING TYPE 1 DIABETES FOR MANY, MANY YEARS. CHRIS WILL BE A GREAT ADDITION TO THAT PANEL. WE'RE ALSO THINKING ABOUT A NUMBER OF OTHER ONES NEXT YEAR. ULTIMATELY THE GOAL IS TO HAVE A GOOGLE HANGOUT IN PRETTY NEARLY EVERY DISEASE THAT WE'RE FUNDING. AND OBVIOUSLY BY THE TIME WE GET TO THE END, IT WILL BE LIKE PAINTING THE GOLDEN GATE BRIDGE. WE'LL HAVE TO GO BACK TO THE BEGINNING BECAUSE EVERYTHING IS MOVING ALONG SO FAST.

AND FINALLY AND SADLY, WE'RE SAYING GOODBYE TO AMY ADAMS, WHO HAS BEEN WITH THE AGENCY FOR A LITTLE OVER FIVE YEARS AND HAS DONE EXTRAORDINARY WORK. AMY IS LEAVING US TO GO TO STANFORD TO TAKE UP A GREAT POSITION THERE. IT'S A WONDERFUL OPPORTUNITY FOR HER AND IT'S SEVEN MILES AWAY FROM HER CHILDREN. SO NO MATTER WHAT I TRIED TO BRIBE HER WITH, NOTHING WOULD INDUCE HER TO STAY.

EVERY TIME YOU LOOK AT THE WEBSITE, THAT'S AMY. EVERY TIME YOU LOOK AT ANYTHING THAT WE DO ONLINE, THAT'S AMY. SHE'S BEEN A TREMENDOUS PART OF

EVERYTHING WE'VE DONE, AND WE'RE GOING TO MISS HER TERRIBLY. SO THANK YOU, AMY.

(APPLAUSE.)

MR. SHEEHY: I JUST WANT TO REALLY RECOGNIZE AMY FOR HER INCREDIBLE SKILL AND LEADERSHIP AS A COMMUNICATIONS PROFESSIONAL IN REALLY MANAGING THIS TRANSITION THAT'S GONE AT THE SAME TIME CIRM HAS HAPPENED, WHICH IS INTO THE SOCIAL MEDIA LANDSCAPE. AND IT'S REQUIRED THE UPTAKE AND USE OF NEW TOOLS THAT CREATE VERY DYNAMIC RELATIONSHIPS WITH STAKEHOLDER COMMUNITIES. WHAT SHE'S DONE IS CREATED A REALLY UNBELIEVABLE MODEL OF HOW TO USE THESE TOOLS TO REALLY GIVE US THE TYPE OF CONTACT AND OUTREACH AND COMMUNICATION WITH OUR STAKEHOLDER COMMUNITIES THAT I DON'T SEE HAPPENING IN VERY MANY OTHER INSTITUTIONS. SHE'S REALLY DONE A PHENOMENAL JOB AND IS A REAL LEADER IN HER FIELD. AND IT'S A TERRIBLE LOSS FOR US.

MR. MC CORMACK: SO AS YOU LOOK AT THE WEBSITE OVER THE NEXT FEW WEEKS, IF YOU NOTICE PROBLEMS OR FLAWS, BLAME AMY. SHE LEFT. DON'T EMAIL HER. AMY HAS BEEN SLOWLY KIND OF GOING THROUGH ALL THE THINGS THAT SHE DOES AND EXPLAINING TO DON AND TODD AND MYSELF ON THE TEAM WHAT IT IS WE'RE GOING TO HAVE TO PICK UP. AND EVERY DAY WE'RE

JUST STANDING THERE SHAKING OUR HEADS. THE LEVEL OF DETAIL AND THE AMOUNT OF WORK SHE'S BEEN DOING IS EXTRAORDINARY. SO WE CERTAINLY WILL MISS HER.

MR. TORRES: MR. CHAIRMAN.

CHAIRMAN THOMAS: YES, SIR.

MR. TORRES: I HAVE DAILY CONTACT WITH AMY AT THE OFFICE, AND I JUST WANT TO ECHO THE WORDS OF JEFF AND KEVIN. BUT ALSO PEOPLE DON'T REALIZE WHAT AN INCREDIBLE HUMAN BEING SHE IS. SHE GIVES SO MUCH TO CHARITABLE WORK, TO PEOPLE FROM UNDERDEVELOPED COUNTRIES THAT SOMETIMES PEOPLE DON'T KNOW ABOUT, BUT I KNOW HER PASSION. SO WE WILL DEFINITELY MISS HER.

DR. DULIEGE: IF I MAY BRIEFLY ADD TO EVERYTHING THAT WAS SAID ABOUT AMY AND THE STAFF OF CIRM. YOU MAY NOT HAVE HAD A CHANCE TO READ WHAT I WROTE, AND MY COMMENT WAS I WANT TO SUPPORT STEM CELL BECAUSE THE CIRM STAFF IS FANTASTIC AND IS COOL, AND REALLY APPLIES TO THE ENTIRE CIRM STAFF, BUT PARTICULARLY ACTUALLY, AMONG OTHERS, FOR YOU, AMY, AS YOU ARE JUST LEAVING.

I ALSO WANTED TO MAKE A FEW COMMENTS ABOUT THE WORLD STEM CELL SUMMIT. I HAD THE PRIVILEGE TO ATTEND IT FOR THE FIRST TIME. AND NOT ONLY WAS IT, AS YOU SAID THIS MORNING OR YESTERDAY, AN INCREDIBLE

MEETING WHERE SCIENTISTS MEET WITH PATIENTS, PATIENT ADVOCATES, JOURNALISTS, AND SO FORTH, BUT I WAS REALLY IMMENSELY APPRECIATIVE OF THE FACT THAT THE CIRM STAFF WAS EVERYWHERE AND REPRESENTING CIRM SO WELL. NOT ONLY THERE WAS A BOOTH THAT WAS EXTREMELY WELL ATTENDED, BUT EVERYONE WHO WAS THERE PARTICIPATED IN SEVERAL MEETINGS, PANEL SESSIONS OF VERY HIGH QUALITY. I JUST WANTED EVERYBODY TO KNOW THAT.

ALAN, YOU DID A SPECTACULAR PLENARY SESSION, THE KEYNOTE ADDRESS ABOUT THE FUTURE OF STEM CELL RESEARCH. AS ALWAYS, VERY INSPIRING.

AND, J.T., YOU WERE IN THAT PARTICULAR PANEL THAT WAS MEMORABLE AMONG OTHER PHILANTHROPISTS, AND YOU REMINDED EVERYBODY THAT CIRM WAS AN INCREDIBLE PHILANTHROPIC ADVENTURE AS WELL. SO FOR ALL OF THAT, THANK YOU SO MUCH.

CHAIRMAN THOMAS: THANK YOU. ANY OTHER COMMENTS? THANK YOU VERY MUCH, KEVIN, FOR YOUR FINE WORK. AND DON AND TODD AND OBVIOUSLY AMY. I ECHO EVERYTHING. YOU KNOW MY REACTION WHEN I HEARD YOU WERE LEAVING WAS NOT VERY POSITIVE, LET'S PUT IT THAT WAY. REALLY GOING TO MISS YOU. THANK YOU VERY MUCH.

HAVING YOU AND LYNN BOTH GO AT THE SAME

TIME, VERY, VERY DIFFICULT SHOES TO FILL. SO THANK YOU AGAIN TO BOTH OF YOU.

PROCEED NOW TO THE PRESIDENT'S REPORT.

DR. TROUNSON: SO AS I USUALLY DO OR I HAVE DONE EVER SINCE I'VE BEEN HERE, SEVERAL OF THE PAPERS WHICH HAVE APPEARED IN THIS LAST MONTH HAVE BEEN WHAT I THINK ARE EXTRAORDINARY. SO THE FIRST ONE COMES FROM THE SALK INSTITUTE AND RUSTY GAGE'S LAB, SHOWING THAT IN THE BRAIN THERE ARE MOSAIC COPY VARIATION AMONG NEURONS. AND THIS IS REALLY FOR THE FIRST TIME BECAUSE THEY WERE STUDYING SINGLE CELL NEURONS FOR THEIR GENOME. AND IT'S BEEN PRETTY DIFFICULT TO DO THAT IN SINGLES CELLS, BUT THEY MANAGED TO DO IT.

SO THEY DID SINGLE CELL GENOMICS USED TO MAP NEURONS FROM IPS CELLS IN POSTMORTEM HUMAN BRAIN. AND THEY FOUND ANEUPLOIDY, WHICH IS MIXED CHROMOSOME NUMBERS, NOT THE CORRECT NUMBER THAT YOU WOULD NORMALLY EXPECT, AND OTHER COPY NUMBER VARIATIONS OF GENES AS WELL AS EUPLOID. THAT'S NORMAL NEURON, NORMAL CHROMOSOME NUMBERS IN THE NEURONS. IPS CELL NEURONS HAD LARGER COPY NUMBER VARIATIONS THAN THE FIBROBLASTS THEY MADE THEM FROM, BUT ALSO FROM THE NEURAL PROGENITORS WHICH GO ON TO FORM NEURONS.

AND 13 TO 41 PERCENT OF THESE ALL HAD ONE MEGABASE SCALE DELETION. IMPORTANT PART OF THIS HAS PROBABLY GOT TO DO WITH THE FUNCTIONING OF NEURONS, I THINK. AND THAT'S AN IMPORTANT QUESTION BECAUSE THE NEURONS REALLY ARE A VERY DIVERSE FUNCTIONAL SOURCE OF CELLS, PARTICULARLY IN THE CENTRAL NERVOUS SYSTEM. AND HOW DO THEY GET TO BE SO DIFFERENT? PARTLY MAYBE BECAUSE THEY TAKE ON THESE VARIATIONS AND MIX UP THE GENOME SO THAT THEY'RE ACTUALLY DIFFERENT ONE FROM ANOTHER.

SO IF YOU LOOK AT THIS PICTURE HERE, THESE ARE THE NEURONS THAT HAVE BEEN MADE FROM THE IPS CELLS. AND THE TOP IS WHERE YOU'VE GOT MULTIPLE COPIES OF THE GENES. YOU CAN SEE THAT THEY'VE GOT MULTIPLE COPIES OF THE GENES HERE. AND ON THE BOTTOM PART YOU'VE GOT DELETIONS OF THEM. AND THESE ONES ARE THE NEURONAL PROGENITOR CELLS THAT GO TO FORM THOSE SO THAT THESE ERRORS ARE NOT -- WHAT WE NORMALLY CALL ERRORS ARE NOT PRESENT IN THESE NEURAL PROGENITOR CELLS, NOR ARE THEY PRESENT REALLY IN THE FIBROBLASTS THAT THEY WERE MADE OF.

IF YOU LOOK OVER HERE, YOU CAN SEE THIS GRAPH. THIS IS THE SIZE OF THE DELETION. IN THE NEURONS THAT ARE IN THE BRAIN, THESE ARE THE NEURONS, FUNCTIONAL NEURONS, YOU CAN SEE THAT

THEY'VE GOT VERY LARGE DELETIONS; WHEREAS, THE NEURAL PROGENITORS LESS SO AND FIBROBLASTS FROM WHICH THEY'RE MADE LESS SO AS WELL.

IF YOU LOOK IN THE ACTUAL HUMAN BRAIN, AND THEY'VE TAKEN ON THE LEFT-HAND SIDE AS YOU LOOK AT THIS, THE LEFT-HAND SIDE, FIVE NEURONS TAKEN FROM A MALE AND ON THE RIGHT-HAND SIDE FIVE NEURONS TAKEN FROM A FEMALE. ODDLY ENOUGH IN THIS PICTURE, AND I REALLY DIDN'T GET THE SIGNIFICANCE OF THIS, THAT THERE IS MULTIPLICATIONS OF GENES AMONGST THESE FIVE NEURONS HERE SHOWN ON THE UPPER PART OF THESE PICTURES HERE. THESE ARE ALL ADDITIONAL COPIES OF THE GENE. AND YOU CAN SEE THE DELETIONS. THEY APPEAR UNDERNEATH.

SO IN THE NEURONS OF THE HUMAN BRAIN, YOU CAN SEE BOTH MULTIPLICATIONS AND DELETIONS AMONGST THE NEURONS THAT ARE THERE. AND IT'S REALLY VERY, VERY FREQUENT. SO I THINK IT IS RELATED TO THEIR FUNCTIONAL HETEROGENEITY, AND IT MAKES AN INTERESTING PERSPECTIVE ABOUT HOW YOU WOULD EXPECT THOSE CELLS TO FORM IF YOU'RE TRYING TO GROW THEM IN CULTURE. HOW ARE YOU GOING TO GET THEM TO ADD OR DELETE IF THIS IS PART OF THEIR FUNCTIONAL CAPACITY? IT'S SOMETHING THAT WE'RE GOING TO HAVE TO START TO LEARN MORE ABOUT, BUT CLEARLY THERE ARE A LOT OF

ADDITIONS AND SUBTRACTIONS SHOWN HERE. THIS IS THE AVERAGE NUMBER OF DELETIONS AND ADDITIONS HERE IN BOTH THESE SETS OF SAMPLES.

SO IT IS MUCH MORE COMPLEX, I THINK, THAN WHAT WE THOUGHT. AND THIS JUST ADDS ANOTHER DEGREE OF COMPLEXITY TO THE WHOLE STORY. BUT I DO THINK IT MIGHT BE RELATED TO THE FUNCTIONALITY OF THESE CELLS. AND SO IF IT ISN'T, THEN IT SEEMS VERY ODD THAT IT'S HAPPENING IN THE STAGES WHERE YOU MOVE FROM A PROGENITOR IN THE BRAIN TO A FUNCTIONAL NEURON.

THE NEXT PAPER THAT I WANTED TO SORT OF DRAW YOUR ATTENTION TO WAS A PAPER BY JUAN CARLOS BELMONTE'S LAB AT THE SALK INSTITUTE, AGAIN, PUBLISHED IN *NATURE*, WHERE THEY SHOWED DIRECTED DIFFERENTIATION OF HUMAN PLURIPOTENTIAL CELLS TO URETERIC BUD KIDNEY PROGENITOR CELLS. SO GROWING A NEW KIDNEY OR REGENERATING A KIDNEY LOOKS TO BE A VERY COMPLEX MATTER. IT LOOKS LIKE A VERY DIFFICULT MATTER TO REPAIR KIDNEYS BECAUSE THEY'RE FUNCTIONALLY VERY COMPLEX LITTLE ORGANS.

BUT THE GROUP USED A MONOLAYER CULTURE TECHNOLOGY WITHOUT ANY FEEDERS, ADDING THE GROWTH FACTORS BMP4, FGF2 AND DIFFERENTIATED THEM INTO WHAT WE KNOW AS MESODERM. AND THEN THEY USE ANOTHER SET

OF FACTORS, RETINOIC ACID, ACTIVIN A AND BMP2 TO DRIVE THEM INTO RENAL-LIKE LINEAGES. AND WHEN THEY WERE COMBINED IN CO-CULTURE WITH MOUSE URETERIC BUDS, THAT IS EMBRYONIC MOUSE URETERIC BUDS, THE HUMAN RENAL-LIKE CELLS INTEGRATED INTO THE TRUNK AND TIP, INDUCING NEUROGENESIS.

I THINK THIS IS INTERESTING BECAUSE IT'S A POSSIBLE PROGRESS TOWARDS KIDNEY REPAIR. IT'S ON THE WAY. AND SO I THINK THIS IS THE FIRST TIME WE'VE SEEN DEVELOPMENT INTO THOSE KIDNEY STRUCTURES OF ANY OF OUR PLURIPOTENTIAL STEM CELLS. SO I THINK IT'S AN INTERESTING AND IMPORTANT STEP.

I TALKED TO CARLOS, JUAN CARLOS, ABOUT IT. HE DIDN'T THINK THIS METHOD WAS GOING TO END UP BEING ABLE TO GROW A WHOLE KIDNEY, BUT HE DID THINK MAYBE YOU COULD EFFECT SOME KIDNEY REPAIR USING A CELL APPROACH.

THE OTHER PAPER I WANTED TO DRAW YOUR ATTENTION TO, I THINK, IS REALLY A VERY IMPORTANT ONE AND PROBABLY WON'T BE SEEN IF YOU JUST LOOKED AT THE LITERATURE BY A LOT OF PEOPLE AS BEING THAT WAY. BUT THIS IS A DERIVATION OF NOVEL HUMAN GROUND STATE FOR PLURIPOTENTIAL STEM CELLS. WE KNOW THAT HUMAN PLURIPOTENTIAL STEM CELLS, EMBRYONIC STEM CELLS OR IPS CELLS, ARE DIFFERENT TO THE MOUSE. THEY RESPOND

TO DIFFERENT GROWTH FACTORS. THEY DIFFERENTIATE IN DIFFERENT WAYS. HUMAN OR PRIMATE CELLS CANNOT MAKE CHIMERAS WHEN THEY'RE COMBINED IN THE EMBRYO AND MOUSE CAN. THERE ARE DIFFERENCES. MAJOR DIFFERENCE IS IN THE GROUND STATE OF THAT PLURIPOTENTIALITY.

SO THIS GROUP AT THE WEIZMANN INSTITUTE, WHICH IS HEADED BY DR. HANNA, HAS BEEN STUDYING VERY CLOSELY THIS GROUND STATE OF HUMAN AND MOUSE. AND THEY DEFINED CULTURE CONDITIONS WHICH ARE REALLY QUITE COMPLEX IN THEIR PAPER, WORKING OUT THE CULTURE CONDITIONS THAT COULD DERIVE WHAT ARE KNOWN AS GENETICALLY NAIVE HUMAN PLURIPOTENTIAL STEM CELLS. SO GROUND STATE LIKE MOUSE, NOT LIKE HUMAN.

SO THESE CELLS RESPONDED TO THE SAME FACTORS THAT MOUSE DID IN THEIR RESPONSE TO GROWTH FACTORS. SO INSTEAD OF BEING TYPICALLY HUMAN, WHICH IS FURTHER DOWN THE TRACK, THEY WERE TYPICALLY LIKE MOUSE EARLY ON IN DEVELOPMENT.

WHAT'S THE IMPORTANT PART OF THAT IS THAT THESE CELLS WERE ABLE TO BE INCLUDED. WHEN THESE CELLS, WHEN THEY'RE INJECTED INTO A MOUSE EMBRYO, THEY ACTUALLY INTEGRATED INTO THAT MOUSE EMBRYO, AND EVENTUALLY THEY PRODUCED HUMAN CELLS IN THOSE MOUSE TISSUES. THEY FORMED CHIMERAS, AND THIS HAS NEVER BEEN DONE BEFORE. SO THESE CELLS NOW ARE REALLY

VERY MUCH LIKE MOUSE EMBRYONIC STEM CELLS. THEY CAN FORM ALL OF THE CELLS THAT THE MOUSE CAN, BUT THEY DO IT IN THE SAME KIND OF WAY.

SO JUST TO SHOW YOU, TO DO THESE STUDIES, THEY INJECTED THESE FLUORESCENT NAIVE HUMAN PLURIPOTENTIAL STEM CELLS, SHOWN IN THE GREEN HERE, INTO AN EMBRYO. THIS WAS A EARLY STAGE EMBRYO; IT'S JUST PREBLASTOCYST. AND YOU CAN SEE THE GREEN TURNS UP IN THE INNER CELL MASS OF THESE BLASTOCYSTS, AND IT APPEARS TO BE INTEGRATING. AND IF YOU LOOK, IF THOSE BLASTOCYSTS ARE THEN TRANSFERRED TO THE MOUSE TO PRODUCE A FETAL MOUSE, YOU CAN SEE THAT THE CELLS, THESE ARE THE HUMAN CELLS SHOWING UP IN WHITE, AND THESE ARE ALL IN THE NEURAL FOLD OF THE MOUSE. SO THEY'RE IN THE NEURAL FOLD OF THE CENTRAL NERVOUS SYSTEM, AND YOU CAN SHOW IN OTHER DEVELOPMENTS, HERE ARE THE WHITE ONES SHOWING UP IN OTHER REGIONS OF THE BODY OF THE MOUSE. SO THEY BECOME INTEGRATED LIKE A CHIMERA. THIS IS THE CONTROLS. THERE ARE NO WHITE CELLS HERE SHOWING UP AT ALL.

I THINK IT'S VERY SIGNIFICANT, AND YOU MIGHT REMEMBER THIS IN, SAY, THREE OR FOUR YEARS TIME WHEN WE COME BACK AND TELL YOU HOW IT'S GOING TO BE USED BECAUSE I DEFINITELY THINK THIS GROUND

STATE IS GOING TO BE ANOTHER REVOLUTION IN STEM CELL MEDICINE.

MOVING ON FROM THOSE INTERESTING PAPERS, THERE'S A NEW APPOINTMENT AT CIRM. ELENA WHITE, WHO'S RETURNING TO CIRM AS A GRANTS MANAGEMENT SPECIALIST, AND DID IT IN SEPTEMBER. SO WE WELCOME HER BACK AGAIN TO US. SHE'S BEEN OFF FOR TWO YEARS AND HAS COME BACK TO US AND IS WORKING ACTUALLY PART TIME WITH US TO ENABLE US TO PERFORM IN OUR GRANTS MANAGEMENT TEAM AS EFFECTIVELY AS WE NORMALLY DO.

THE RFA PROGRAM, WE'VE ALREADY HAD THE DISEASE TEAM. THAT'S ALREADY PAST. THE BASIC BIOLOGY V, THERE WILL BE AN ICOC FUNDING DECISION IN JANUARY. THE GENOMICS WILL COME TO THE BOARD IN JANUARY AS WELL. THERE'S A STRATEGIC PARTNERING GRANTS REVIEW APPLICATION, WHICH IS IN FEBRUARY 5TH TO 7TH, SOMETHING LIKE THAT. AND SOME OF THE BOARD HAVE BEEN ATTENDING THESE MEETINGS. AND, MIKE, I THOUGHT YOU THOUGHT IT WAS REALLY WORTHWHILE, AND I'M ENCOURAGING ANNE-MARIE TO MAYBE COME AS WELL BECAUSE THAT WOULD BE GOOD JUST TO SEE THE PROCESS IN PLACE. I THINK YOU GET A BETTER UNDERSTANDING FOR WHAT'S GONE ON THERE THAT THEN COMES HERE.

SO I ENCOURAGE THE BOARD TO GO THERE IF THEY HAVE A CHANCE AND JUST SEE WHAT THE PROCESS IS

AND GET A FEELING FOR HOW IT HAPPENS.

THE RESEARCH LEADERSHIP EXTENSION, THE GRANTS WORKING GROUP REVIEW OF THOSE APPLICATIONS SHOULD BE IN MARCH.

ALPHA CLINICS, THE GRANTS WORKING GROUP REVIEW SHOULD BE IN JUNE. AND TOOLS AND TECHNOLOGIES II SHOULD BE IN SEPTEMBER.

SO THERE HAVE BEEN A NUMBER OF MEETINGS. I JUST WANTED TO REPORT ON A FEW OF THOSE. OTHERS THAT I WON'T TALK ABOUT ARE IN YOUR FOLDERS. THERE'S A COUPLE OF VERY INTERESTING ONES THAT I WAS AT. FIRST OF ALL, THE NATURE MEDICINE SYMPOSIUM ON STEM CELLS IN HANOVER, GERMANY, WHERE AN INVITED GROUP OF PEOPLE, AROUND 20 OF US, GOT TOGETHER TO DISCUSS THE MAJOR ISSUES AND QUESTIONS THAT NEED TO BE ADDRESSED FOR TRANSLATIONAL RESEARCH IN STEM CELL RESEARCH TO ADVANCE AND, IF POSSIBLE, DEVELOP ANSWERS FOR THE QUESTIONS AT HAND.

SO THIS IS NOW BEING WRITTEN UP IN A SERIES OF PAPERS BY THE PEOPLE WHO WERE ATTENDING THAT. AND THE FOCUS OF THE DISCUSSION WAS IN THOSE VERY INTERESTING AREAS OF EITHER CELL DIFFERENTIATION, MECHANISMS OF REGENERATION, DISEASE MODELING, CLINICAL TRANSLATION, AND REPROGRAMMING, AND PLURIPOTENTIALITY. THEY WERE VERY, VERY

INTERESTING. WE COULD SEE WHERE THE PROBLEMS WERE. THERE WILL BE DEVELOPMENTS THAT WILL BE REPORTED IN *NATURE MEDICINE* AS THESE REPORTS COME THROUGH.

THE OTHER ONE WAS THE WORLD SUMMIT ON REGENERATIVE MEDICINE WHICH ARE REALLY TARGETING THE GLOBAL BARRIERS TO THE IMPLEMENTATION OF THERAPIES OF REGENERATIVE MEDICINE. SO THOSE PAPERS ARE AVAILABLE IF YOU WANT FROM THE CHINA STUDY, AND THERE WILL BE SOME MORE COMING FORWARD, BUT, AGAIN, AN INCREDIBLY INTERESTING AREA. THIS WAS MOSTLY POPULATED BY TISSUE ENGINEERS AND CELL BIOLOGISTS. SO IT WAS A VERY, VERY INTERESTING MEETING.

OTHER CELL CONFERENCES THAT WE'VE HAD JUST RECENTLY WAS ONE ON "PARKINSON'S DISEASE: FROM DISCOVERY TO THE CLINIC," WHICH CIRM HAD A MODERATED WEBINAR WITH EXPERTS FROM FDA, INDUSTRY, ACADEMIA, SLIDES, AUDIOTAPE, AND QUESTION AND ANSWERS WERE POSTED. SO YOU CAN PICK THAT UP ON THE WEBSITE NOTED THERE. AND THERE'S A WHITE PAPER FROM CIRM, WHICH SPONSORED THE WORKSHOP, AS A REFERENCE. SO THAT WILL BE ON THE WEBSITE IN DUE COURSE.

THEN 2013 WORLD ALLIANCE FORUM IN SAN FRANCISCO ON THE FUTURE OF STEM CELLS, THIS IS AN ORGANIZATION WHICH IS MOSTLY CENTERED IN JAPAN, BUT THEY HAD THEIR MEETING IN SAN FRANCISCO. IT WAS A

FANTASTIC MEETING OF REALLY SOME OF THE BEST PEOPLE IN THE WORLD. AND IT FEATURED A LOT OF REALLY INTERESTING ADVANCES IN STEM CELL TECHNOLOGY AND CHALLENGES TO OVERCOME BEFORE THE PROMISE CAN BE TURNED INTO PRACTICAL APPLICATION, AND IT INCLUDED COMPANIES AND IT INCLUDED PEOPLE WHO ARE REALLY BROADLY INTERESTED IN THE AREA. AND IT SERVED AS A CATALYST FOR CREATING NEW BUSINESSES BY NURTURING NEW TECHNOLOGIES EMERGING OUT OF BOTH THE U.S. AND JAPAN.

SO I THOUGHT IT WAS ONE OF THOSE REALLY FANTASTIC MEETINGS. IT WAS A DAY MEETING IN SAN FRANCISCO. THERE ARE OTHERS IN YOUR BOARD PAPERS THERE.

NOW, I JUST WANTED TO REPORT ON EXTRAORDINARY SUPPLEMENTS AWARDS BECAUSE THAT'S WHAT WE'RE REQUIRED TO DO FOR THE ICOC. JUST TO REMIND YOU, IN DECEMBER 2012 YOU APPROVED $16 MILLION FOR EXTRAORDINARY SUPPLEMENTS, $12 MILLION FOR THE MAJOR SUPPLEMENTS AND $4 MILLION FOR MINOR SUPPLEMENTS. AND IN THE MINOR SUPPLEMENTS, A PRESIDENTIAL DECISION COULD BE MADE AFTER RECEIVING RECOMMENDATIONS FROM TWO MEMBERS OF A GRANTS WORKING GROUP ALONG WITH SENIOR MANAGEMENT.

AND JUST TO LET YOU KNOW, IN THE AREA OF

TOOLS AND TECHNOLOGIES, AN AWARD TO RT 21975, DEVELOPMENT OF PRECLINICAL TESTING OF A NEW DEVICE FOR CELL TRANSPLANTATION TO THE BRAIN TO DANIEL LIM AT UCSF. HE REQUESTED A MINOR SUPPLEMENT OF $163,402 TO COVER MOST OF THE COST OF DEVELOPING A DESIGN HISTORY FILE FOR THE DEVICE AND A SET OF DOCUMENTS REQUIRED FOR COMMERCIALIZATION OF MEDICAL DEVICES. IS REBUDGETING THE REMAINING FUNDS IN THE CURRENT AWARD TO COVER THE REMAINING DHF COST AND TO CONDUCT STUDIES IN SUPPORT OF A 5, 10K FILING.

SO THE PROCESS WAS THE APPLICATION AND BUDGET WAS REVIEWED BY EXPERT MEMBERS OF THE GRANTS WORKING GROUP, AND THERE WAS EXTERNAL AND INTERNAL RECOMMENDATION TO FUND, AND THEN I APPROVED THAT. SO I APPROVED THAT MINOR AWARD.

SO CAN I INVITE CHILA WITH A REASONABLE VOICE TODAY TO GIVE YOU THE FINANCIAL REPORT.

MS. SILVA-MARTIN: THANK YOU, DR. TROUNSON. GOOD AFTERNOON, MR. CHAIR AND MEMBERS OF THE BOARD, MEMBERS OF THE PUBLIC, AND STAFF. I WILL BE REPORTING ON CIRM'S FINANCES FOR THE '13-'14 FISCAL YEAR.

THE FIRST THING I DO WANT TO DO THOUGH IS ACKNOWLEDGE THE REST OF THE CIRM TEAM THAT WORKS REALLY HARD TO ENSURE THAT WE GET UNQUALIFIED,

UNMODIFIED AUDIT REPORTS. AND IT REALLY STARTS FIRST WITH CYNTHIA SCHAFFER, WHO IS OUR CONTACT AND PROCUREMENT MANAGER, AND IS RESPONSIBLE FOR ENSURING THAT SHE ISSUES CONTRACTS AND PROCUREMENTS IN COMPLIANCE WITH NOT ONLY CIRM POLICIES, BUT THE MYRIAD OF STATE RULES AND REGULATIONS, AND SHE DOES AN EXCELLENT JOB.

AND THEN WE HAVE THREE FINANCE STAFF WHO INCLUDES CELESTE HYDLER, SHEILA CHADWICK, AND ODEL BARRY. AND THEY'RE RESPONSIBLE FOR REVIEWING, AUDITING, PROCESSING THOUSANDS OF PAY MEMOS, INVOICES, HONORARIA REQUESTS, TRAVEL EXPENSE CLAIMS, AND NOT ONLY MAKING SURE THAT THEY'RE IN COMPLIANCE WITH THOSE CONTRACT NPO'S THAT CYNTHIA ISSUES, BUT ALSO ENSURING THAT THEY GET CODED TO THE RIGHT POCKETS OF MONEY SO THAT WHEN WE GET OUR FINANCIAL AUDIT COMPLETED, WE HAVE THIS GREAT REPORT. SO I DO WANT TO ACKNOWLEDGE THEM FIRST AND FOREMOST.

THIS FIRST SLIDE COVERS WHAT WE'VE PROVIDED IN GRANT DISBURSEMENTS AND WHAT OUR CASH RESERVES ARE. SO FOR THE FIRST FIVE MONTHS OF THE FISCAL YEAR, WE HAVE DISBURSED $93 MILLION IN GRANT PAYMENTS, WHICH IS ABOUT $28 MILLION MORE THAN WE DID DURING THE SAME PERIOD IN THE '12-'13 FISCAL YEAR. WE CONTINUE TO RECEIVE COMMERCIAL PAPER

FUNDING EACH MONTH BASED ON FORECASTS AND REPORTS THAT ARE PREPARED BY THE OFFICE OF THE CHAIR. AND SO AS A RESULT, WE HAVE A VERY HEALTHY CASH RESERVE. AS OF NOVEMBER 30TH, WE HAD $53 MILLION AND WE WILL CONTINUE TO RECEIVE MONTHLY COMMERCIAL PAPER ALLOCATIONS ANYWHERE FROM 13 TO $22 MILLION GENERALLY BASED ON THOSE REPORTS THAT ARE PROVIDED BY THE OFFICE OF THE CHAIR.

JUST TALKING ABOUT OUR OPERATIONAL EXPENDITURES AT A VERY HIGH LEVEL. OUR '13-'14 EXPENDITURES ARE REALLY ON TRACK. AT THE NEXT MEETING I DO HOPE TO PROVIDE YOU WITH A YEAR-END FORECAST SO THAT YOU'LL KNOW WHERE I THINK WE'RE GOING TO END UP. BASED ON THE FIRST FIVE MONTHS OF EXPENDITURES, THOUGH, I AM SEEING A LITTLE BIT OF SAVINGS. THE MAJORITY OF SAVINGS IS FROM EMPLOYEE EXPENSES, AND IT'S REALLY ATTRIBUTED TO THE FACT THAT WE HAVE A COUPLE OF POSITIONS THAT ARE VACANT, BUT ALSO THAT WE BUDGETED FOR MERIT ADJUSTMENTS FOR THE FULL YEAR, AND THEY WERE NOT IMPLEMENTED TILL THE NOVEMBER PAY PERIOD.

NOW, THIS NEXT CHART PROVIDES YOU THE OPERATING EXPENDITURES BY THE CATEGORIES, AND IT COMPARES IT TO THE SAME PERIOD IN THE '12-'13 FISCAL YEAR. I'M NOT GOING TO COVER ALL OF THE CATEGORIES.

I'M JUST GOING TO POINT OUT A COUPLE OF THEM.

OVERALL OUR EXPENDITURES ARE UP BY $245,000 OVER LAST YEAR. OUR EMPLOYEE EXPENSES ARE UP, BUT THAT'S BECAUSE LAST NOVEMBER, I BELIEVE, WE HAD 55 STAFF ON BOARD, AND THIS NOVEMBER WE HAVE 57. SO WE HAVE A COUPLE MORE STAFF ON BOARD. WE ALSO HAD SOME OF OUR BENEFIT COST THAT INCREASED. FOR EXAMPLE, RETIREMENT WENT UP AS WELL AS SOME OF OUR HEALTH BENEFITS. YOU WILL NOTICE, HOWEVER, THAT OUR EXTERNAL SERVICES HAVE GONE DOWN SIGNIFICANTLY. AND THAT'S REALLY ATTRIBUTED TO TWO AREAS. A BIG PORTION OF IT IS THE I.T. PROGRAMMING. LAST YEAR WE HAD HALF A MILLION DOLLARS BUDGETED FOR I.T. PROGRAMMING. THIS YEAR WE ONLY HAVE $75,000 BUDGETED BECAUSE WE DID, IN FACT, BRING A COUPLE OF STAFF ON BOARD A COUPLE OF YEARS AGO, AND THAT'S WORKING OUT GREAT.

AND THEN THE OTHER CATEGORY THAT I WANTED TO POINT OUT IS THAT OUR COSTS THIS YEAR ARE HIGHER IN TRAVEL THAN THEY WERE DURING THE SAME PERIOD LAST YEAR, AND I THINK THAT'S ATTRIBUTED TO A NUMBER OF DIFFERENT REASONS. ONE OF THEM BEING MORE THAT WE HAVE STAFF THAT ARE TRAVELING. WE ALSO HAD -- THE COST CENTERS SUBMITTED TRAVEL PLANS, AND I THINK THEY'RE ADHERING TO THEM MORE CLOSELY. AND SO WE'RE

SEEING MORE EXPENDITURES.

AND THEN THE THIRD IS THAT WE REALLY HAVE BEEN ENCOURAGING STAFF TO SUBMIT THEIR TRAVEL EXPENSE CLAIMS ON A MONTHLY BASIS, AND WE'RE SEEING THAT. SO THAT MEANS THE EXPENDITURES ARE BEING RECORDED MORE TIMELY.

THE NEXT CHART PROVIDES YOU COST CENTER DETAILS. WE HAVE EIGHT COST CENTERS, AND THIS CHART REFLECTS THE BUDGET FOR EACH OF THE COST CENTERS AND THEN EXPENDITURES THAT HAVE BEEN RECORDED THROUGH NOVEMBER. I DO WANT TO POINT OUT THAT RECORDED IS NOT NECESSARILY WHAT THEY HAVE INCURRED BECAUSE WE HAVE EVERY MONTH ABOUT A 400 TO $600,000 LAG. FOR NOVEMBER I THINK IT WAS ABOUT $4,000. SO WHAT I CAN SAY ABOUT ALL OF THE COST CENTERS IS THAT THEIR EXPENDITURES ARE PRETTY MUCH ON TRACK, BUT NEXT MONTH I WILL BE ABLE TO GIVE YOU SOME MORE DETAILS ONCE I'VE DONE A THOROUGH ANALYSIS AND WE LOOK AT ALL OF THE COSTS FOR THE REST OF THE YEAR.

THEN FINALLY, ALTHOUGH WE'RE SIX MONTHS INTO THE FISCAL YEAR, IT'S REALLY TIME FOR US TO BEGIN THE BUDGET DEVELOPMENT FOR THE '14-'15 FISCAL YEAR. SO THIS IS THE TENTATIVE SCHEDULE. THE FINANCE STAFF PLANS TO DISTRIBUTE TO EACH OF THE COST CENTERS SOME CURRENT YEAR DATA AS WELL AS SOME

TEMPLATES SO THAT THEY CAN DEVELOP THE BUDGET. WE'LL GIVE THEM ABOUT THREE TO FOUR WEEKS TO TURN THOSE REQUESTS AROUND. WE WILL DO AN INTERNAL REVIEW WITH THE PRESIDENT AND THE CHAIR. FROM THAT WE THEN WILL BRING THE BUDGET PROPOSAL TO THE FINANCE SUBCOMMITTEE HOPEFULLY SOMETIME IN MARCH. WE'LL FINALIZE THE BUDGETS DURING APRIL BASED ON INPUT FROM THE FINANCE SUBCOMMITTEE, AND THEN WE PLAN TO BRING IT TO THIS BOARD IN MAY 2014.

THAT CONCLUDES MY PRESENTATION. ARE THERE ANY QUESTIONS?

MR. SHEEHY: SO THE TRAVEL BUDGET, SO THAT'S UP 66 PERCENT?

MS. SILVA-MARTIN: IT'S NOT UP 66 PERCENT. THE EXPENDITURES THAT HAVE BEEN RECORDED ARE UP 66 PERCENT. WHAT YOU HAVE TO KEEP IN MIND IS THAT THEY PLAN FOR TRIPS, AND SOMETIMES THEY'RE TAKEN LATER ON IN THE YEAR. THIS YEAR I THINK THAT THE COST CENTERS ARE KEEPING MORE TO THE PLAN OF WHAT THEY SUBMITTED IN THEIR TRAVEL PLANS, AND WE ALSO ARE GETTING OUR TRAVEL EXPENSES SUBMITTED TO THE FINANCE OFFICE EARLIER.

MR. SHEEHY: IS IT POSSIBLE TO KNOW HOW THE TRAVEL BUDGETS MATCH -- TRAVEL EXPENDITURES MATCH THE BUDGETS BY COST CENTER? ARE WE EXCEEDING

BUDGETS, I GUESS, IS MY QUESTION FOR TRAVEL? ARE WE EXCEEDING OUR BUDGETS?

MS. SILVA-MARTIN: ABSOLUTELY NOT. IN OUR TRAVEL BUDGET, WE HAVE $533,000 FOR BOTH IN-STATE AND OUT-OF-STATE TRAVEL AND INTERNATIONAL TRAVEL THAT YOU AUTHORIZED. AND AS YOU CAN SEE, EXPENDITURES THAT HAVE BEEN RECORDED AS OF NOVEMBER ARE ONLY 122,000, SO WE'RE WAY UNDER BUDGET, AND WE WILL NOT EXCEED THE TRAVEL BUDGETS, PARTICULARLY THE IN-STATE AND OUT-OF-STATE BECAUSE THOSE ARE REGULATED, AND WE CANNOT EXCEED THOSE COSTS. AND I CAN BRING YOU MORE DETAILS AT THE JANUARY MEETING IF YOU WOULD LIKE.

MR. SHEEHY: YEAH. I THINK MAYBE IN JANUARY WE SHOULD TAKE A LOOK AT THE TRAVEL BUDGET. THAT JUST SEEMS -- TO BE UP 66 PERCENT OVER THIS POINT LAST YEAR IS NOT CLEAR TO ME. I KNOW THAT'S ALWAYS BEEN A SORE SPOT FOR THE GOVERNOR. I THINK WE SHOULD BE ON TOP OF THAT.

MS. SILVA-MARTIN: WHAT I CAN SAY IS THAT OVER THE YEARS, WE HAVE MADE SIGNIFICANT EFFORTS. AS YOU MAY RECALL, WHEN MR. THOMAS CAME ON BOARD, HE DID REQUIRE THAT WE REDUCE OUR OUT-OF-STATE TRAVEL BUDGET, AND WE HAVE DONE THAT. WE'VE BEEN KEEPING EVERY YEAR IN LINE WITH THAT. SO IT'S VERY

CAREFULLY REVIEWED, BUT I'M HAPPY TO PROVIDE YOU NEXT MONTH IN JANUARY WITH ADDITIONAL INFORMATION.

MR. SHEEHY: JUST BECAUSE THAT NUMBER KIND OF JUMPS OUT.

MS. SILVA-MARTIN: SURE. I UNDERSTAND. ABSOLUTELY. NO OTHER QUESTIONS?

DR. DULIEGE: JUST TO UNDERSTAND, JEFF, IT MAY JUMP OUT TO BE HIGHER THAN WHAT WAS SPENT THE YEAR BEFORE, IS THAT WHAT IT IS? THE TRAVEL BUDGET, WHAT SURPRISES YOU IN THE TRAVEL BUDGET?

MR. SHEEHY: THE VARIANCE IS 66 PERCENT. SO I LOOK AT THAT.

DR. DULIEGE: BUT IT'S, HOWEVER, WAY UNDER THE PLANNED BUDGET FOR 2013; IS THAT RIGHT?

MS. SILVA-MARTIN: THAT'S CORRECT. WE HAVE 533 AUTHORIZED.

DR. DULIEGE: I LOOK AT IT A SOMEWHAT DIFFERENT WAY, WHICH IS FOR ME THERE'S SOMETHING STRANGE ABOUT PLANNING FOR SUCH A POSSIBLY HIGH BUDGET AND ONLY SPENDING ABOUT 25 PERCENT OF IT. I'M JUST CURIOUS ABOUT WHAT HAPPENED.

MS. SILVA-MARTIN: WHAT I CAN SAY ABOUT THE TRAVEL BUDGET IS THAT I INDICATED THAT WE REALLY HAVE BEEN TRYING TO ENCOURAGE PEOPLE TO TURN THEIR TRAVEL EXPENSE CLAIMS IN ON A TIMELY BASIS. SO

WHAT'S HAPPENED IN THE PAST IS SOMETIMES, PARTICULARLY WHEN INDIVIDUALS ARE TRAVELING INTERNATIONALLY, WE MAY NOT SEE THEIR TRAVEL EXPENSE CLAIMS FOR TWO TO THREE MONTHS. SO THAT MEANS THAT THERE'S A LAG IN THE RECORDING OF THE EXPENDITURES. BUT I THINK THAT WE'RE ON TRACK WITH OUR BUDGET, AND WE WILL NOT EXCEED WHAT'S BEEN AUTHORIZED FOR THAT.

DR. DULIEGE: THAT I UNDERSTAND. I DON'T THINK YOU WILL EXCEED. IF WE'RE THAT MUCH UNDER THE PLANNED BUDGET, THERE'S NO WAY YOU WILL EXCEED IT IN A FEW MONTHS, FOR SURE.

MS. SILVA-MARTIN: RIGHT. THE OTHER THING THAT I WOULD LIKE TO POINT OUT IS ONE OF THE TRIPS THAT WE TAKE THAT SEVERAL OF THE STAFF ATTEND ISSCR, FOR EXAMPLE, BUT THAT DOESN'T OCCUR TILL JUNE. SO IT'S NOT LIKE A STRAIGHT LINE EVERY MONTH. YOU'RE GOING TO HAVE 12 MONTHS, ONE-TWELFTH OF THE EXPENDITURE. SO IT KIND OF GOES UP AND DOWN.

MR. SHEEHY: YEAH, BUT IN THIS FISCAL YEAR, JUNE IS STILL AHEAD OF US, WHICH IS USUALLY THE MAJOR INTERNATIONAL TRAVEL EVENT. I THINK WE JUST -- IT WOULD BE GOOD TO HAVE SOME MORE DETAIL AT THE NEXT MEETING. I THINK THAT'S PROBABLY THE BEST WAY TO HANDLE IT, AND THAT WILL FEED INTO THE BUDGET DISCUSSION THAT'S COMING UP SHORTLY THEREAFTER.

MS. SILVA-MARTIN: SURE. I'LL BE HAPPY TO PROVIDE THAT INFORMATION.

MR. SHEEHY: DOES THAT MAKE SENSE? DOES THAT SOUND REASONABLE?

CHAIRMAN THOMAS: THANK YOU, CHILA. AND THANK YOU TO YOUR ENTIRE TEAM. AND THANK YOU FOR CALLING THEM OUT. THAT WAS GREAT. SO WE APPRECIATE ALL THE HARD WORK EVERYBODY DOES.

WE SHOULD NOTE THAT, I BELIEVE, MARIA, AM I RIGHT ON THIS, THAT BETWEEN NOW AND THE NEXT BOARD MEETING ON THIS THEME, THE CFAOC WILL BE MEETING. SO WE'LL HAVE OUR ANNUAL VISIT WITH THE CONTROLLER AND HIS PANEL TO ADDRESS FISCAL ISSUES AND OVERSIGHT MATTERS RELEVANT TO THE CONTROLLER'S OFFICE, WHICH WE ALWAYS LOOK FORWARD TO THAT AS A CHANCE TO SHOW THEM WHAT A GREAT JOB EVERYBODY IS DOING. SO WE'LL BE BACK TO YOU WITH THAT IN OUR NEXT BOARD MEETING IN LATE JANUARY.

OKAY. NOW, QUORUM ISSUES HAVE BEEN RESOLVED FOR THE TIME BEING. SO WE'RE GOING TO PROCEED WITH, AS JAMES WOULD SAY, ALL DELIBERATE SPEED TO ITEM NO. 9, WHICH IS CONSIDERATION OF SUPPLEMENT OF RFA 12-03, HUMAN EMBRYONIC STEM CELL DERIVATION AWARD. DR. YAFFE.

DR. YAFFE: MR. CHAIRMAN, MEMBERS OF THE

BOARD, MEMBERS OF THE PUBLIC, I BRING FOR YOUR CONSIDERATION REQUESTS FOR A SUPPLEMENT TO THE HIPSC DERIVATION AWARD. DR. TROUNSON EARLIER REVIEWED OUR HIPS DERIVATION AND BANKING INITIATIVE, WHICH IS NOW UNDER WAY. I JUST WANT TO BRIEFLY TOUCH ON THE FEATURES OF THAT INITIATIVE AGAIN.

THE GOAL IS TO ESTABLISH A HIGH QUALITY DISEASE-SPECIFIC HIPSC RESOURCE IN CALIFORNIA. AND THIS RESOURCE OR THIS EFFORT HAS THREE KEY COMPONENTS. THE FIRST IS TISSUE COLLECTION FROM 3,000 INDIVIDUALS. TISSUES WILL BE COLLECTED WITH AN EYE TO PREVALENT GENETICALLY COMPLEX DISEASES. THERE WILL BE BROAD DONOR CONSENT FOR USE OF THE TISSUE AND DERIVED LINES, AND THERE WILL BE ASSOCIATED TISSUE DONOR MEDICAL INFORMATION COLLECTED.

THE SECOND COMPONENT IS HUMAN INDUCED PLURIPOTENT STEM CELL LINE GENERATION BY A SINGLE DERIVER AND USING A SINGLE DERIVATION METHOD.

AND THE THIRD COMPONENT IS BANKING OF THE CELLS IN A CIRM-SUPPORTED HUMAN PLURIPOTENT STEM CELL REPOSITORY. THESE CELL LINES WILL THEN BE AVAILABLE FOR A MYRIAD OF STUDIES INVOLVING DISEASE MODELING, TARGET DISCOVERY, AND DRUG DISCOVERY AND DEVELOPMENT.

YOU WILL RECALL THAT WE BROUGHT THE RESULTS OF THE GRANTS WORKING GROUP TO YOU LAST, I THINK IT WAS, MARCH, AND YOU APPROVED THE FOLLOWING AWARDS. THERE ARE SEVEN TISSUE COLLECTING AWARDS, AND I'LL JUST GO OVER THEM BRIEFLY IN A MOMENT, A CELL LINE DERIVATION AWARD, ONE, TO THOMAS NOVAK AS THE PROGRAM DIRECTOR AT CELLULAR DYNAMICS INTERNATIONAL, CDI, AND ONE REPOSITORY AWARD TO STEVEN MADORE OF CORIELL INSTITUTE. I SHOULD NOTE ALTHOUGH BOTH OF THOSE ORGANIZATIONS ARE CENTERED OUTSIDE CALIFORNIA, THEY ARE ESTABLISHING PRESENCE IN CALIFORNIA. THE WORK IS GOING TO BE DONE AT THE BUCK INSTITUTE IN NOVATO, CALIFORNIA.

THERE ARE SEVEN TISSUE COLLECTORS INVOLVED AND FUNDED THROUGH THIS INITIATIVE. AND AS YOU CAN SEE ON THE SLIDE OR IN YOUR NOTES, A RANGE OF IMPORTANT DISEASES AND CONDITIONS, INCLUDING NEURODEVELOPMENTAL DISORDERS IN CHILDREN, AND IDIOPATHIC AUTISM, AGAIN, IN A PEDIATRIC POPULATION, IDIOPATHIC PULMONARY FIBROSIS, LUNG DISEASE, SUSCEPTIBILITY TO VIRAL HEPATITIS, AND ALCOHOLIC STEATOHEPATITIS, NONALCHOLIC STEATOHEPATITIS, A TYPE OF HEART DISEASE, IDIOPATHIC FAMILIAL DILATED CARDIOMYOPATHY, AS WELL AS ALZHEIMER'S DISEASE, AND BLINDING EYE DISEASES, PARTICULARLY IN ELDERLY

POPULATIONS.

IN TOTAL THERE WILL BE 3,000 TISSUE DONORS. OF THESE 2450 WILL BE DONATIONS FROM AFFECTED INDIVIDUALS AND 550 FROM HEALTHY CONTROL INDIVIDUALS.

A RECOMMENDATION OF THE GRANTS WORKING GROUP WHEN THEY REVIEWED THESE PROPOSALS WAS THAT CIRM ASSEMBLE A GROUP OF EXPERTS TO ADVISE ON THE COLLECTION OF CONTROLS AND IN PARTICULAR TO TRY AND SET UP SOME CONTROL COHORTS SO THERE COULD BE SHARED CONTROLS SO THAT EVERY STUDY DIDN'T NEED ITS OWN CONTROLS. THERE COULD BE GROUPS OF CONTROLS, FOR EXAMPLE. CONTROLS FROM PEDIATRIC PATIENTS COULD SERVE FOR BOTH THE NEURODEVELOPMENTAL DISORDERS IN CHILDREN AND THE IDIOPATHIC AUTISM.

AND WE TOOK THAT RECOMMENDATION AND ASSEMBLED A GROUP OF SEVEN INDEPENDENT HUMAN GENETICS, GENOMICS, AND STEM CELL EXPERTS. SOME OF THESE INDIVIDUALS ARE ALSO MEMBERS OF OUR GRANTS WORKING GROUP. THIS GROUP DID ADVISE ON THE COLLECTION AND THE ASSEMBLY OF THE CONTROL COHORTS, BUT THEY ALSO MADE A VERY STRONG RECOMMENDATION THAT WE UNDERTAKE GENOMICS ANALYSIS OR SNP ANALYSES ON ALL TISSUE SAMPLES AND DERIVED CELL LINES. SNP, OR SINGLE NUCLEOTIDE POLYMORPHISM, ANALYSIS DETECTS DNA

SEQUENCE VARIATIONS THROUGHOUT THE GENOME. SNP'S ARE AT THE CORE OF GENETIC VARIATION IN INDIVIDUALS AND BETWEEN INDIVIDUALS AND, IN FACT, CAN INDICATE IMPORTANT FEATURES OF DISEASE SUSCEPTIBILITY AND THE RESPONSE TO THERAPEUTIC TREATMENT.

SNP ANALYSIS WILL FACILITATE CASE CONTROL, SAMPLE MATCHING FOR THIS COLLECTION, THE ANALYSIS OF GENETIC ANCESTRY AND GENETIC DIVERSITY, BOTH OF INDIVIDUAL LINES AND OF THE COLLECTION AS A WHOLE. IT WILL FACILITATE THE IDENTITY MATCHING, HIGH PRECISION IDENTITY MATCHING OF DERIVED LINES AND THE ORIGINAL TISSUES. IT WILL ALLOW A DETERMINATION OF CELL LINE GENOMIC INTEGRITY AND ALLOW THE IDENTIFICATION AND ANALYSIS OF DISEASE-ASSOCIATED MARKERS.

THE SNP DATA WILL BE DEPOSITED AND AVAILABLE THROUGH DBSNP, A DATABASE MAINTAINED BY THE NATIONAL CENTER FOR BIOTECHNOLOGY INFORMATION, A COMPONENT OF THE NIH.

IT WAS THE OPINION OF OUR ADVISORY GROUP AND OF OUR SCIENTIFIC STAFF THAT WHOLE GENOME SNP DATA WILL SIGNIFICANTLY INCREASE THE VALUE AND UTILITY OF CIRM'S HIPS COLLECTION. I WOULD GO FURTHER TO SUGGEST THAT THIS WOULD BE A LEVERAGING OF OUR INVESTMENT IN THE HIPSC INITIATIVE TO BOTH

ENHANCE THE VALUE OF THE SAMPLES THAT WE ARE ASSEMBLING AND ALSO CREATE A DISTINCTIVE RESOURCE. A NUMBER OF SCIENTISTS WE'VE TALKED TO ABOUT THE SNP ANALYSIS HAVE SUGGESTED THAT THE SNP ANALYSIS ALONE, TOGETHER WITH THE MEDICAL INFORMATION WE'RE GATHERING, IS ALREADY A REALLY VALUABLE RESOURCE TO EXPLORE DISEASE MECHANISM, ANALYZE SUSCEPTIBILITY, AND MAKE MEDICAL ADVANCE.

SO WE'RE ASKING FOR SUPPLEMENTAL FUNDS THAT WILL ENABLE WHOLE GENOME SNP ANALYSIS ON DNA FROM THE 3,000 TISSUE SAMPLES AND 9,000 DERIVED LINES. I WANT TO NOTE THAT THIS REQUEST DID NOT COME FROM THE GRANTEE. THIS REQUEST IS COMING FROM SCIENTIFIC STAFF AT THE SUGGESTION AND ENCOURAGEMENT OF INDEPENDENT SCIENTIFIC ADVISORS.

I AM REQUESTING -- WE ARE REQUESTING $2 MILLION AS A SUPPLEMENT TO THE HIPSC DERIVATION AWARD TO CELLULAR DYNAMICS INTERNATIONAL, CDI, THE DERIVER, WITH THOMAS NOVAK AS THE PROGRAM DIRECTOR. AND THIS MONEY WOULD BE USED -- I SHOULD SAY UP TO $2 MILLION WOULD BE USED TO SUPPORT THIS ADVANCED GENOMIC ANALYSIS. I'LL BE HAPPY TO TAKE QUESTIONS.

MR. SHEEHY: I HAVE A LOT OF PROCESS QUESTIONS. THERE'S NO BUDGET. I MEAN WE'RE JUST GIVING OUT $2 MILLION TO TWO PRIVATE ENTITIES.

DR. YAFFE: I CAN BREAK THAT DOWN FOR YOU, IF YOU WOULD LIKE.

MR. SHEEHY: WELL, THERE SHOULD BE A BUDGET THAT'S BEEN DISTRIBUTED TO THE PUBLIC. WE SHOULD HAVE A BUDGET IN OUR BOOK. WE SHOULD HAVE A REQUEST FOR -- THEY ASK FOR THE MONEY, FRANKLY, I THINK, AND WE SHOULD HAVE REVIEWED THE REQUEST. THERE WAS A GENOMICS REVIEW WHICH WOULD HAVE AFFORDED THE CHANCE TO HAVE REVIEW. I JUST DON'T THINK WE JUST HAND OUT $2 MILLION TO A PRIVATE ENTITY BECAUSE PEOPLE SAID IT WAS A GOOD IDEA. I THINK IN TERMS OF GOOD STEWARDSHIP, AS A PUBLIC OFFICIAL, I JUST FIND THIS TO BE STUNNING.

THE EVIDENCE BASIS FOR PROVIDING THIS IS JUST REALLY THIN. I'VE GOT A COUPLE OF PAGES AND THAT'S IT. WE HAD JEANNE LORING SAYING SOME GENETIC ANALYSIS CAN BE DONE FOR A HUNDRED FIFTY BUCKS. I JUST -- WE SHOULD HAVE HAD -- FOR $2 MILLION, I MEAN IF THIS WAS A HUNDRED THOUSAND DOLLARS, I CAN UNDERSTAND IT, BUT FOR $2 MILLION, THERE SHOULD BE AN ACTUAL PROPOSAL THAT GETS REVIEWED BY THE WORKING GROUP, ESPECIALLY SINCE YOU HAD A GENOMICS REVIEW NOT TWO MONTHS AGO. BUT THIS IS JUST NOT ACCEPTABLE, FROM MY PERSPECTIVE, AS A PROCESS FOR HANDING OUT GOVERNMENT MONEY FROM THE TAXPAYERS OF

CALIFORNIA.

DR. KRONTIRIS: I'D LIKE TO AGREE WITH THAT. I WONDER HOW MUCH THE CURRENT CHIPS COST FOR HUNDREDS OF THOUSANDS OF SNP'S.

I HAVE A QUESTION. HOW MANY DISEASES ARE REPRESENTED IN THIS 2450 AFFECTEDS?

DR. YAFFE: ELEVEN DISEASES.

DR. KRONTIRIS: ELEVEN DISEASES, SO THAT'S ROUGHLY 200.

DR. YAFFE: IT VARIES. SOME DISEASES THERE ARE FEWER PATIENTS, AND SOME DISEASES THERE ARE MORE.

DR. KRONTIRIS: SO EVEN -- THAT'S AN EXCEEDINGLY SMALL NUMBER. IT'S A USELESS NUMBER FOR A CASE CONTROL STUDY NOWADAYS. COUPLE HUNDRED CASES, 500 CONTROLS. SO I'M REALLY SURPRISED THAT YOU HAD EXPERTS TELL YOU THAT THAT WOULD ALLOW YOU TO IDENTIFY DISEASE. SO THIS IS, I THINK, FURTHER SUPPORTING WHAT YOU SAY IN TERMS OF REALLY NEEDING TO GET THIS TO REAL REVIEW. THE FACT THAT THERE ARE SO MANY DISEASES WITHIN THIS SMALL GROUP OF CASES MEANS THAT ITS VALUE IN SEARCHING FOR DISEASE MARKERS IS LIMITED. AND I THINK THAT SUPPORTS WHAT JEFF IS SAYING ABOUT SOMETHING LIKE THIS NEEDING REAL SCIENTIFIC REVIEW.

DR. YAFFE: WE DIDN'T ANTICIPATE THAT THIS COLLECTION WOULD BE USED FOR GWAS, THE LARGE GENOME STUDIES. THE USE OF THE SAMPLES AND THE DATA FOR DISEASE MARKER ANALYSIS IS AN AUGMENTED AND ADDITIONAL USE, BUT THAT'S NOT THE PRIMARY USE. THE PRIMARY USE WOULD BE FOR CASE CONTROL MATCHING, FOR GENOMIC INTEGRITY, FOR GENOMIC IDENTITY OF CELL LINES AND DERIVED CELLS, AND FOR GENETIC ANCESTRY AND GENOMIC DIVERSITY.

DR. KRONTIRIS: SO ALL OF THOSE USES, BUT DETERMINATION OF INTEGRITY DON'T REQUIRE LOTS OF SNP'S.

MR. SHEEHY: COULD I MAKE A MOTION?

DR. YAFFE: I JUST, IN RESPONSE, MR. SHEEHY, AND I'M SORRY THAT WE DIDN'T HAVE THIS DATA AVAILABLE TO YOU EARLIER, AND I COULD MAKE IT AVAILABLE, JUST PUT ON THE BOARD A BREAKDOWN OF THE BUDGET AND WHERE WE -- HOW WE DERIVED AT THE NUMBER OF $2 MILLION. THE MAJORITY OF THE MONEY IS GOING TO PURCHASE THE ARRAYS FOR SNP CHIPS. THERE ARE TWO TYPES, HIGH DENSITY FOR THE TISSUES, A LOWER DENSITY AND LESS EXPENSIVE ARRAY FOR THE DERIVED CELL LINES. THE REMAINING COSTS ARE FOR SAMPLE PREPARATION, FOR DNA PURIFICATION, SAMPLE PROCESSING, AND DATA ANALYSIS.

AGAIN, I WANT TO REITERATE THAT CDI DID NOT COME TO US, ALTHOUGH WE'VE HAD A DIALOGUE WITH THEM ABOUT WHETHER THEY WOULD BE WILLING TO DO THIS WORK. EVERYONE WE'VE TALKED TO FROM THE BANK, BANKING INDIVIDUALS, THE TISSUE COLLECTORS, AND THE DERIVER, AS WELL AS OUTSIDE GENETICISTS AND GENOMICS EXPERTS, HAVE EXPRESSED THE OPINION THAT THIS WOULD BE A VALUABLE ADDITION TO OUR EFFORT TO ENHANCE AND LEVERAGE MONEY WE'RE ALREADY PUTTING INTO IT.

MR. SHEEHY: AGAIN, I COME TO THE -- YOU HAVE A FACTUAL BASIS THAT IS NOT IN EVIDENCE HERE. SO WE HAVE ANONYMOUS CASE REPORTS. WE GIVE OUT MONEY AFTER PEER REVIEW. THAT'S HOW IT WORKS. THAT'S WHAT PROP 71 SAYS. RESEARCH MONEY IS SUPPOSED TO BE PEER REVIEWED. YOU HAD A PEER REVIEW WHERE YOU COULD HAVE DONE THIS. THE FACT THE COMPANY IS NOT ASKING FOR IT MAKES IT EVEN DODGIER TO ME.

I WOULD LIKE TO MOVE THAT WE NOT ACCEPT THIS PROPOSAL. I THINK IF THIS REALLY IS SOMETHING THAT SHOULD BE DONE, THEN THE COMPANY OR SOMEONE SHOULD PUT TOGETHER A REAL PROPOSAL WITH A REAL BUDGET AND WE SHOULD HAVE IT PEER REVIEWED BY OTHER EXPERTS SO THAT WE ACTUALLY HAVE A PROPOSAL. THERE'S NOT EVEN A PROPOSAL HERE. THIS IS JUST LIKE

$2 MILLION, AND WHO'S GOING TO DECIDE WHAT TESTS ARE DONE ON WHAT SAMPLES? ARE WE SURE THAT THOSE ARE THE RIGHT TYPES OF TESTS TO BE DONE ON THOSE SAMPLES? WHO'S GOING TO GO THE TEST, CDI?

I DON'T WANT TO ARGUE THIS OUT. JUST IN TERMS OF PROCESS, THIS IS AN INAPPROPRIATE WAY TO GIVE OUT $2 MILLION. I CANNOT SUPPORT IT. I WILL NOT SUPPORT IT, AND I'M MOVING THAT WE NOT SUPPORT IT. AND I HOPE I HAVE A SECOND.

DR. STEWARD: SECOND.

CHAIRMAN THOMAS: FURTHER DISCUSSION BY MEMBERS OF THE BOARD ON THIS TOPIC?

DR. JUELSGAARD: SO, TOASTER, MICHAEL, THIS IS FROM YESTERDAY. BUT ANYWAY, JUST A SERIES OF QUESTIONS. SO WE'RE THE SOLE FUNDING SOURCE FOR THIS INITIATIVE; IS THAT RIGHT, CIRM IS?

DR. YAFFE: THAT IS CORRECT.

DR. JUELSGAARD: AND WHEN WE DID THIS, DO WE HAVE CONTRACTUAL AGREEMENTS WITH THE TWO ENTITIES THAT ARE INVOLVED?

DR. YAFFE: WE DO.

DR. JUELSGAARD: HOW IS THE -- HOW DO WE PAY THEM? SO IT'S $20 MILLION, AS I RECALL, THAT WAS FUNDED IN EACH ONE OF THEM, OR IS THAT UP TO $20 MILLION? HOW DOES THAT WORK?

DR. YAFFE: THE DERIVATION IS 16 MILLION, THE BANKING IS 10 MILLION. HOW DO WE PAY THEM?

DR. JUELSGAARD: NO. NO. NO. SO WE'VE CLEARLY MAPPED OUT THAT WE'RE GOING TO SPEND THE TOTAL $40 MILLION ON 3,000 SAMPLES THE WAY THINGS ARE CURRENTLY ARRANGED; IS THAT RIGHT?

DR. YAFFE: ACTUALLY I BELIEVE THE TOTAL BUDGET IS $32 MILLION.

DR. JUELSGAARD: 32 MILLION.

DR. YAFFE: YES. IT'S A BARGAIN AT $32 MILLION.

DR. JUELSGAARD: WAIT A MINUTE, THEN. SO IF WE'RE ALREADY ON AN UNDER-SPEND RUN AND WE'VE APPROVED 40, WHY DO WE EVEN ASK FOR MORE MONEY? WE'VE GOT EIGHT MILLION -- YOU'VE GOT EIGHT MILLION, WE'VE GOT $8 MILLION THAT WE'VE ALREADY APPROVED TO SPEND ON THIS PROJECT. RIGHT? YOU JUST SAID 32 MILLION AND WE APPROVED 40. LET'S START WITH THAT.

DR. YAFFE: I'M NOT AWARE THAT WE HAVE THE FREEDOM TO TAKE MONEY THAT HAS NOT BEEN AWARDED, EVEN THOUGH YOU MAY HAVE CONCEPTED IT, AND THEN APPLY IT TO PROJECTS.

DR. JUELSGAARD: SO WHAT YOU'RE PROPOSING IS JUST TO EXPAND THE SCOPE OF THE UNDERLYING PROJECT TO INCLUDE THIS, BUT STAY WITHIN THE

APPROVED AMOUNT?

DR. YAFFE: THAT'S CORRECT.

DR. JUELSGAARD: GOT IT. WASN'T CLEAR ABOUT THAT.

CHAIRMAN THOMAS: OS.

DR. STEWARD: SO I HAVE GENERALLY THE SAME SENSE THAT JEFF HAS ABOUT THIS. IT SEEMS LIKE THIS IS SOMETHING THAT HAS TO BE COMPETED. IF YOU'RE BUYING ANY PRODUCT OR SERVICE WITH STATE MONEY, IT'S GOT TO BE A COMPETITIVE PROCESS AND NOT JUST KIND OF AN AWARD.

I'M ALSO -- MAYBE THIS HAS ALREADY BEEN WORKED OUT, AND I APOLOGIZE IF IT. IT'S OBVIOUSLY CORRECT THAT THIS COULD BE A HUGE RESOURCE FOR MINING DATA RELATING CLINICAL CONDITION WITH GENOMICS. HOWEVER, THAT DEPENDS CRITICALLY ON THE CONSENTING GOING IN AT THE TIME OF TISSUE COLLECTION. AND HAS THAT ACTUALLY BEEN WORKED OUT IN A WAY THAT ALL MAKES SENSE?

I'M SAYING THAT BECAUSE THAT'S REALLY -- THAT WOULD ACTUALLY NORMALLY BE PART OF A PROPOSAL THAT WOULD COME FORWARD TO HAVE PEOPLE LOOK AT IT AND SAY, YES, THIS ACTUALLY MAKES SENSE.

DR. YAFFE: YES. AND THIS CONSENT WOULD INCLUDE GENETIC AND GENOMIC ANALYSIS OF DNA FROM THE

TISSUE SAMPLES. SO IT'S BEEN APPROVED, IN FACT, BY A NUMBER OF THE IRB'S OF THE TISSUE COLLECTORS INCLUDES THIS ACTIVITY.

DR. STEWARD: THAT'S ONE THING. BUT RELATING THAT TO CLINICAL DATA IS ANOTHER ENTIRELY. AND I'M JUST SAYING THAT AT THE STAGE OF THE CONSENTING, THERE ACTUALLY HAS TO BE A PRETTY CLEAR AND CAREFULLY WORDED STATEMENT TO THAT REGARD. I'M JUST ASKING IF ALL THAT'S IN PLACE.

DR. YAFFE: AS I UNDERSTAND IT, ALL OF IT IS IN PLACE. UNFORTUNATELY GEOFF LOMAX IS NOT HERE, WHO'S OUR OFFICER WHO HANDLES MUCH OF THIS WORK ON CONSENT AND IRB. BUT FROM MY UNDERSTANDING, THAT IS IN PLACE IN FACT.

DR. STEWARD: AGAIN, I WOULD STILL SAY THAT THAT'S SOMETHING THAT WOULD NORMALLY BE A REVIEWED SET OF THINGS RATHER THAN JUST, YES, IT'S IN PLACE AND LET'S GIVE TWO MILLION BUCKS. SO JUST TO SUPPORT WHAT JEFF SAID, I THINK HAS TO BE -- IT'S FINE IF IT'S AN RFP OR A CONTRACT PROPOSAL OR SOMETHING LIKE THAT. I THINK IT'S A GREAT IDEA, BUT JUST SAYING, OKAY, THESE GUYS GET THE MONEY, I'M UNCOMFORTABLE WITH THAT.

MR. SHEEHY: AND YOU RAISE THE QUESTION TOO WITH CONSENT. SO IF THE IRB'S HAVE CONSENTED TO

THE COLLECTION OF THIS TYPE OF INFORMATION, BUT THIS WASN'T IN THE ORIGINAL BUDGET, IT MAKES ME WONDER IF WE PICKED THE RIGHT GRANTEE IN THE FIRST PLACE, I MEAN HONESTLY. THE CONTRADICTIONS HERE AND THE LACK OF INFORMATION AND JUST THE NONGOVERNMENTAL PROCESS THAT'S BEING DEPLOYED HERE IS VERY TROUBLING.

CHAIRMAN THOMAS: SO, MR. YAFFE, WHAT I WOULD THINK IS A GOOD IDEA HERE, BECAUSE THE UNDERLYING SUGGESTION AS TO THE VALUE OF WHAT YOU'RE LOOKING FOR, I THINK, HAS A LOT OF MERIT. I DON'T THINK ANYONE CONTESTS THAT. BUT WE HAVE SERIOUS PROCEDURAL ISSUES. WHAT I WOULD RECOMMEND HERE IS, IN THE EVENT MR. SHEEHY'S MOTION PASSES, IS THAT YOU GO BACK TO THE -- GIVE THIS A BIT MORE THOUGHT, PUT IT TOGETHER IN SOMETHING THAT CONFORMS TO NORMAL PROCESS, AND THEN BE PREPARED TO BRING IT BACK AND HAVE DISCUSSION AT THAT POINT ON THE THEORY THAT THE ACTUAL SUBSTANTIVE ISSUE IS A PROFOUND ONE, WHICH I THINK IT IS.

MR. SHEEHY: THAT'S WHY I WOULD LIKE TO HAVE IT PEER REVIEWED BECAUSE THAT WILL CONFIRM THAT SUPPOSITION.

CHAIRMAN THOMAS: THAT'S RIGHT. SO I THINK WITH THAT IN MIND, I DON'T KNOW THAT WE NEED ANY --

DR. STEWARD: JUST ONE OTHER THING. I THINK IT SHOULD BE A COMPETITIVE PROCESS AS WELL. THEY'RE SORT OF THE OBVIOUS PEOPLE, BUT MAYBE SOMEBODY ELSE CAN DO THE SAME THING CHEAPER.

CHAIRMAN THOMAS: OKAY. ANY FURTHER DISCUSSION BY MEMBERS OF THE BOARD? COMMENTS FROM MEMBERS OF THE PUBLIC? OKAY. DO WE NEED A ROLL CALL ON THIS? NO. COULD YOU PLEASE RESTATE THE MOTION, MR. HARRISON.

MR. HARRISON: AS I UNDERSTAND IT, THE MOTION IS NOT TO FUND THE SUPPLEMENT TO HIPSC DERIVATION AWARD.

CHAIRMAN THOMAS: OKAY. EVERYBODY GOT THAT? VOICE VOTE. ALL THOSE IN FAVOR OF THAT MOTION PLEASE SAY AYE. OPPOSED? ABSTENTIONS?

MS. BONNEVILLE: WE JUST NEED A ROLL CALL VOTE FOR THOSE ON THE PHONE.

ART TORRES.

MR. TORRES: AYE.

MS. BONNEVILLE: SUE BRYANT.

DR. BRYANT: YES.

MS. BONNEVILLE: LARS BERGLUND.

DR. BERGLUND: YES.

MS. BONNEVILLE: THANK YOU.

DR. YAFFE: THANK YOU FOR YOUR

CONSIDERATION.

CHAIRMAN THOMAS: MR. YAFFE, YOU HAVE YOUR MARCHING ORDERS. THANK YOU.

WE'RE NOW GOING TO PROCEED TO ITEM NO. 10. SO YOU WILL RECALL, THIS IS ON THE CRITERIA FOR THE SELECTION OF OUR NEXT PRESIDENT. AS YOU RECALL FROM YESTERDAY, I MENTIONED THE PRESIDENTIAL SEARCH SUBCOMMITTEE HAS BEEN BUSILY AT WORK. WE'VE HAD TWO MEETINGS, ONE OF WHICH ENDED UP IN THE ELECTION OF KORN FERRY AS OUR SEARCH FIRM. WHAT REMAINS TO BE ADOPTED HERE IS THE SET OF CRITERIA.

YOU HAVE IT. IT'S TAB 10 IN YOUR PACKAGE. WE HAD A LOT OF DISCUSSION ON THIS.

MR. HARRISON: JUST FOR MEMBERS, IF YOU'RE LOOKING IN YOUR BINDER, YOU HAVE TWO COPIES OF IT, ONE OF WHICH HAS A REDLINE TO REFLECT THE CHANGES MADE AT THE PRESIDENTIAL SEARCH SUBCOMMITTEE ON TUESDAY EVENING. SO THAT'S WHAT YOU SHOULD LOOK AT.

CHAIRMAN THOMAS: THANK YOU. SO WE HAD QUITE EXTENSIVE DISCUSSION ON THIS, WHICH I'M HAPPY TO SUMMARIZE. BUT IF YOU READ THROUGH THE CRITERIA, I THINK YOU WILL HAVE A COMPREHENSIVE FEEL FOR ALL THE DIFFERENT ELEMENTS WE PROPOSE LOOKING FOR IN THE NEXT PRESIDENT. AND THIS IS SOMETHING THAT WE DO NEED TO FORMALLY ADOPT THROUGH A MOTION. SO I WOULD

ASK THAT SOMEBODY MAKE A MOTION THAT WE APPROVE THE CRITERIA.

MR. SHEEHY: SO MOVED.

MR. TORRES: SO MOVED.

DR. PRIETO: SECOND.

CHAIRMAN THOMAS: IT'S BEEN MOVED IN A TIE BY MR. SHEEHY AND SENATOR TORRES AND SECONDED BY DR. PRIETO.

SO IF EVERYBODY COULD JUST TURN AND LOOK AT THAT AND JUST SEE IF ANYBODY HAS PARTICULAR QUESTIONS OR COMMENTS OR WOULD LIKE FURTHER EXPLANATION ON THE VARIOUS ITEMS LISTED ON THAT DOCUMENT. SEEING NO COMMENTS, DO WE HAVE COMMENTS FROM MEMBERS OF THE PUBLIC? ANY COMMENT BY MEMBERS ON THE PHONE? OKAY. THANK YOU. I THINK WE CAN PROCEED TO A VOTE. MR. HARRISON, VOICE VOTE IS FINE. ALL THOSE IN FAVOR OF ADOPTING THE LIST OF CRITERIA IN TAB 10 FOR OUR PRESIDENTIAL SEARCH PLEASE SAY AYE. OPPOSED? ABSTENTIONS? VERY GOOD. MOTION PASSED UNANIMOUSLY.

MS. BONNEVILLE: ART TORRES.

MR. TORRES: AYE.

MS. BONNEVILLE: SUE BRYANT.

DR. BRYANT: YES.

MS. BONNEVILLE: LARS BERGLUND.

DR. BERGLUND: YES.

MS. BONNEVILLE: THANK YOU.

CHAIRMAN THOMAS: OKAY. LIKE I WAS SAYING, UNANIMOUS APPROVAL. I DIDN'T HEAR WHAT YOU SAID. GIL WOULD LIKE TO PRESENT THE NEXT ITEM, IS THAT WHAT YOU'RE SAYING, WHICH IS ITEM NUMBER WHAT?

MR. HARRISON: ELEVEN.

CHAIRMAN THOMAS: ELEVEN. PERFECT. FIRST TIME IN THIS ENTIRE TWO DAYS WE'VE ACTUALLY MOVED SEQUENTIALLY IN THE RIGHT ORDER AS LISTED ON THE AGENDA.

DR. SAMBRANO: THANK YOU VERY MUCH, MR. CHAIR, MEMBERS OF THE BOARD. I'M BRINGING TO YOU THREE NOMINEES FOR GRANTS WORKING GROUP MEMBERSHIP, WHO BRING US EXPERTISE IN STEM CELL THERAPY DEVELOPMENT, REGULATORY AFFAIRS IN CARDIOVASCULAR DISEASE. THEIR BRIEF BIOS ARE IN YOUR BOOKS UNDER ITEM 11.

THE NOMINEES ARE DRS. STEWART ABBOTT, CAROL DANIELSON, AND WARREN SHERMAN. SO WE SEEK YOUR APPROVAL OF THESE INDIVIDUALS AS OUR MEMBERS OF OUR WORKING GROUP.

DR. PRIETO: MOVE APPROVAL.

MR. SHEEHY: SECOND.

CHAIRMAN THOMAS: IT'S BEEN MOVED AND

SECONDED. ANY DISCUSSION BY MEMBERS OF THE BOARD? LIKE THE LATEST IN THE SERIES OF EMINENTLY QUALIFIED MEMBERS FOR THIS, DR. SAMBRANO, THANK YOU. ANY COMMENTS FROM MEMBERS OF THE PUBLIC? COMMENTS BY MEMBERS ON THE PHONE? ALL THOSE IN FAVOR OF THE MOTION PLEASE SAY AYE. OPPOSED? ROLL CALL.

MS. BONNEVILLE: ART TORRES. SUE BRYANT.

DR. BRYANT: YES.

MS. BONNEVILLE: LARS BERGLUND.

DR. BERGLUND: THANK YOU.

CHAIRMAN THOMAS: THANK YOU. THAT MOTION PASSES. THANK YOU, DR. SAMBRANO.

LET'S SEE HERE. WE'RE DOWN TO THE VERY CONTROVERSIAL ITEM OF APPROVING THE BOARD MINUTES FOR THE LAST MEETING. DO I HEAR A MOTION?

DR. STEWARD: SO MOVED.

CHAIRMAN THOMAS: MOVED BY DR. STEWARD. SECONDED BY?

MR. ROWLETT: SECOND.

CHAIRMAN THOMAS: BY MR. ROWLETT. I'M NOT EVEN GOING TO ASK FOR COMMENT. ALL THOSE -- GROSSLY BREACHING MR. HARRISON'S ROBERT'S RULES OF ORDER. ALL THOSE IN FAVOR PLEASE SAY AYE. OPPOSED? THOSE ON THE PHONE?

DR. BRYANT: AYE.

CHAIRMAN THOMAS: I HEARD SUE. AND I HEARD LARS TOO.

DR. BERGLUND: YES.

CHAIRMAN THOMAS: THERE YOU GO. MOTION APPROVED.

ITEM 17, CONSIDERATION OF ADOPTION OF AMENDMENTS TO SECTION 100601. IF ANYBODY KNOWS WHAT THAT IS BEFORE MR. TOCHER SPEAKS, YOU GET EXTRA BONUS POINTS.

MR. TOCHER: THANK YOU, CHAIRMAN AND MEMBERS. THIS IS JUST A QUICK ITEM, HOUSEKEEPING ITEM. EARLIER THIS YEAR AT YOUR LAST MEETING, YOU APPROVED A FINAL SET OF AMENDMENTS TO OUR INTELLECTUAL PROPERTY REGULATIONS THAT, AMONG OTHER THINGS, DEFINE THE FORMULA FOR COMPUTING LICENSING REVENUE THAT IS SHARED WITH THE STATE FROM OUR GRANTEES.

AS PART OF THE FORMAL ADOPTION PROCESS, AS SOME OF YOU MAY KNOW, THE OFFICE OF ADMINISTRATIVE LAW TAKES A LOOK AT THESE REGULATIONS BEFORE THEY GO INTO EFFECT. AND IN THIS CASE WITH THIS REGULATION 601, THEY HAD A RECOMMENDATION TO PROVIDE FURTHER CLARITY TO ONE OF THE SUBDIVISIONS. AND THAT'S FOUND ON PAGE 5 OF THE ATTACHMENT IN ITALICS.

THEIRS IS JUST SIMPLY TO MAKE CLEAR THE

OPERATION OF THE FORMULA WITH RESPECT TO NONPROFIT GRANTEES. IT IS A POLICY THAT HAS ALWAYS BEEN EMBODIED IN OUR REGULATIONS, BUT THEY FELT THE TEXT COULD BE CLEARER ON THAT POINT. SO AS A RESULT, CIRM RECIRCULATED WITH OAL'S PROPOSED CLARIFICATION, WE CIRCULATED THAT FOR PUBLIC COMMENT. AND NOT SURPRISINGLY, NONE WAS RECEIVED. AND SO AS A FINAL STEP, WE BRING THOSE OAL-INSPIRED AMENDMENTS BACK FOR YOUR APPROVAL SO THAT WE CAN THEN RETURN IT TO OAL FOR FINAL APPROVAL. SO SEEKING A MOTION TO APPROVE THE AMENDMENTS.

DR. STEWARD: MOVE TO APPROVE.

DR. PRIETO: SECOND.

CHAIRMAN THOMAS: IT'S BEEN MOVED AND SECONDED. DO WE HAVE ANY DISCUSSION BY MEMBERS OF THE BOARD? ALL THOSE IN FAVOR PLEASE SAY AYE. OPPOSED? ABSTENTIONS? I THINK I HEARD SUE AND LARS ON THE PHONE.

DR. BRYANT: YES.

DR. BERGLUND: YES.

MR. TORRES: TORRE IS AYE. YES. I THINK I WAS NOT RECORDED ON THE LAST VOTE BECAUSE I WAS ON MUTE BY ACCIDENT.

CHAIRMAN THOMAS: WE'LL SO NOTE AND AMEND.

OKAY. SO I BELIEVE WE'RE DOWN TO GENERAL

PUBLIC COMMENT ON ANYTHING AND EVERYTHING. ITEM 8 WE ARE DEFERRING, MR. JUELSGAARD, BECAUSE MR. LOMAX IS NOT HERE. YOU WILL NOTE THERE IS AN AGENDIZED SPOT FOR CLOSED SESSION. WE HAVE NO NEED FOR ONE.

MR. HARRISON: FOR THE RECORD, THE MOTION TO APPROVE AMENDMENT TO REGULATION 100601 PASSED.

CHAIRMAN THOMAS: I MUST HAVE MISSED SAYING THAT. THANK YOU, MR. HARRISON. AS ALWAYS ON TOP OF YOUR GAME.

HOWEVER, I WOULD LIKE TO NOTE THAT THE HIGH ACHIEVEMENT AWARD FOR THIS LENGTHY TWO-DAY SESSION GOES TO DIANE WINOKUR, WHO DID SOMETHING THAT, AS FAR AS I KNOW, NEVER HAPPENED IN MR. KLEIN'S TENURE AND HADN'T HAPPENED YET IN MY TENURE, WHICH WAS TO ASK A QUESTION THAT ACTUALLY STUMPED MR. HARRISON AND REQUIRED THAT HE RESEARCH BEFORE RESPONDING. SO, DIANE, YOU GET THE AWARD.

(APPLAUSE.)

CHAIRMAN THOMAS: SO WITH THAT, I WOULD LIKE TO THANK EVERYBODY. THIS HAS BEEN A VERY LONG COUPLE OF DAYS, HIGHLY SUBSTANTIVE COUPLE OF DAYS. WE GOT THROUGH A GREAT MANY THINGS, HAD VERY EARNEST DISCUSSION. I WANT TO THANK EVERYBODY FOR STICKING IT OUT. AND TO THOSE OF YOU ON THE PHONE AS WELL, WISH EVERYBODY A VERY HAPPY HOLIDAY AND WE WILL SEE

YOU ALL ON JANUARY 29TH. WE STAND ADJOURNED.

(THE MEETING WAS THEN CONCLUDED AT 02:38 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 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

LUXE HOTEL
11461 SUNSET BOULEVARD
LOS ANGELES, CALIFORNIA
ON
DECEMBER 11, 2013

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.

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