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

REGULAR MEETING

LOCATION: KABUKI HOTEL
1625 POST STREET
SAN FRANCISCO, CALIFORNIA

DATE: FEBRUARY 28, 2008
9 A.M.

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

BRS FILE NO.: 80559

I N D E X

SAN FRANCISCO, CALIFORNIA

THURSDAY, FEBRUARY 28, 2008

9 A.M.

CHAIRMAN LO: LET'S GET STARTED. WE HAVE A FULL AGENDA, AND I THINK THERE WILL BE A LOT OF INTERESTING DISCUSSIONS AND LOOKING FORWARD TO THE DAY.

FIRST, I WANT TO WELCOME EVERYBODY TO SAN FRANCISCO. WE PARTICULARLY ARRANGED GOOD CALIFORNIA WEATHER FOR THOSE OF YOU FROM THE EAST COAST TO KNOW WHAT YOU ARE MISSING. AND IF ANYONE IS THINKING OF RELOCATING TO CALIFORNIA, IT'S LIKE THIS 364 DAYS A YEAR. I'M NOT IMMUNE FROM A LITTLE BIT OF WHAT WE CALL CREATIVE EXAGGERATION, ALTA. BUT I WANT TO WELCOME EVERYBODY. IT'S GREAT TO SEE EVERYBODY AGAIN, AND HOPE THAT YOU ALL HAVE BEEN WELL SINCE OUR LAST MEETING.

A LOT HAS HAPPENED SINCE OUR LAST MEETING. AND PART OF WHAT WE'RE GOING TO DO TODAY IS TO SORT OF GET CAUGHT UP WITH SOME SCIENTIFIC ADVANCES. TWO OF OUR MEMBERS, JOHN WAGNER AND KEVIN EGGAN, HAVE ACTUALLY BEEN INVOLVED WITH SOME VERY EXCITING, VERY IMPORTANT SCIENTIFIC WORK, AND THEY'VE VERY GRACIOUSLY AGREED TO SORT OF GIVE US

SORT OF A THUMBNAIL SKETCH OF SOME OF THE EXCITING DEVELOPMENTS.

THERE'S BEEN ADMINISTRATIVE CHANGES. ALAN TROUNSON WAS LURED HERE FROM THE DISMAL WEATHER IN AUSTRALIA TO TAKE OVER AS THE PRESIDENT AND CEO OF CIRM. THIS IS OUR FIRST CHANCE TO ALL MEET HIM, AND WE CERTAINLY WELCOME ALAN. AND HE'S GOING TO PROVIDE DYNAMIC LEADERSHIP AND HAS SOME IDEAS FOR US TO THINK ABOUT IN TERMS OF THE STRATEGIC PLAN FOR CIRM AND HOW SWG MIGHT BE ABLE TO HELP WITH SOME NEW INITIATIVES THAT HE'S THINKING ABOUT AT CIRM.

BUT I WANT TO ASK SHERRY TO ADD HER WELCOME.

MS. LANSING: WELL, AGAIN, I ALSO WANT TO WELCOME EVERYBODY AND SAY HOW HAPPY I AM TO SEE EVERYBODY AGAIN. I MISSED, I GUESS, TWO MEETINGS, AND I WANT TO APOLOGIZE; BUT WHEN WE TOOK THE VOTE, I WAS THE ONLY ONE THAT HAD A PROBLEM ON THOSE DAYS. SO RELUCTANTLY I WAS NOT ABLE TO ATTEND. PLEASE DON'T INTERPRET THAT AS A LACK OF PASSION OR ENTHUSIASM FOR THE WORK THAT WE'RE DOING BECAUSE LITERALLY IT WAS 15 TO 1 WHO COULDN'T ATTEND THAT DAY.

I TOO WANT TO SAY THAT THIS MEETING

REPRESENTS WHAT WE'VE ALWAYS TALKED ABOUT, THAT WE ARE A CONSTANT WORK IN PROGRESS, AND THAT WHAT WE DECIDE TODAY, DUE TO THE SCIENCE MOVING SO FAST, WE MAY CHANGE, YOU KNOW, IN TWO OR THREE MONTHS, THAT QUICKLY, BECAUSE THE SCIENCE IS MOVING SO QUICKLY AND THINGS THAT HAVE HAPPENED WITH THE CHEEK CELL AND ALL THESE THINGS ARE THINGS WE DIDN'T KNOW ABOUT TWO YEARS AGO WHEN WE BEGAN OUR WORK.

AND SO, ONCE AGAIN, I GUESS I SAY WHAT I ALWAYS SAY IS WE'LL BE MEETING, AND FOR ME HAPPILY BECAUSE I LIKE SEEING ALL OF YOU, UNTIL THE LAST PATIENT IS CURED IS HOW I LIKE TO THINK OF IT. DO YOU KNOW?

AGAIN, I ALSO WANT TO WELCOME ALAN AND SAY HOW LUCKY WE ALL FEEL AT CIRM TO HAVE HIM AS OUR NEW LEADER AND THAT HE BRINGS A FRESH PERSPECTIVE. AND SO I THINK YOU'RE GOING TO SEE THROUGH OUR AGENDA THAT WE HAVE A LOT OF ISSUES THAT WE NEVER HAD BEFORE BECAUSE OF HOW FAST THE SCIENCE IS MOVING. AND THAT'S WHAT'S GREAT ABOUT OUR GROUP, THAT THEY CAN HAVE AN OPEN AND HONEST DISCUSSION, A TRANSPARENT DISCUSSION, AND PERHAPS COME TO SOME CONCLUSIONS OR, EVEN MORE LIKELY, CONTINUE TO HAVE SUBCOMMITTEES EXPLORING THEM AND

COME BACK TO US. SO, AGAIN, THANK YOU FOR YOUR TIME. THANK YOU FOR YOUR EXPERTISE. AND I'M JUST HONORED TO BE PART OF IT.

CHAIRMAN LO: GREAT. I THINK SHERRY, AS SHE ALWAYS DOES, SORT OF HIT THE NOTE THAT I THINK IS THE KEYNOTE FOR OUR MEETING TODAY, AND THAT'S HAVING FINISHED OUR MES REGULATIONS, OUR JOB IS NOT DONE. THE SCIENCE HAS PROGRESSED. THERE HAVE BEEN POLICY CHANGES IN OTHER COUNTRIES AROUND THE WORLD, AND WE'RE GOING TO NEED TO REVISIT SOME ISSUES THAT WE'VE DISCUSSED BEFORE. AND I'M NOT SURE HOW WE'RE GOING TO COME OUT, BUT I THINK WE ARE ALL COMMITTED TO CONSIDERING ISSUES IN LIGHT OF NEW SCIENTIFIC DEVELOPMENTS, NEW POLICY DEVELOPMENTS, AND MAKING SURE OUR ETHICAL STANDARDS ARE AS UP TO DATE AS THE SCIENCE.

I WANT TO QUICK, IF SOMEONE CAN PUT THE NEXT SLIDE ON, SORT OF GIVE YOU AN OVERVIEW OF WHAT I HOPE TO ACCOMPLISH TODAY, SORT OF HOW THE MEETING WILL BE SET OUT. SO THE FIRST THING WE'RE GOING TO DO IS TO HAVE SOME PRESENTATIONS THAT REALLY GIVE THE SWG SORT OF A BACKGROUND ON ALL THAT'S BEEN GOING ON. AND SO FIRST GEOFF IS GOING TO GIVE US SOME UPDATES ON REGULATORY CONSIDERATIONS, AND THEN WE'RE GOING TO HAVE TWO

PRESENTATIONS TO HELP US GET UP TO DATE ON THE SCIENCE.

JOHN WAGNER IS GOING TO TALK ABOUT SOME WORK HE HAS DONE WITH SORT OF MOVING IMPORTANT SCIENTIFIC DISCOVERIES IN THE LAB INTO CLINICAL TRIALS IN AN EXPEDITIOUS MANNER, BUT DOING THESE TRIALS IN A WAY THAT ALLOW HIM TO EVALUATE THE EFFECTIVENESS AND THE SAFETY OF THE INTERVENTION. I THINK IT'S A REAL MODEL FOR SORT OF MOVING QUICKLY TO CLINICAL TRIALS AND YET PROVIDING RIGOROUS DATA FROM THOSE RESULTS.

AND THEN KEVIN EGGAN, WHO WITH HIS LAB HAS BEEN IN THE FOREFRONT OF SORT OF DISCOVERIES, NEW WAYS TO DERIVE PLURIPOTENT CELL LINES, WILL SORT OF PRESENT THAT TO US. I THINK ONE OF THE THINGS WE'RE GOING TO THINK ABOUT IS HOW THESE NEW DEVELOPMENTS WITH WAYS TO DERIVE PLURIPOTENT CELLS MAY OR MAY NOT CHANGE OUR WAY OF THINKING ABOUT SOME OF THE ETHICAL POLICY ISSUES.

WE'RE ALSO GOING TO HEAR A LITTLE ABOUT WHAT OTHER GROUPS THAT ARE TRYING TO SET GUIDELINES AND POLICY ARE DOING. SO THERE'S A MEETING OF THE INTERNATIONAL STEM CELL FORUM, INTERSTATE ALLIANCE FOR STEM CELL RESEARCH, AND THE NATIONAL ACADEMIES PANEL, WHICH ALTA IS THE

CO-CHAIR, HEAR A LITTLE BIT ABOUT WHAT SOME OF THE ISSUES THEY'RE THINKING ABOUT ARE.

AND THEN THERE'S SOME SPECIFIC ISSUES THAT I THINK WE NEED TO THINK ABOUT AFRESH. ONE IS THE USE OF STEM CELL LINES, PLURIPOTENT STEM CELL LINES, DERIVED IN OTHER JURISDICTIONS UNDER CONDITIONS WHICH MAY NOT HAVE BEEN ACCEPTABLE FOR CIRM FUNDING IN CALIFORNIA. MAY CIRM-FUNDED RESEARCHERS USE THOSE LINES? IT'S GOING TO BE AN INCREASINGLY IMPORTANT ISSUE THAT WE NEED TO MAKE SURE WE'VE THOUGHT THROUGH CAREFULLY.

AND THEN ALAN TROUNSON IS GOING TO TALK TO US ABOUT THE ISSUE OF OOCYTE DONATION OR SHARING FOR RESEARCH PURPOSES, AND HE'S GOING TO TALK ABOUT HOW HE FEELS THAT IT'S VERY IMPORTANT FOR SCIENTIFIC PURPOSES TO BE ABLE TO DERIVE FRESH NEW PLURIPOTENT LINES USING FRESH OOCYTES AND HOW OUR CURRENT REGULATIONS MAKE THAT DIFFICULT.

SO A LOT OF WHAT THE FIRST PART OF THE MEETING IS GOING TO BE IS THE MEMBERS OF THE COMMITTEE REALLY SORT OF HEARING INFORMATION, BEING UPDATED. STARTING, I THINK, WITH OUR WORKING LUNCH, AFTER WE HAVE A TIME TO GET REACQUAINTED, I WANT US TO DEVELOP A STRATEGIC PLAN FOR THE STANDARDS WORKING GROUP. ALAN, I

THINK, IS VERY MUCH IMPLEMENTING THE STRATEGIC VISION FOR CIRM AS A WHOLE. I THINK SWG NEEDS TO SORT OF BE PART OF THAT EFFORT, BUT I THINK IT'S IMPORTANT WE SET PRIORITIES OF WHAT WE WANT TO BE WORKING ON OVER THE NEXT YEAR. I WANT TO MAKE SURE WE SORT OF DECIDE THAT BY SORT OF MIDAFTERNOON, EARLY AFTERNOON.

AND THEN I THINK WE NEED TO DEVELOP A WORK PLAN FOR HOW WE'RE GOING TO GO ABOUT ACCOMPLISHING OUR PLANS, OUR OBJECTIVES FOR THE YEAR, AND WE NEED TO MAKE SOME CONCRETE SUGGESTIONS, ONCE WE'VE DECIDED WHAT WE'RE GOING TO STUDY, WHAT ADDITIONAL INFORMATION WE'RE GOING TO NEED TO GATHER, WHETHER WE'RE GOING TO NEED TO CONVENE EXPERTS AND STAKEHOLDERS TO MAKE SURE OUR POLICY RECOMMENDATIONS ARE BASED ON THE BEST EVIDENCE AND DELIBERATION. WE MAY WANT TO BREAK UP INTO SUBCOMMITTEES TO SORT OF TACKLE SOME MORE SPECIFIC ISSUES, AND THEN I THINK WE'RE GOING TO MAKE SOME ASSIGNMENTS AS TO WHAT WE'RE ALL DOING BEFORE THE NEXT MEETING.

ALTHOUGH I DON'T THINK WE'RE GOING TO DECIDE POLICIES TODAY, WE'RE GOING TO DECIDE WHAT TOPICS WE WANT TO ADDRESS AND HOW WE'RE GOING TO WORK ON DEVELOPING POLICIES FOR THOSE TOPICS. I

THINK THAT WAS MY LAST SLIDE.

I GUESS I SHOULD HAVE FIRST FORMALLY CONVENED THE MEETING, BUT WE SHOULD DO A FORMAL ROLL CALL.

MS. PACHTER: GOOD MORNING. BERNARD LO.

CHAIRMAN LO: HERE.

MS. PACHTER: SHERRY LANSING.

MS. LANSING: HERE.

MS. PACHTER: MARCY FEIT. ROBERT KLEIN. FRANCISCO PRIETO.

DR. PRIETO: HERE.

MS. PACHTER: JEFF SHEEHY.

MR. SHEEHY: HERE.

MS. PACHTER: JONATHAN SHESTACK. ALTA CHARO.

MS. CHARO: HERE.

MS. PACHTER: PATRICIA KING. TED PETERS.

DR. PETERS: HERE.

MS. PACHTER: JOSE CIBELLI.

DR. CIBELLI: HERE.

MS. PACHTER: KEVIN EGGAN.

DR. EGGAN: HERE.

MS. PACHTER: ANN KIESSLING.

DR. KIESSLING: HERE.

MS. PACHTER: JEFFREY KORDOWER. KENNETH OLDEN.

DR. OLDEN: HERE.

MS. PACHTER: JANET ROWLEY.

DR. ROWLEY: HERE.

CHAIRMAN LO: HI, JANET. WELCOME ON THE PHONE.

MS. PACHTER: ROBERT TAYLOR.

DR. TAYLOR: HERE.

MS. PACHTER: JOHN WAGNER.

DR. WAGNER: HERE.

MS. PACHTER: JAMES WILLERSON.

CHAIRMAN LO: BOB KLEIN JUST WALKED IN. DO WE HAVE A QUORUM IN FACT?

MS. PACHTER: YES, WE DO.

CHAIRMAN LO: THANK YOU. GEOFF, YOU WANT TO GET US STARTED HERE ON A STAFF REPORT.

DR. LOMAX: YES, I WILL. THANKS FOR THE INTRODUCTION, BERNIE. I'D JUST LIKE TO ACKNOWLEDGE PAT BECKER FOR ALL THE ORGANIZATION AND ALL THE HELP GETTING YOU ALL IN THE ROOM TODAY.

MS. KING: SHE'S ACTUALLY OFF DOING SOMETHING RELATED TO THAT RIGHT NOW.

DR. LOMAX: AS WE SPEAK. IT'S HARD TO

ACKNOWLEDGE PAT BECAUSE SHE'S ALWAYS DOING SOMETHING. WE WILL REACKNOWLEDGE HER WHEN WE HAVE THE OPPORTUNITY.

I AM FOR THIS PORTION OF THE MEETING GOING TO VERY QUICKLY GO THROUGH A REGULATORY UPDATE ON THE AMENDMENTS THAT WERE RECOMMENDED AND HAVE SUBSEQUENTLY NOW BEEN PUT THROUGH THE PROCESS. THESE WERE THE RECOMMENDATIONS OF JULY 2007.

BRIEFLY, TO REMIND YOU ALL OF THE TOPICS THOSE AMENDMENTS COVERED, IT WAS THE USE OF THE JAPANESE STEM CELL LINES AND APPROVING LINES DERIVED UNDER THE JAPANESE REGULATIONS AS ACCEPTABLE FOR CIRM-FUNDED RESEARCH, WHICH WILL ALLOW THEM TO BE USED BY GRANTEES WITHOUT ADDITIONAL REVIEWS. THERE WAS CLARIFICATION OF LANGUAGE REGARDING PAYMENT FOR CELLS, AND THESE WERE -- THIS LANGUAGE SPECIFICALLY ADDRESSED CELLS FROM THIRD-PARTY PROVIDERS. IT WAS MAKING THE REGULATIONS MORE CONSISTENT WITH PROPOSITION 71. THESE AMENDMENTS NO WAY IMPACT PAYMENTS TO EGG DONORS OR ANY DIRECT DONORS. IT WAS A FAIRLY NUANCED AREA COVERING, FOR EXAMPLE, THE ACQUISITION OF CELLS FROM A THIRD-PARTY VENDOR, AN ACT-TYPE VENDOR.

IN ADDITION, WE MODIFIED OUR REQUIREMENTS FOR USE OF SOMATIC CELLS AND HUMAN TISSUE. SPECIFICALLY THIS CHANGE IN THE REGULATIONS WOULD ALLOW ANONYMIZED CELLS THAT ARE ESSENTIALLY IN TISSUE BANKS TO BE USED FOR REPROGRAMMING-TYPE EXPERIMENTS. THE ORIGINAL REGULATIONS HAD VERY STRICT REQUIREMENTS WITH REGARD TO CONSENT, AND THESE CHANGES ALLOW SORT OF A LIMITED SET OF CELLS THAT COMPLY WITH FEDERAL STANDARDS TO BE USED IN RESEARCH.

AND I'LL POINT OUT I DO HAVE SORT OF MORE DETAILED SLIDES FOR EACH OF THESE ITEMS, BUT I'VE GIVEN YOU THE ABRIDGED VERSION. IF THERE ARE ANY QUESTIONS ON ANY OF THESE ITEMS, I COULD GO TO A MORE DETAILED SLIDE, BUT I HOPE OVER THE COURSE OF OUR DELIBERATIONS THIS WAS ALL CLEAR. I JUST WANTED TO PROVIDE A REMINDER. SO IF THAT'S CLEAR, I WILL JUST MOVE FORWARD.

WE ALSO IN THE LAST ROUND OF REGULATIONS, BECAUSE OF THE CHANGES WE MADE TO THE LANGUAGE IN THE PRECEDING SECTIONS, WE HAD TO COME BACK TO SECTION 1000120, AND WE REVISED THAT SECTION JUST A BIT REALLY TO CALIBRATE THE REFERENCES IN THAT SECTION TO THE CHANGES. WHEN WE MADE CHANGES TO THE REGULATIONS, SOME OF THE

NUMBERING IN THE REGULATIONS CHANGED. THIS IS FAIRLY TYPICAL.

AGAIN, TO REMIND YOU OF THE PROCESS, I THINK IT'S ALWAYS USEFUL TO REMEMBER THE WORK WE HAVE TO DO WITHIN THE REGULATIONS. SO IN JULY YOU RECOMMENDED THE CHANGES. THEY WERE SUBSEQUENTLY APPROVED BY THE ICOC IN, I THINK, AUGUST AND SEPTEMBER. WE HAD EXTENSIVE -- I THINK IT WENT ACTUALLY THROUGH NOVEMBER. WE HAD PUBLIC COMMENTS. WE ACTUALLY HAD TWO PUBLIC COMMENT PERIODS, WHICH MEANT WE PUT THE ORIGINAL COMMENTS TO THE ORIGINAL REGULATIONS OUT, WE RECEIVED COMMENTS, WE MADE MODIFICATIONS, WE THEN PUT OUT THE REGULATIONS AGAIN FOR PUBLIC COMMENT. ANY TIME YOU MAKE A SIGNIFICANT CHANGE, YOU HAVE TO THEN HAVE THEM COMMENTED ON.

YOU HAVE A COPY IN YOUR FOLDER OF THE COMMENTS THAT WE RECEIVED, OUR RESPONSE TO THEM. AGAIN, I HOPE THOSE ARE SORT OF DETAILED AND SATISFACTORY. AND THE OAL WILL BE THE FINAL DETERMINANT OF THAT, BUT I HOPE WE'VE DONE AN APPROPRIATE JOB WITH OUR RESPONSE TO COMMENTS.

THE ICOC APPROVED THE FINAL RECOMMENDED LANGUAGE IN JANUARY OF THIS YEAR, AND WE ARE JUST NOW MOVING INTO THE OAL REVIEW PROCESS. AND WE

HOPE THAT GOES SUCCESSFULLY. ANY QUESTIONS AT THIS POINT?

SO, AGAIN, THE PUBLIC COMMENTS WERE -- YOU HAVE THEM AT YOUR DISPOSAL. THEY'RE ALSO AVAILABLE TO THE PUBLIC ON THE TABLE. I THINK I'VE ESSENTIALLY SAID THIS. TO SUMMARIZE, THERE'S NO FURTHER ACTIVITY REQUIRED AT THIS TIME UNLESS THE OAL WERE TO COME BACK AND INDICATE THERE WAS SOME PROBLEM WITH THE REGULATORY PACKAGE, WHICH MIGHT REQUIRE US TO COME BACK TO YOU ALL. IF THAT DOES NOT HAPPEN, THEN I THINK WE'VE SUCCESSFULLY BEEN ABLE TO MOVE THROUGH A ROUND OF MODIFICATION, WHICH, I THINK AS YOU ALL HAVE SAID, THAT WE WILL HAVE TO MODIFY FROM TIME TO TIME TO KEEP UP WITH THE SCIENCE. AND, AGAIN, THIS, I THINK, WAS AN EXAMPLE OF US DOING THAT.

WITH THAT SAID, I SORT OF COVERED THE REGULATORY UPDATE, AND I'LL TURN IT BACK OVER TO BERNIE.

CHAIRMAN LO: ANY QUESTIONS FOR GEOFF? I WANT TO THANK GEOFF AS WELL AS OUR LEGAL CONSULTANTS, TAMAR AND SCOTT, FOR THEIR HELP IN SORT OF GETTING OUR IDEAS INTO APPROPRIATE REGULATORY LANGUAGE. IT'S A LOT OF STAFF WORK. THEY'VE SPARED THOSE ON THE COMMITTEE SORT OF THE

MINUTE-BY-MINUTE DETAILS. WE DO APPRECIATE ALL THE HARD WORK YOU'VE PUT IN.

DR. LOMAX: ALSO, I THINK WE HAVE TO ACKNOWLEDGE, I THINK, ALTA FROM TIME TO TIME CHIMES IN WITH HER LAWYERLY EXPERTISE AND REMINDS US OF THE CORRECT WORDS AND THINGS LIKE THAT.

MS. CHARO: THAT'S VERY KIND, BUT THIS TIME AROUND YOU ALL DID IT ENTIRELY ON YOUR OWN.

DR. LOMAX: WITH PAT NOW BACK IN THE ROOM, I'D JUST LIKE TO ACKNOWLEDGE, PAT, YOUR EFFORT FOR THIS MEETING. WE COULDN'T HAVE DONE IT WITHOUT YOU.

CHAIRMAN LO: WITH THAT, I WANT TO MOVE ON TO THE SORT OF SCIENTIFIC PART OF OUR AGENDA. AND I'M GOING TO ASK JOHN WAGNER TO START. MANY OF US HAVE SEEN IN THE NEWS AND PERHAPS ON JOHN'S WEBSITE THE VERY INNOVATIVE CLINICAL TRIAL HE AND HIS COLLEAGUES HAVE DONE WITH EPIDERMOLYSIS BULLOSA, A VERY SEVERE, VERY RARE CHILDHOOD DISEASE, SORT OF MOVING FROM THE LAB TO A STEM CELL CLINICAL TRIAL. JOHN, THANKS VERY MUCH.

DR. WAGNER: THANK YOU FOR HAVING ME SPEAK ON THIS TOPIC. THIS IS THE FIRST TIME IT'S EVER BEEN PRESENTED, SO IT'S NOT GOING TO BE AS SMOOTH A PRESENTATION PERHAPS. THIS REALLY GOES

TO POINT OUT TO YOU THAT THIS IS REALLY HOT OFF THE PRESS. SO YOU MAY HAVE QUESTIONS I CAN'T ANSWER, BUT I THINK WHAT WAS ASKED OF ME WAS TO REALLY GIVE YOU AN IDEA WHAT IT'S LIKE TO MOVE SOME OF THESE NOVEL THERAPIES INTO CLINICAL TESTING AND SOME OF THE OBSTACLES THAT WE HAVE TO AT LEAST CONSIDER. I DON'T NECESSARILY HAVE THE ANSWERS, BUT I CAN AT LEAST TELL YOU WHAT I'VE DONE. SOME OF IT IS GOING TO BE PROBABLY CORRECT AND SOME OF IT MAY NOT BE AS OPTIMAL AS WE'D LIKE IT TO BE.

JUST AS A WAY OF STARTING OFF, JUST SO THAT SOME OF YOU WHO DON'T KNOW ME VERY WELL, WHAT MY AREA OF INTEREST IS REALLY DOING PHASE I CLINICAL TRIALS. THEY'RE THE TYPES OF CLINICAL TRIALS WHERE WE ARE DESIGNING NEW THERAPIES FOR BASICALLY PATIENTS WHO HAVE INCURABLE DISEASES. SO THE MAJORITY OF MY WORK IS REALLY IN CANCER THERAPY. I TAKE CARE OF CHILDREN PRINCIPALLY, ALTHOUGH ADULTS AS WELL. SO WHAT WE'RE TRYING TO DO IS FIGURE WAYS OF TRYING TO OBVIOUSLY IMPACT UPON THEIR DISEASE; BUT IN REALITY WHEN YOU'RE DOING A VERY HIGH RISK PHASE I TRIAL, YOU TAKE THE WORST RISK PATIENTS. AND SO TYPICALLY MY PATIENTS HAVE ADVANCED LEUKEMIA OR OTHER SIMILAR TYPE OF

HORRIBLE DISEASE WHERE THE OUTCOME IS EXPECTED TO BE POOR.

SO WITH THAT IN MIND, I WANT TO TAKE YOU THROUGH A STORY. THIS IS PERHAPS MORE NOT YOUR TYPICAL SCIENTIFIC PRESENTATION, BUT I THINK IT WILL ILLUSTRATE A FEW THINGS, AT LEAST I HOPE IT WILL. SO IT'S BASICALLY JUST TO GIVE YOU AN IDEA, EPIDERMOLYSIS BULLOSA IS A DISEASE I PREVIOUSLY KNEW NOTHING ABOUT. I WAS PRESENTING STEM CELL THERAPIES IN A MEETING IN NEW YORK CITY IN 2004. AND AT THE END OF THE MEETING, THIS MOTHER COMES UP TO ME AND SAYS, "HERE'S MY CHILD. SAVE MY CHILD."

SO THIS WAS ACTUALLY QUITE TRAUMATIC BECAUSE THIS CHILD WHO HAS THIS DISEASE CALLED EPIDERMOLYSIS BULLOSA WAS ABOUT TWO YEARS OF AGE, IS BLEEDING, HIS SKIN IS COMING OFF, AND, YOU KNOW, IT WAS REALLY NOT ONLY TRAUMATIC TO ME, BEING IN FRONT OF THIS AUDIENCE, BUT IT'S TRAUMATIC TO THE AUDIENCE AS WELL. I THINK THAT WHAT HAPPENED THOUGH WAS THAT THIS REALLY BRINGS HOME A POINT THAT THERE ARE MANY, MANY HORRIBLE DISEASES OUT THERE FOR WHICH WE'RE GOING TO BE ASKED TO DEVELOP SOMETHING FOR. AND ALTHOUGH IT WAS NOT IN MY AREA OF EXPERTISE, WHAT I DECIDED TO

DO AFTER THIS EVENT WAS REALLY TO BEGIN A PROCESS OF SAYING CAN WE ANSWER A QUESTION IN THIS PARTICULAR DISEASE. AND THE ANSWER AT THAT POINT MAY HAVE BEEN NO, BUT THIS IS HOW THE STORY BEGAN.

TO GIVE YOU A LITTLE BIT OF BACKGROUND, DEB, DYSTROPHIC EPIDERMOLYSIS BULLOSA, AND THERE ARE SEVERAL FORMS, BUT THIS IS ONE OF THE MORE SEVERE FORMS, IS BASICALLY A DISORDER WHERE BASICALLY THERE IS NO ANCHORING BETWEEN THE EPIDERMIS AND DERMIS, AND SO SIMPLY BY THE SHEAR TRAUMA OF RUBBING THE SKIN, THE SKIN WILL COME OFF. IN ADDITION, THESE CHILDREN VOMIT. THEY SLOUGH UP THEIR ENTIRE MUCOSA. MOST OF THESE CHILDREN WILL DIE EARLY IN LIFE. AND FOR THOSE THAT I GUESS ARE LUCKY ENOUGH TO LIVE INTO THEIR TWENTIES WILL TYPICALLY DIE OF SQUAMOUS CELL CARCINOMA THAT IS RAPIDLY PROGRESSIVE AND FATAL. IT'S VERY MUTILATING. THERE'S TREMENDOUS SCARRING ASSOCIATED WITH IT. AND THIS IS A DISEASE WHICH, I THINK OF ALL THE DISEASES I TAKE CARE OF, THIS HAS GOT TO BE ONE OF THE WORST ONES I'VE BEEN FACED WITH PERSONALLY.

THIS IS ACTUALLY PICTURES FROM THE PATIENT I TOOK CARE OF. AND YOU CAN SEE ALSO WHEN YOU LOOK AT THE TOES, WHAT YOU FIND IS THAT, WHEN

YOU LOOK AT THE FINGERS, IT'S CALLED MITTEN HANDS OR MITTEN TOES. BASICALLY WHAT HAPPENS OVER TIME BECAUSE OF THE CONSTANT INFLAMMATION IS THAT THEY ACTUALLY FUSE TOGETHER, AND THE TOES TYPICALLY WILL DISAPPEAR OVER TIME.

SO IN ANY EVENT, THIS IS A DISEASE WHERE THERE IS NO CURRENTLY CURATIVE THERAPY. WHEN I WENT BACK TO LOOK TO SEE WHAT THE ALTERNATIVES WERE, THERE IS A TRIAL GOING ON AT STANFORD LOOKING AT GENE THERAPY. THIS PATIENT WOULD NOT HAVE QUALIFIED FOR THAT TRIAL AND THE TRIAL AT THAT POINT HAD NOT YET BEGUN.

SO WHEN YOU INITIALLY HAVE THIS TRAUMATIC STORY OCCUR, YOU CAN IMAGINE A MOTHER COMES UP TO ME AND SAYS, "SAVE MY CHILD. I'M WILLING TO DO ANYTHING" BECAUSE THE ALTERNATIVE IS CERTAIN HORRIBLE LIFE AND DEATH VERSUS TRYING SOMETHING. SHE JUST WANTED ME TO TRY SOMETHING AND DIDN'T REALLY CARE WHAT I WAS TRYING. BUT TO PUT IT IN HER OWN WORDS, SHE'D RATHER GO DOWN KICKING AND SCREAMING THAN DOING NOTHING AT ALL AND WATCHING HER CHILD HAVE THIS INEVITABLE OUTCOME.

MS. LANSING: HOW OLD WAS THE CHILD?

DR. WAGNER: TWO YEARS OF AGE. SO

BASICALLY MY FIRST RESPONSE WAS EMOTIONAL. ONE THING I WAS TELLING BERNIE A LITTLE BIT EARLIER WAS THE FACT THAT THERE'S A PART OF ME THAT BELIEVES THE SAME THING SHE WAS ASKING. I'D RATHER GO DOWN KICKING AND SCREAMING THAN DOING NOTHING AT ALL BEYOND THE EMOTIONAL RESPONSE BECAUSE THERE IS AN INTERNAL STRUGGLE THAT AS AN INVESTIGATOR, AND PERHAPS I'M GIVING YOU TOO MUCH DETAIL AND PERHAPS THIS IS MORE ME THAN ANYTHING ELSE, BUT I THINK IT'S SOMETHING WE'RE GOING TO BE FACED WITH WHEN YOU HAVE THESE NEW STEM CELL THERAPIES MOVE FORWARD.

THE POINT IS THAT YOU HAVE TO THEN STEP BACK AND SAY HOW CAN I DO THIS SCIENTIFICALLY. SO THE FIRST QUESTION WAS WHAT WAS THE PROOF OF PRINCIPLE BY WHICH WE COULD SAY, YES, THERE IS A HOPE THAT WHATEVER THERAPY IS DEVELOPED MIGHT HAVE A POSITIVE EFFECT? SO THE HYPOTHESIS WAS IS THAT WE BELIEVE THAT THERE WOULD BE A STEM CELL POPULATION THAT WOULD EXIST THAT WOULD BE ABLE TO SECRETE THE MISSING PROTEIN OR COLLAGEN TYPE VII THAT WOULD IN TURN FORM ANCHORING FIBRILS THAT WOULD ANCHOR THE DERMIS TO THE EPIDERMIS AND HOPEFULLY CHANGE THE CLINICAL MANIFESTATIONS OF THIS DISEASE.

SO THEN THE NEXT STEP WAS THAT, AGAIN, I KNEW NOTHING ABOUT THIS DISEASE. AND I BEGAN INVESTIGATING AND FOUND THAT THERE WAS AN ANIMAL MODEL ASSOCIATED WITH THIS TYPE OF DISEASE; HOWEVER, THE ANIMALS ALL DIED BY TWO WEEKS OF LIFE. SO THAT CREATED ANOTHER DILEMMA BECAUSE WHATEVER CELL THERAPY I WOULD GIVE THEM, THE ANIMALS AFTER BIRTH, IT WAS NOT GOING TO BE A VERY QUICK TIMELINE FOR THESE CELL THERAPIES TO WORK.

SO FORTUNATELY I HAD A GROUP IN OUR PROGRAM WHO WAS USED TO DOING IN UTERO TRANSPLANTS, USED TO LOOKING AT DIFFERENT TYPES OF ANIMAL MODELS. WE HAVE ACCESS TO ADULT STEM CELL POPULATIONS, WHICH AT THE UNIVERSITY OF MINNESOTA IS TERMED THE MAPC, FROM CATHERINE VERFAILLIE'S WORK, AS WELL AS MESENCHYMAL STEM CELL, EPIDERMAL STEM CELL, AND MARROW CELL POPULATIONS, WHICH WE WERE GOING TO INVESTIGATE TO SEE WHETHER ANY OF THOSE HAD ANY IMPACT WHATSOEVER.

I ALSO WANT TO POINT OUT TO YOU THAT DESPITE THE FACT THAT I HAVE A CONSIDERABLE AMOUNT OF GRANT FUNDING, NONE OF IT'S IN EB, AND I DON'T HAVE ACCESS TO EASILY TRANSFERRING WORK THAT WAS DESIGNED FOR LEUKEMIA INTO TAKING CARE OF EB, SO, THEREFORE, WE BASICALLY HAD TO SCRAPE TO GET THE

FUNDING TOGETHER. MOTHER, NOT ONLY DOES SHE HAVE A CHILD WITH EB, BUT IS OUT FUND-RAISING AND RAISES $40,000 TO SUPPORT TO RESEARCH. AND THOSE OF YOU THAT DO ANIMAL MODEL WORK KNOW THAT THAT DOESN'T GO VERY FAR.

THIS IS WHAT THE ANIMAL MODEL LOOKS LIKE. BASICALLY JUST SHOWING YOU THESE PICTURES, YOU CAN SEE THAT THERE IS EXTENSIVE BLISTERING ON THE PAWS OF THESE ANIMALS, THERE'S CONTRACTURES, AND THESE ANIMALS ALL DIE QUITE QUICKLY. NOW, THE ANIMAL MODEL IS QUITE SIMILAR TO THE HUMAN COUNTERPART.

SO THE PLAN WAS IS THAT WE WOULD TAKE THESE MICE, DO IN UTERO INFUSIONS OF A VARIETY OF DIFFERENT POPULATIONS OF CELLS. AND TO MAKE A LONG STORY SHORT, THAT WE TRANSPLANTED HUNDREDS OF ANIMALS, OBVIOUSLY NOT ONLY WITH THE 40,000 FROM THE MOTHER, BUT WE SCRAPED AROUND 20,000 HERE, 10,000 THERE. WE WERE ABLE TO DO THE EXPERIMENTS. WHAT YOU CAN SEE HERE IS THAT FOR THE ANIMALS THAT WERE IN THE CONTROL POPULATION, THE ADULT STEM CELL POPULATION, THE MESENCHYMAL STEM CELLS, OR EPIDERMAL STEM CELLS, NOTHING WORKED. THE ANIMAL DIED WITHIN TWO WEEKS OF LIFE.

WE THEN LOOKED AT DIFFERENT SELECTED

POPULATIONS OF CELLS. ALTHOUGH I ANTICIPATED THAT IT WOULD BE AN ADULT STEM CELL POPULATION THAT WOULD WORK, IT WAS ONLY WHEN I USED WHOLE BONE MARROW THAT ACTUALLY THE CELLS SHOWED SOMETHING DIFFERENT. NOW, YOU'D LOOK AT THAT AND YOU MAY SAY ONLY THREE OF 13 ACTUALLY SURVIVED TWO WEEKS OF LIFE AND BEYOND. BUT WHAT WAS EXTRAORDINARY IS THAT THIS HAD NEVER EVER OCCURRED BEFORE. THERE HAD BEEN NO THERAPY EVER DONE BEFORE THAT EVER HAD DEMONSTRATED ANY SURVIVAL.

WE THEN SENT THESE ANIMALS FOR EVALUATION TO COLUMBIA UNIVERSITY. BASICALLY LOOKING AT THOSE ANIMALS WITH FRESH BLISTERS, AS SHOWN ON THE LEFT, AND THE ANIMALS THAT WERE ONE OF THE THREE SURVIVORS, IT WAS SOMETHING UNIQUELY DIFFERENT. YOU COULD SEE WHERE THEY PREVIOUSLY HAD BLISTERS IN UTERO, AND YET THEY WERE NO LONGER BLISTERING AT THIS POINT. THIS JUST SHOWS YOU MORE OF THE PICTURES.

SO THE BOTTOM LINE IS IS THAT WE THEN HAVE A PROOF OF PRINCIPLE THAT SOMETHING COULD WORK. I'M CUTTING THIS SHORT FOR PURPOSES OF TIME HERE BECAUSE WHAT WE DID IS WE ACTUALLY HAVE GONE BACK AND ACTUALLY LEARNED MORE ABOUT THE CELL POPULATION THAT'S RESPONSIBLE. IT'S NOT THE

HEMATOPOETIC STEM CELL POPULATION PER SE. THERE IS OTHER CELL POPULATIONS PRESENT IN THE BONE MARROW SPACE THAT WE'RE FURTHER DEFINING AT THIS POINT.

BUT THE BOTTOM LINE IS THAT WE COULD SEE THAT WITH WHOLE BONE MARROW AND WITH SELECTED SUBPOPULATIONS OF CELLS THAT WE'RE ABLE THEN TO CREATE A CIRCUMSTANCE WHERE COLLAGEN TYPE VII COULD BE REPLACED WITH DEVELOPMENT OF ANCHORING FIBRILS AND CORRECTION OF THE CLINICAL MANIFESTATIONS IN THIS DISEASE MODEL.

AS BERNIE WAS ASKING ME IS HOW DO WE PROCEED TO THIS CLINICAL TRIAL, THIS WAS THE PROOF OF PRINCIPLE BY WHICH YOU COULD SAY SOMETHING COULD BE DONE THAT WOULD AT LEAST PROVIDE US WITH A RATIONALE FOR TRYING SOMETHING QUITE SIGNIFICANTLY RISKY.

GOING BACK TO WHAT THE HYPOTHESIS NOW IS IN HUMANS, AGAIN, WE HAVE THE PROOF OF PRINCIPLE, WE WERE NOW GOING TO USE WHOLE BONE MARROW AS A WAY OF TREATING THESE PATIENTS AND CORRECTING THEIR UNDERLYING DISEASE. THE OTHER THING, AS A BACKUP STRATEGY, IS THAT IF WE DO AN ALLOGENEIC TRANSPLANT, WE ALSO WILL BE CREATING TOLERANCE. THEREFORE, THAT DONOR WOULD BE POTENTIALLY

AVAILABLE FOR SKIN GRAFTING SHOULD THAT BE NEEDED AS A SECONDARY OUTCOME, ALTHOUGH WE WERE HOPING THAT THIS WOULD NOT BE NEEDED.

THIS GIVES YOU AN IDEA OF WHAT THE THERAPEUTIC PROTOCOL WAS FOR THIS GROUP. IT'S NOT THAT IMPORTANT OTHER THAN THE FACT WE LISTED IT WITH CLINICALTRIALS.GOV, WHICH ACTUALLY WAS QUITE SIGNIFICANT ONLY FROM THE STANDPOINT THAT THAT WAS THE ONE THING THAT ALLOWED THE INSURANCE COMPANY TO MOVE FORWARD WITH FUNDING THE ACTUAL CLINICAL TRIAL. WITHOUT THAT, THEY SAID THEY WOULD NOT HAVE ALLOWED SUCH A TRIAL TO OCCUR.

SO WHAT ARE THE RISKS WITH ALLOGENEIC TRANSPLANTATION WITH HIGH DOSE CHEMOTHERAPY FOLLOWED BY AN INFUSION OF HEMATOPOETIC OR BONE MARROW CELLS, I SHOULD SAY? WELL, THERE IS VOMITING, AND CLEARLY VOMITING WITH CHEMOTHERAPY WOULD BE A MAJOR RISK. THERE COULD BE A RISK OF GRAFT FAILURE, GRAFT VERSUS HOST DISEASE WHERE THE IMMUNE SYSTEM OF THE DONOR REJECTS THE PATIENT. REMEMBER, THIS IS ALREADY A DISEASE WHERE THE PATIENT HAS A DISRUPTIVE MUCOSA AND A DISRUPTED SKIN, SO OBVIOUSLY INFECTION WAS A MAJOR RISK. CLEARLY THIS MOTHER WAS MADE AWARE OF THE RISK OF DEATH.

BUT THERE WERE A NUMBER OF MAJOR HURDLES THAT WE HAD TO OVERCOME, AND YOU MIGHT BE ABLE TO GUESS THEM, BUT THE ETHICS, THE COST, AND ALSO JUST DEVELOPING A CARE TEAM AT AN INSTITUTION WHERE EPIDERMOLYSIS BULLOSA WAS NOT REALLY A HIGH PRIORITY DISEASE -- NOT A PRIORITY, BUT A DISEASE BY WHICH WE SAW A LARGE NUMBER. AND, THEREFORE, WE HAD TO RECREATE THAT PARTICULARLY FOR THE BONE MARROW TRANSPLANT TEAM THAT WAS GOING TO BE ACTUALLY TAKING CARE OF THIS PATIENT.

BUT WHEN I TALK ABOUT THE ETHICS BEHIND IT, IS THAT IT REALLY IS A VULNERABLE POPULATION OF PATIENTS. AS YOU CAN IMAGINE, THESE PATIENTS ARE WILLING TO DO ANYTHING TO TRY TO HAVE A CHANCE TO DO SOMETHING POSITIVE.

DR. KIESSLING: WHAT'S THE INCIDENCE OF THIS?

DR. WAGNER: ABOUT ONE IN 500,000.

DR. KIESSLING: HOW MANY PEOPLE ALTOGETHER?

DR. WAGNER: I HAVEN'T DONE THAT CALCULATION. I CAN'T TELL YOU. REMEMBER, THIS IS ALL NEW. I DON'T KNOW THAT ANSWER. IT'S A VERY SMALL, RARE. IT MAKES SOME OF THE OTHER GENETIC DISEASES LOOK COMMON COMPARED TO THESE PEOPLE.

DR. CIBELLI: I DON'T KNOW IF YOU CAN TAKE QUESTIONS NOW, OR ARE YOU GOING TO WAIT?

DR. WAGNER: WE'RE MAKING THIS UP AS WE GO ALONG.

DR. CIBELLI: I'M CURIOUS WHEN YOU LISTED THIS IN CLINICALTRIAL.GOV, DID YOU GET FEEDBACK? WAS THAT OPEN FOR PEOPLE TO SEND YOU MORE REQUESTS TO BRING IN MORE PEOPLE INTO THE CLINICAL TRIAL?

DR. WAGNER: THE REASON WHY WE SUBMITTED IT TO CLINICALTRIALS.GOV WAS MAINLY BECAUSE OF PUBLICATION PURPOSES.

DR. CIBELLI: BUT OTHER THAN THAT, DO YOU THINK THAT PEOPLE BECAME MORE AWARE OF THAT THERE WAS SOME SOLUTION ON STEM CELLS WITH THIS?

DR. WAGNER: REALLY AS A RESULT OF PUBLICITY THAT OCCURRED AS A RESULT OF THE FIRST PATIENT IN THE LAY PRESS, WE RECEIVED A HUGE, I CAN'T TELL YOU THE NUMBER, BUT A HUGE NUMBER OF PEOPLE FROM ALL OVER THE WORLD ASKING FOR THIS THERAPY, WHICH IS ANOTHER ISSUE THAT I'LL GET TO AT THE VERY END.

SO IN TERMS OF THE ETHICS BEHIND IT, OBVIOUSLY THERE'S MORE THAN JUST BEING A VULNERABLE POPULATION, BUT THERE'S ALSO THE COST

OF AN EXPERIMENTAL THERAPY. WE WERE VERY LUCKY THAT THE INSURANCE COMPANY WOULD ALLOW SUCH A PROCEDURE BECAUSE, REMEMBER, THIS IS REALLY FOR ALL INTENTS AND PURPOSES A CLASSIC BONE MARROW TRANSPLANT WHERE THE AVERAGE COSTS ARE GOING TO BE SOMEWHERE AROUND 500,000.

SO IN ANY EVENT, WE WENT THROUGH AND GOT OUR REGULATORY APPROVALS FOR MOVING IT FORWARD. AND IN TERMS OF THE OUTCOME, WHAT HAPPENED FOR THIS PARTICULAR PATIENT IS THAT THERE WAS RAPID CHIMERISM; THAT IS, WE FOUND THAT THE DONOR CELLS ENGRAFTED, HEMATOPOETIC RECOVERY WAS RAPID, THERE WAS NO SIGNIFICANT VOMITING, THERE WAS NO SIGNIFICANT INFECTION, THERE WAS NO GRAFT VERSUS HOST DISEASE. THIS WAS AS EASY A TRANSPLANT AS IT EVER COULD HAPPEN, BUT JUST KNOW WE WERE LUCKY.

THERE'S NOTHING PECULIAR ABOUT THIS COMPARED TO A LEUKEMIA PATIENT OTHER THAN THE FACT THIS PATIENT WOULD HAVE A RISK OF LEUKEMIA RELAPSE. NONETHELESS, WE WERE VERY LUCKY TO NOT HAVE ANY OF THESE CLINICAL COMPLICATIONS OCCUR.

MS. LANSING: DOES THE AGE OF THE PATIENT HAVE ANYTHING TO DO WITH IT?

DR. WAGNER: THERE ARE. SO THE YOUNGER YOU ARE, THE MORE LIKELY THAT YOU WILL HAVE A GOOD

OUTCOME. I LEFT OUT SOMETHING VERY SIGNIFICANT IN ALL THIS IS THAT IT WAS AN HLA-MATCHED SIBLING DONOR THAT WAS AVAILABLE. I SHOULD POINT OUT TO YOU, AND AGAIN THIS IS BECAUSE IN PART THIS IS A BRAND-NEW TALK THAT I'VE NEVER GIVEN BEFORE FOR THIS PARTICULAR DISEASE, BUT ALSO, AS IT TURNS OUT, THE CHILD THAT WAS PRESENTED TO ME IN 2004, WHO IS NOW OBVIOUSLY OLDER, WAS NOT THE RECIPIENT OF THIS TRANSPLANT. IT HAPPENED TO BE HIS BROTHER.

SO WHAT HAD HAPPENED BETWEEN 2004 AND THE TIME THAT WE ACTUALLY DESIGNED AND IMPLEMENTED AND WERE READY FOR OPENING THE CLINICAL TRIAL, THE MOTHER HAD ANOTHER CHILD WITH THE SAME DISEASE, WHO HAPPENED TO BE HLA MATCHED WITH AN IN-BETWEEN SIBLING THAT HAPPENED TO BE A CASE WHERE THE UMBILICAL CORD BLOOD WAS COLLECTED BY ACCIDENT. AND WHAT WE DID IS, BECAUSE OF THE FACT THAT ALL OF OUR WORK WAS WITH BONE MARROW IN THE ANIMAL MODEL, WE ACTUALLY USED THE BONE MARROW AND SUPPLEMENTED WITH THE CORD BLOOD, ALTHOUGH THE CORD BLOOD WAS ONLY ADDED BECAUSE IT WAS THERE.

MS. LANSING: WHAT HAPPENED TO THE OLDER CHILD?

DR. WAGNER: THE OLDER CHILD HAS NOT

BEEN TREATED YET.

IN TERMS OF THE CLINICAL OUTCOME, PICTURES TELL EVERYTHING. ON THE LEFT IS BEFORE AND ON THE RIGHT IS AFTER.

DR. ROWLEY: JOHN, FOR THOSE WHO CAN'T SEE IT, WOULD YOU DESCRIBE IT?

DR. WAGNER: WE SHOW, I THINK, SIGNIFICANT IMPROVEMENT. WHEN YOU LOOK AT THE HANDS AND YOU LOOK AT THE OTHER PARTS OF THE BODY THAT I'LL SHOW, WHAT YOU SEE ON THE LEFT-HAND SIDE IS YOU SEE SIGNIFICANT DESQUAMATION ON SIGNIFICANT SURFACES OF THE BODY. AND WHAT YOU SEE ON THE RIGHT-HAND SIDE, WHICH IS NOW THREE MONTHS AFTER THE INFUSION OF THESE HEMATOPOETIC STEM CELLS OR BONE MARROW POPULATIONS, YOU FIND THAT THERE IS MARKED IMPROVEMENT.

I SHOULD POINT OUT TO YOU THAT HIS SKIN IS NOT COMPLETELY NORMAL, BUT IT'S EVOLVING. SO EVEN THOUGH THIS MAY BE THREE MONTHS AFTER THE INFUSION OF THE CELLS, IT CONTINUES TO IMPROVE, AND WE JUST DON'T KNOW EXACTLY WHERE IT WILL END. BUT THAT'S WHAT YOU SEE ON THE PHOTOGRAPHS, JANET.

DR. ROWLEY: HOW OLD WAS THE CHILD AT TRANSPLANTATION?

DR. WAGNER: EIGHTEEN MONTHS.

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SO I THINK THAT FOR THE CLINICAL MANIFESTATIONS, I WANT TO BE CONVINCED, I WANT TO SAY THIS IS BETTER; HOWEVER, TO BE COMPLETELY HONEST ABOUT IT, I COULD IMAGINE THAT BECAUSE AFTER TRANSPLANT, HE MAY NOT BE AS ACTIVE AS WE WAS BEFORE TRANSPLANT, ALTHOUGH I THINK THAT HE IS, MAYBE IT'S JUST LESS BLISTER FORMATION BECAUSE OF DECREASED ACTIVITY AND DECREASED FRICTION WITH OTHER SURFACES. HOWEVER, AGAIN, WHERE THE PROOF IS IS IN THE BIOPSY. ALTHOUGH I CAN'T TELL YOU, IF YOU CAN SEE IT VERY WELL, IN PANEL D IS THE PRESENCE OF ANCHORING FIBRILS. IN THE OTHER PANELS ARE THE PRESENCE OF COLLAGEN TYPE VII. AND WITH EVERY BIOPSY BETWEEN DAY 30, 60, AND 100 WE FOUND INCREASING AMOUNTS OF COLLAGEN TYPE VII THAT PREVIOUSLY WAS ZERO.

SO ANY WAS CERTAINLY A MAJOR FINDING; HOWEVER, IT WAS REALLY FUNCTIONALLY THE PRESENCE OF ANCHORING FIBRILS WHICH REALLY MEANS THAT WE'VE DONE SOMETHING, NOT ONLY CLINICALLY APPEARS TO BE A BENEFIT, BUT BIOCHEMICALLY AND BIOLOGICALLY AS WELL.

SO WHAT IS THE NEXT STEP? SO THE FIRST THING IS WE SAY WE WAIT BECAUSE OF THE FACT THAT WE DON'T KNOW HOW THIS IS GOING TO EVENTUALLY END

UP. WILL WE HAVE COMPLETE RESOLUTION OF THIS DISEASE? TO GIVE YOU AN IDEA, AND ALTHOUGH I DON'T KNOW THIS RIGHT NOW, BUT IT MAY BE, LET'S SAY, FOR A NORMAL INDIVIDUAL, THAT YOU WILL HAVE 100 ANCHORING FIBRILS PER FIELD. I'M MAKING THAT UP. I DON'T KNOW THAT NUMBER AS A POINT OF REFERENCE. IT MAY BE POSSIBLE THAT THERE WILL ONLY BE TEN ANCHORING FIBRILS PER FIELD OR SOMEWHERE IN BETWEEN.

WE KNOW THAT CARRIERS HAVE A LOWER NUMBER THAN NONCARRIERS. BUT WHAT I DON'T KNOW, WHAT NO ONE KNOWS, IS HOW MANY IS ENOUGH TO MAKE A CLINICAL DIFFERENCE. SO ONLY TIME WILL TELL AS TO HOW SIGNIFICANTLY IMPROVED THIS PATIENT WILL BE. ONLY TIME OR OTHERS WILL FIGURE OUT WHETHER THE CLINICAL IMPROVEMENT IS SATISFACTORY. OF COURSE, WE ARE ENCOURAGED BY THE RESULTS WE HAVE SO FAR. HE'S CURRENTLY 130 DAYS OUT AFTER HIS INFUSION OF CELLS. BUT, NONETHELESS, THAT'S WHERE WE ARE NOW.

THE OTHER THING THAT WE NEED TO DO OR WHAT WE WOULD LIKE TO HAVE DONE IS BEING PREPARED FOR THE NEXT GENERATION. I THINK THAT FROM THE VERY BEGINNING WHEN YOU DECIDE WHAT DO YOU CONSIDER TO BE THE BEST OUTCOME YOU CAN MAKE IT, AND OBVIOUSLY WHAT I WOULD LIKE TO BE ABLE TO DO

IS TO FIGURE OUT WHAT IS THE SPECIFIC POPULATION OF CELLS THAT WE'D LIKE TO BE ABLE TO GIVE OUR PATIENTS, AND HOPEFULLY MAYBE EVEN EXPAND THEM SO THAT YOU HAVE MORE RAPID RECOVERY. NONETHELESS, THERE IS NO FUNDING TO SUPPORT THIS AS YET, AND SO THIS WORK IS GOING ON AT VERY SLOW RATES.

AND THEN IN ADDITION, BECAUSE OF, I THINK, THE RESULTS WE HAVE SO FAR, WE'RE NOW GOING TO CONSIDER NOW BRINGING ON A SECOND PATIENT. AND THE SECOND PATIENT WILL ACTUALLY BE A 16-YEAR-OLD THAT WILL BE COMING IN WITH A CONSIDERABLY MUCH MORE ADVANCED DISEASE, BUT ALSO HAS AN HLA-MATCHED SIBLING. YOU MAY GO BACK AND ASK WHAT HAPPENS TO THE PATIENT WHO IS THE ONE WHO INCITED THIS WORK TO BEGIN WITH. THERE IS NO HLA-MATCHED SIBLING. WE WOULD HAVE TO GO FOR ONE ANTIGEN MISMATCHED UNRELATED DONOR, WHICH MAKES ME VERY NERVOUS. THERE IS A TREMENDOUS PRESSURE TO NOT ONLY TAKE CARE OF HIM, BUT ALSO THERE ARE PROBABLY ABOUT 50 OR 60 OTHER PATIENTS WAITING IN THE QUEUE.

WHAT I HAD TO DO IS STEP BACK AND SAY, EVEN THOUGH MY EMOTIONAL RESPONSE IS TAKE CARE OF ALL OF THEM, THE SCIENTIFIC RESPONSE IS YOU HAVE TO JUST DO ONE THING AT A TIME AND WAIT TO SEE HOW THIS EVOLVES BECAUSE IF I KNEW FOR SURE

UNEQUIVOCALLY THAT WE HAD A GOOD OUTCOME IN THIS PATIENT, THEN I WOULD FEEL BETTER ABOUT TAKING IT TO THE NEXT STEP AND TRYING FOR A MORE DIFFICULT TRANSPLANT WITH THE ONE ANTIGEN MISMATCHED UNRELATED DONOR.

SO I WANT TO SAY QUESTIONS. I'M DONE WITH THE PRESENTATION AND LIST THE QUESTIONS AND LESSONS TO BE LEARNED.

DR. PRIETO: I GUESS I DO HAVE A QUESTION, SORT OF WONDERING HOW TO GET AN IDEA OF THE TIMELINES FOR MOVING A THERAPY LIKE THIS FORWARD. IF YOU HAVE SOME SORT OF A RESPONSE IN THE SECOND PATIENT, THEN HOW FAR DO YOU THINK YOU ARE FROM BEING ABLE TO DEVISE A PROTOCOL THAT OTHER TEAMS COULD USE?

DR. WAGNER: WELL, THERE'S A LOT OF PRESSURE NOW FROM OTHER TEAMS THAT ARE ALREADY ASKING BOTH IN EUROPE AND THE UNITED STATES. AND I THINK IT'S TOO DIFFICULT -- AT LEAST I COULD BE WRONG, BUT IT'S TOO DIFFICULT FOR ME TO JUST SAY HERE'S THE PROTOCOL WHEN, IN FACT, IT'S OUR WORK THAT WE'RE TRYING TO FIGURE OUT. AND WE HAVE NOW A TEAM INVOLVED. WHAT HAPPENS IF WE THEN, FOR EXAMPLE, INITIATE THE PROTOCOL AT CENTER X IN SOUTHERN CALIFORNIA OR WHEREVER AND IT FAILS? YOU

KNOW, YOU WON'T KNOW -- WE NEED TO HAVE A CORE COMPETENCY AT LEAST AT ONE SITE TO BE ABLE TO SAY WHAT ARE THE SUPPORTIVE CARE MEASURES? AS YOU KNOW, PROTOCOLS DON'T ADDRESS EVERYTHING. AND SO WE'RE TRYING TO FIGURE OUT IS THIS WORKING? IS THIS THE RIGHT THERAPY? WILL THIS WORK JUST FOR MISMATCHED SIBLING DONORS OR PERHAPS UNRELATED DONORS?

SO WE'VE NOT -- WE'RE NOT READY TO EXPORT THE PROTOCOL AS YET. IS IT SOMETHING OTHER PEOPLE COULD DO? YES. AND WE'RE TRYING TO MAKE SURE THAT WE DO THINGS, WE CREATE REGIMENS THAT OTHERS COULD ADOPT PRETTY EASILY RATHER THAN DEVELOPING TECHNOLOGIES THAT ARE SO DIFFICULT THEY COULD ONLY BE DONE ONE PLACE. IT'S A GOOD QUESTION. AT LEAST PERSONALLY I DON'T FEEL COMFORTABLE GIVING IT OUT QUITE YET.

DR. TAYLOR: QUESTION FOR YOU IN TERMS OF -- IT'S FASCINATING STUFF. WHAT CAN YOU TELL ME A LITTLE BIT ABOUT THE GENETIC DEFECT IN DEB AND THE BIOLOGY? AND REALLY WHAT I'M GETTING TO IS CAN YOU BE SURE THAT THIS IS ACTUALLY A STEM CELL CURE BASED ON THE FACT THAT THE ONLY TREATMENT THAT SEEMED TO WORK WAS WHOLE BONE MARROW TRANSPLANTATION? I CAN IMAGINE OTHER

MECHANISMS THAT COULD, THEY'RE CONVOLUTED, FRANKLY, SO WHAT ABOUT THE COLLAGEN VII DEFECT? IS IT A GENE DELETION?

DR. WAGNER: IT IS A GENE DELETION. UNFORTUNATELY, I CAN'T TELL YOU MUCH. I CAN'T TELL YOU WHICH GENE. I JUST DON'T RECALL OFF THE TOP OF MY HEAD, BUT IT IS A GENE DELETION.

AND IN TERMS OF YOUR SECOND QUESTION, IS IT -- I THINK THAT IN THE ANIMAL MODELS, WE NEVER LET THE ANIMALS LIVE LONG ENOUGH TO BE ABLE TO SAY WHETHER OR NOT THIS WAS A LIFELONG CURATIVE THERAPY. COULD THIS BE SOME TRANSIENT PHENOMENON? AND THE ANSWER IS POSSIBLY YES. BECAUSE IN OUR ENTHUSIASM TO TRY TO MOVE THIS CLINICAL TRIAL FORWARD, WE SACRIFICED THREE ANIMALS TO SHOW THAT WE WERE ABLE TO PRODUCE ANCHORING FIBRILS. WHAT HAPPENS IF IT'S NOT A TRUE STEM CELL WHICH DOESN'T PROVIDE US WITH A LIFELONG THERAPY? WE DON'T KNOW THAT ANSWER. WE'LL FIND OUT.

DR. TAYLOR: IF IT'S THE GENE DELETION AND YOU'VE GOT COLLAGEN VII THERE NOW, THAT'S ACTUALLY A GREAT STEP, IT SOUNDS.

DR. WAGNER: WE CLEARLY HAVE COLLAGEN VII. WHAT WE WERE AFRAID OF, WHAT HAPPENS IF WE GET COLLAGEN VII, BUT THE COLLAGEN VII WASN'T ABLE

TO BECOME ANCHORING FIBRILS? BUT WE'VE DEMONSTRATED THAT WELL.

DR. OLDEN: A QUESTION ABOUT YOUR ANIMAL MODEL. DO YOU INTEND TO EXPAND YOUR BONE MARROW STEM CELL POPULATION USING SPECIFIC GROWTH STIMULATING FACTORS TO GET AT WHICH COMPONENT OF THE ENTIRE GRAFT IS REALLY EFFECTIVE?

DR. WAGNER: CLEARLY YOUR QUESTION IS IF THIS WERE IN THE SETTING OF LEUKEMIA WHERE I HAD THE GRANT FUNDING TO DO THIS, IT WOULD HAVE BEEN A MUCH LARGER SCALE TO DO EXACTLY WHAT YOU ARE SAYING, TO FIND OUT WHAT THE MECHANISM OF WHY DID THIS WORK, AND CAN WE MAKE IT BETTER THAN WHAT IT ALREADY IS BY EITHER USING DIFFERENT GROWTH FACTORS, EXPANDING THE SELECTED POPULATION OF CELLS? BUT I WANTED TO POINT OUT TO YOU THAT THIS WAS, FIRST OFF, NO. 1, THIS WAS EXCEPTIONALLY LUCKY THAT THINGS WORKED OUT AS WELL AS THEY DID WITH THE SMALL AMOUNT OF A BUDGET THAT WE HAD FOR THIS PARTICULAR PROGRAM.

NONETHELESS, TO REALLY DO THIS RIGHT, YOU WANT TO HAVE A LARGER BUDGET. AND, AGAIN, YOU HAVE ACCESS TO MONEY IN THIS STATE THAT NOT EVERYONE IS GOING TO HAVE ACCESS TO TO ALLOW YOU TO DO THINGS IN A BETTER WAY THAN WHAT WE'VE DONE

SO FAR.

OTHER QUESTIONS?

IN TERMS OF WHAT I THOUGHT WERE THE LESSONS, YOU TELL ME. THIS IS JUST MY TAKE ON IT, AND THERE'S PROBABLY MANY MORE THINGS. WHAT GEOFF AND I WERE TALKING ABOUT ON THE PHONE WAS WHAT CAN WE TAKE AWAY FROM THIS LESSON OR FROM THIS EXAMPLE? WELL, ONE IS I THINK ONE OF THE THINGS THAT WE CAN THINK ABOUT WHEN WE'RE TALKING ABOUT STEM CELL THERAPIES WHICH HAVE THE POTENTIAL FOR IMPACTING SO MANY DIFFERENT DISEASES AND SO MANY DIFFERENT PEOPLE IS WE HAVE TO FIGURE A WAY OF GETTING THE BASIC TRANSLATIONAL CLINICAL TEAMS TO TALK TOGETHER. AS A PERSON INVOLVED IN A STEM CELL INSTITUTE MYSELF, THIS IS NO EASY TASK, BUT IT'S BEEN DONE BEFORE.

I THINK CANCER CENTERS ARE ONE EXAMPLE OF HOW YOU CAN MAKE THAT HAPPEN. WHAT MAKES THIS UNIQUELY DIFFERENT IS THAT THERE ARE SO MANY DIFFERENT DISEASES THAT CAN BE IMPACTED. HOW DO YOU GET THE RIGHT PEOPLE TALKING TOGETHER? IN THIS PARTICULAR EXAMPLE, IT WAS ME TRYING TO FIND PEOPLE. I DIDN'T KNOW THE DERMATOLOGISTS. I DIDN'T KNOW THIS DISEASE. AND SO IT WAS REALLY A STRUGGLE TO FIND THE RIGHT PEOPLE AND BRING THEM

TOGETHER AND CONVINCE THEM THIS WAS THE RIGHT THING TO DO.

WE'VE ALREADY TALKED ABOUT THE FUNDING ISSUE. NONETHELESS, IT SLOWS PROGRESS BECAUSE OF THE FACT THAT WE'RE TRYING TO GET TO THE NEXT STEP, AND THAT'S YET TO BE ACCOMPLISHED.

BUT THERE'S SOME OTHER TOPICS THAT WE HAVE TO DISCUSS, AND I'VE ALREADY TALKED ABOUT NO. 1. THE OTHER THING TO TALK ABOUT IS WHAT ARE YOUR EXPECTATIONS FOR A PHASE I CLINICAL TRIAL? THIS WAS EXCEPTIONALLY LUCKY, AND I THINK THAT WHAT YOU ARE GOING TO SEE IS THAT AS WE BEGIN DESIGNING NEW STEM CELL THERAPIES FOR TREATING PATIENTS FOR WHATEVER DISEASE IT IS, YOU SHOULDN'T HAVE THIS AS YOUR EXPECTATION. IT'S GOING TO REQUIRE MANY GENERATIONS, AND I DON'T WANT THE PUBLIC TO BE DISMAYED BY THE FACT THAT THE FIRST GENERATION MAY NOT BE THE ONE THAT WORKS. IT MAY TAKE MANY ITERATIONS BEFORE YOU MAKE IT WORK.

AND AS LONG AS WE DESIGN CLINICAL TRIALS THAT ALLOW US TO ANSWER A QUESTION, AND HOPEFULLY THEN TAKE US TO THE NEXT STEP, THAT'S WHAT WE HAVE TO BE DOING. I ALSO WANT TO MAKE SURE THAT THE PUBLIC DOESN'T FEEL DISAPPOINTED BY THE FACT THAT THE FIRST TRIALS MAY NOT ALWAYS WORK.

THAT GETS, THEN, TO WHAT ARE REASONABLE EXPECTATIONS FOR THE FIRST CLINICAL TRIALS, NOT ONLY FROM THE PUBLIC'S POINT OF VIEW, BUT BY THE FUNDING AGENCIES? BUT ALSO, THEN, AGAIN, WHAT DISEASES ARE TARGETED? I WOULD BET YOU THAT MOST PEOPLE WOULD NOT HAVE HAD EB ON THE TOP OF THEIR LIST IN THIS ROOM. ON THE OTHER HAND, YOU COULD SAY, WELL, YES, WE SHOULD BE INVESTING IN DIABETES OR PARKINSON'S OR SPINAL CORD INJURY, WHICH ARE FAR MORE FREQUENT; BUT, NONETHELESS, THIS GIVES US ACTUALLY SOMETHING QUITE EXTRAORDINARY IN THAT THIS OPENS US UP NOW TO MANY, MANY OTHER DERMATOLOGIC DISEASES FOR WHICH WE HAD NEVER CONSIDERED, AT LEAST WITH BONE MARROW CELLS, IN THE PAST, SO IT OPENS UP A WHOLE NEW PARADIGM.

THERE ARE NUMBER OF REGULATORY ISSUES WE CAN DISCUSS AND HOW THESE REGULATORY ISSUES MIGHT BE INFLUENCED BY OTHER POLITICAL AND THINGS GOING ON TODAY.

ALSO QUALITY OF ACCESS. THE ONE THING THAT REALLY BOTHERS ME MOST OF ALL IS BEING ON THE FRONT LINE OF THESE NEW THERAPIES SO THAT MANY PEOPLE CALL ALL OVER THE WORLD AND SAY, "I WANT THIS. WHAT CAN YOU DO FOR MY CHILD?" IT'S KIND OF HARD TO SAY NO TO SOMEONE SIMPLY BECAUSE OF THE

FACT THAT THEY DON'T HAVE THE $500,000 FOR A TRANSPLANT. YET SAY, "I'VE DANGLED THE CARROT AND SAY I CAN CURE YOU, BUT YOU CAN'T HAVE IT." AND THAT'S PARTICULARLY DIFFICULT FOR ME BEING ON THE FRONT LINES. IT'S MUCH MORE EASY FOR AN ADMINISTRATOR TO SAY NO THAN FOR ME TO SAY NO.

I THINK THE OTHER THING IS IS THAT THE WAY, AS I UNDERSTAND IT, IN CALIFORNIA IS THAT IT IS WRITTEN THAT THE PEOPLE WITHIN THE STATE OF CALIFORNIA WILL HAVE ACCESS TO THE NEW TECHNOLOGIES FIRST, AND THEN WHATEVER IS LEFT OVER OTHERS WILL HAVE ACCESS TO. AND YOU NEED TO KEEP THAT IN MIND, THAT, AGAIN, THERE COULD BE NEW DISCOVERIES THAT OCCUR THAT THE REST OF THE UNITED STATES MAY NOT HAVE IMMEDIATE ACCESS TO, AND THAT WILL BE JUST DIFFICULT.

DR. KIESSLING: DID YOU HAVE TO TALK TO THE FDA TO DO THIS?

DR. WAGNER: WE TALKED TO THE FDA TO FIGURE OUT WHETHER OR NOT WE NEEDED TO HAVE AN IND. AND THE WAY IT WORKED OUT IS THAT WE DIDN'T HAVE TO HAVE AN IND BECAUSE WE DIDN'T MANIPULATE THE MARROW ITSELF. IF WE HAD, WE WOULD HAVE HAD TO. HOWEVER, THE QUESTION THAT REALLY CAME UP IS THAT THIS IS A NEW USE OF MARROW, BUT YET IT WAS

ACTUALLY VERY SIMILAR TO OTHER METABOLIC DISORDERS; THEREFORE, IT WAS UNDER THAT CATEGORY AND, THEREFORE, WE WERE ABLE TO GET BY WITHOUT AN IND.

DR. KIESSLING: WERE THEY HELPFUL?

DR. WAGNER: I GUESS. I CAN'T SAY THAT IT WAS -- IT WAS NOT AN OBSTACLE. LET'S PUT IT THAT WAY. WHERE I THINK I SPENT MOST OF MY TIME WAS REALLY WITH THE IRB. AND THE IRB WAS IMPORTANT BECAUSE OF THE FACT THAT, NOT ONLY DID WE HAVE TO TRAIN THE STAFF ON HOW TO TAKE CARE OF DEB, BUT WE ALSO HAD TO EDUCATE THE IRB BECAUSE THEY WERE VERY NERVOUS ABOUT A VERY VULNERABLE POPULATION, AND HOW ARE WE JUSTIFYING WHAT WE'RE DOING AND JUSTIFYING THE RISKS THAT WERE BEING IMPOSED.

DR. KIESSLING: I ACTUALLY WENT DOWN AND CHATTED WITH THE FDA A COUPLE WEEKS AGO, AND IT WAS TOLD UNIFORMLY THAT THEY WISH THE PEOPLE WOULD COME TO THEM WITH EVERY QUESTION REALLY, REALLY EARLY, THAT THEIR GOAL IS NOT TO BE AN OBSTACLE.

DR. WAGNER: TO BE HONEST WITH YOU, I THOUGHT THAT WHAT WAS GOING TO HAPPEN, MY FEELING WAS IF WE WENT TO THE FDA AND ASKED THEM THE QUESTION, THAT THE AUTOMATIC RESPONSE WAS, YES,

YOU NEED AN IND, AND THE ANSWER WAS NO. AT LEAST IN ONE EXAMPLE, IT'S NOT ALWAYS GOING TO BE AN AUTOMATIC, YES, YOU HAVE TO HAVE AN IND.

IN ANY EVENT, THERE'S OTHER ISSUES. I'D BE HAPPY TO ADDRESS THEM. LET ME JUST GIVE YOU ONE LAST SLIDE, WHICH IS REALLY THE TIMELINE. AS I INDICATED, IN JULY OF 2004 WAS MY FIRST INTRODUCTION TO DEB AT THE END OF MY PRESENTATION, WHICH HAD NOTHING TO DO WITH DEB. THEN I WAS ABLE THEN TO FIND PEOPLE WHO WERE EXPERT IN THE FIELD BY ACCIDENT. I WAS AT A MEETING IN KEYSTONE, COLORADO, AND HAPPENED TO BE SITTING NEXT TO AN EXPERT IN EPIDERMOLYSIS BULLOSA -- WHO WOULD HAVE THOUGHT THAT WOULD HAVE OCCURRED? -- WHO THEN INTRODUCED ME TO THAT THERE WAS AN ANIMAL MODEL THAT EXISTED. I CONTACTED THE PEOPLE AT JEFFERSON UNIVERSITY WHO WERE GOOD ENOUGH TO GIVE US THE ANIMAL MODEL. THE COLONY INITIATED SEVERAL MONTHS LATER. THE FIRST IN UTERO TRANSPLANTS WERE PERFORMED IN JULY. WITHIN THE YEAR THE PROOF OF PRINCIPLE HAD BEEN ESTABLISHED, AND I BEGAN WRITING THE PROTOCOL.

IT TOOK ME ABOUT, AS YOU CAN SEE THERE, APPROXIMATELY A YEAR TO WRITE THE PROTOCOL, IN PART BECAUSE IT WAS ME WRITING THE PROTOCOL AND

IT'S NOT THE ONLY THING I DO, BUT ALSO BECAUSE OF THE FACT THAT IT REQUIRED LOTS OF EDUCATION OF THE IRB AND TALKING TO THE ETHICS COMMITTEE AS WELL AS TALKING TO THE FDA AND MAKING SURE THAT WE WERE DOING THE THINGS IN THE RIGHT WAY BECAUSE IT IS A VERY EMOTIONAL THING TO BE DOING, AND YOU SOMETIMES SECOND-GUESS YOURSELF WHETHER OR NOT YOU'RE RESPONDING EMOTIONALLY OR SCIENTIFICALLY.

WE FINALLY GOT IRB APPROVAL IN MAY, AND THEN THE SHOCK WAS THAT WE WERE ABLE TO GET INSURANCE APPROVAL. WE NEVER ANTICIPATED THAT. WE ANTICIPATED THE NEXT YEAR OR TWO WOULD BE FUND-RAISING, BUT THAT NEVER OCCURRED, AND SO WE RAPIDLY WENT ON TO DOING THE TRANSPLANT IN OCTOBER OF THIS PAST YEAR.

I WANT TO ACKNOWLEDGE ALL THE PEOPLE THAT WERE INVOLVED. THAT'S IT.

CHAIRMAN LO: GREAT.

(APPLAUSE.)

CHAIRMAN LO: QUESTIONS, COMMENTS?

MS. CHARO: JOHN, THIS WAS EXTRAORDINARY. THE PICTURES ARE AGONIZING. I DON'T THINK THIS IS SOMETHING THAT YOU CAN FIX OR THE SWG CAN FIX, BUT IT'S SOMETHING THAT -- IT'S SOMETHING THAT I'M THINKING ABOUT A LOT THESE

DAYS, AND IT HAS TO DO WITH PUBLIC EXPECTATIONS AND HOW TO MANAGE THE PUBLIC EXPECTATIONS. I THINK IT'S LINKED TO WHAT YOU WERE TALKING ABOUT WHEN IT COMES TO THE PRESSURE FROM PARENTS.

I WAS SEARCHING THROUGH MY E-MAILS. I HAPPENED TO BE PRESENT FOR A REALLY FASCINATING PRESENTATION BY A NIGERIAN SOCIAL SCIENTIST WHO'S NOW AT THE UNIVERSITY OF ALBERTA NAMED UBAKA OGBOGU, WHO GAVE A PRESENTATION ON THE RANGE OF WEBSITES AROUND THE WORLD THAT ARE NOW ADVERTISING STEM CELL CURES FOR EVERYTHING FROM SERIOUS DISEASES TO WRINKLES. I'M NOT KIDDING. COSMETIC USES OF STEM CELLS.

AND THESE ARE PROLIFERATING VERY RAPIDLY. IT WAS SHOCKING HOW MANY OF THEM THERE WERE. GRANTED, A FAIR NUMBER OF THEM CAME FROM CHINA OR THE UKRAINE, BUT THEY WERE ALSO SCATTERED AROUND OTHER COUNTRIES AS WELL. AND IN THE U.S. I THINK WE'VE ALL AT VERY VARIOUS MEETINGS RUN INTO FAMILIES WHERE THERE'S A MEMBER OF THE FAMILY THAT'S COMING BASICALLY LOOKING FOR SOMEBODY TO INITIATE SOME KIND OF TRIAL.

AND SINCE YOU WERE WORKING SPECIFICALLY ON PHASE I, WHICH EVEN IN THESE AREAS OF SERIOUS DISEASES IS USUALLY UNDERSTOOD AS NOT OFFERING ANY

REAL PROSPECT OF MEDICAL BENEFIT, YOUR EXTRAORDINARY SUCCESS NOTWITHSTANDING, I'D BE REALLY INTERESTED IN KNOWING A LITTLE BIT MORE ABOUT EXACTLY HOW YOU MANAGED THE EXPECTATIONS OF THESE PARENTS.

ONE LAST THOUGHT, ONE LAST COMMENT IS THAT WE'VE SEEN BOTH IN THE JESSE GELSINGER TRIAL, WE'VE SEEN DISCUSSIONS BY STEM CELLS, INC. IN CALIFORNIA ABOUT BATTEN'S DISEASE TRIALS THAT SOME OF THE TRICKIEST SITUATIONS ARE THE ONES IN WHICH IT'S PARENTS CONSENTING FOR CHILDREN BECAUSE OF THE EMOTIONAL DYNAMIC OF PARENT AND CHILD IN THE SENSE THAT, YES, WE SHOULD GO DOWN FIGHTING AND BE A PROTECTOR. WHAT DID YOU HAVE TO GO THROUGH IN ORDER TO MANAGE THESE EXPECTATIONS BECAUSE WE'RE GOING TO HAVE TO DO THIS OVER AND OVER AND OVER?

DR. WAGNER: THE FIRST PART OF YOUR COMMENT IS RELATED TO, I THINK, FREQUENTLY, IF NOT HIGHLY FREQUENTLY, IS THE USE OF UMBILICAL CORD BLOOD. THAT IS THE SOURCE OF STEM CELLS WHICH SEEMS TO BE TREATING EVERYTHING, WHETHER IT BE ACUTE BRAIN INJURY TO SPINA BIFIDA TO YOU NAME THE DISEASE, AND SOMEHOW IT SEEMS TO BE IMPACTING IT. BECAUSE OF MY RESEARCH, WHICH IS PRIMARILY ON CORD BLOOD, I FREQUENTLY GET THOSE PHONE CALLS. AND

IT'S ACTUALLY THE REASON WHY THIS MOTHER CAME TO ME WAS BECAUSE OF MY WORK IN CORD BLOOD. I WAS GIVING MY PRESENTATION ON CORD BLOOD, WHICH SORT OF LED HER TO THINK THAT, JUST LIKE EVERYONE ELSE, THAT CORD BLOOD WAS GOING TO BE THE END ALL FOR ALL DISEASES.

AND AS IT TURNS OUT, ALTHOUGH WE USED CORD BLOOD, IT'S JUST BECAUSE IT WAS AVAILABLE, BUT REALLY THE FACT IS IT LED US, THEN, TO OPEN A DOOR. BUT WE TOLD THIS MOTHER, DESPITE THE PRESSURE, THAT WE WERE NOT GOING TO PROCEED AHEAD WITHOUT THE PROOF OF PRINCIPLE IN AN ANIMAL MODEL, WHICH IS UNIQUELY DIFFERENT THAN WHAT MOST OF THE STEM CELL THERAPIES HAVE DONE IN OTHER COUNTRIES IN PARTICULAR.

THE PRESSURE, THOUGH, COMES AS INTERNAL AS WELL AS FROM THE PARENTS. BECAUSE THE FACT IS IS THAT, YOU KNOW, IF YOU DO PHASE I THERAPIES, YOU TEND TO BE THE TYPE OF PERSON THAT TAKES RISKS, AT LEAST RISKS FOR OTHER PEOPLE ANYWAY. IT IS A STRUGGLE. AND I DON'T HAVE ANY EASY ANSWER, BUT PERSONALLY IT IS A VERY DIFFICULT THING BECAUSE OF THE FACT THAT YOU NEED TO BE ABLE TO STEP BACK WITH A GROUP TO SAY AM I DOING THE RIGHT THING. I'M NOT SURE IF I'M ANSWERING YOUR

QUESTION BECAUSE IT'S A VERY PERSONAL THING, AND IT'S ONE OF THOSE THINGS WHERE YOU WANT TO DO SOMETHING. AND THEN WHAT YOU ARE DOING IS YOU'RE TRYING TO ALWAYS SECOND-GUESS YOURSELF. ARE YOU DOING THINGS BECAUSE YOU WANT TO DO IT AND BECAUSE IT'S A SCIENTIFICALLY INTERESTING THING? ARE YOU DOING IT BECAUSE IT GIVES YOU NOTORIETY? ARE YOU DOING IT FOR THE RIGHT REASONS? OR ARE YOU REALLY DOING IT BECAUSE YOU HAVE A SCIENTIFIC QUESTION YOU THINK YOU CAN ANSWER?

I DON'T KNOW WHAT THE ANSWER IS BECAUSE OBVIOUSLY WITH THIS CASE, THE MOTHER WAS OUT THERE. SHE WAS TRYING TO FUND-RAISE. SHE WANTED THE PUBLICITY SO THAT GAVE US PUBLICITY, AND THAT BECOMES A CONFLICT. SO THERE'S SO MANY THINGS GOING ON SIMULTANEOUSLY, BUT THE FACT IS IS THAT THERE ARE WAYS WE CAN STEP BACK, ESPECIALLY IN THE GROUP SETTING, WHERE YOU HAVE THESE CHECKS AND BALANCES. SO GOING AND HAVING TO PROVE WHAT WE'VE DONE IN THE THOUGHT PROCESS TO A SCRO OR TO AN IRB, I THINK, IS CRITICALLY IMPORTANT TO MAKE SURE THAT YOU'RE, NO. 1, DOING GOOD SCIENCE AND, SECONDLY, THAT YOU ARE REALLY DOING IT IN A WELL-PLANNED, PHASED APPROACH.

CHAIRMAN LO: ANY OTHER QUESTIONS,

COMMENTS FROM THE COMMITTEE?

MS. LANSING: REMARKABLE WORK. VERY EXCITING.

CHAIRMAN LO: ANY PUBLIC COMMENT?

MR. JANUS: MY NAME IS JEFFREY JANUS. IN YOUR OPINION, YOU MENTIONED THE $500,000 FOR THE TREATMENT. HOW AMENABLE DO YOU THINK THIS WOULD BE TO LOWERING THAT COST IF IT WAS SUCCESSFUL?

DR. WAGNER: I HAVE TO THINK ABOUT THAT A BIT, OTHER THAN I CAN TELL YOU THAT FOR THIS PARTICULAR PATIENT, IT COST US $250,000. BUT, AGAIN, THIS WAS THE BEST TRANSPLANT YOU COULD EXPECT. I DON'T THINK THIS IS GOING TO BE THE NORM.

BUT ON THE OTHER HAND, WILL INCREASED NUMBERS OF PATIENTS DRIVE DOWN THE COST? WE'VE NOT SEEN THAT WITH LEUKEMIA. I DON'T PREDICT THAT IT'S GOING TO DRIVE DOWN COST BECAUSE IT'S NOT GOING TO BE SUCH THAT -- SEE, THE PROBLEM IN TRANSPLANT IS THAT WE'RE TRYING TO TRICK THE IMMUNE SYSTEM. THAT'S WHAT MAKES IT SO COSTLY. IT'S NOT SPECIFICALLY THE CHEMOTHERAPY OR THE STEM CELLS THAT WE'RE GIVING. OVER TIME THE STEM CELL MANUFACTURE MAY BE CHEAPER, BUT THAT'S A DROP IN

THE BUCKET COMPARED TO ALL THE DRUGS YOU GIVE TO TRICK THE IMMUNE SYSTEM TO ACCEPTING CELLS.

FOR ALL STEM CELL THERAPIES, EVEN IF IT'S AUTOLOGOUS, WE MAY HAVE TO STILL TRICK THE IMMUNE SYSTEM DEPENDING UPON WHAT KIND OF CELLS WE GIVE. YOU KNOW, IT'S NOT JUST GIVING THE CELLS THEMSELVES. IT'S ALL THE REST OF IT THAT COSTS SO MUCH.

MS. LANSING: BUT THE INSURANCE COMPANY IS PAYING FOR THIS.

DR. WAGNER: IN THIS PARTICULAR CASE. THIS IS AN EXCEPTIONAL CIRCUMSTANCE BECAUSE YOU CAN IMAGINE WHEN THE INSURANCE COMPANY SAID TO ME IS THIS INVESTIGATIONAL OR EXPERIMENTAL, THERE WASN'T REALLY A GOOD WAY AROUND THAT ONE. I COULD NOT THINK OF THE RIGHT WORDS OTHER THAN TO EXPLAIN SIMPLY THIS IS THE PROOF OF PRINCIPLE, THIS IS WHY WE THINK THAT THIS COULD WORK, THIS IS SIMILAR TO METABOLIC DISEASES WHICH ARE APPROVED. SO I TRIED TO MAKE AN ARGUMENT THAT THIS COULD BE SIMILAR, BUT IN TERMS OF HAS THIS BEEN DONE BEFORE? WELL, NO. AND I CAN TELL YOU THE SAME INSURANCE COMPANY, DESPITE THIS OUTCOME, HAS REFUSED THE BROTHER.

MS. LANSING: REALLY. WHY? HOW CAN

THEY BECAUSE YOU'VE HAD SUCH A SUCCESSFUL OUTCOME?

DR. WAGNER: JUST TO BE COMPLETELY HONEST ABOUT IT, THIS MAY BE A PROCESS BY WHICH THEY HAVE TO GO THROUGH THE FIRST DENIAL AND THAT THEY WILL APPROVE EVENTUALLY. ALL I'VE DONE IS I'VE GIVEN THEM MY APPEAL, AND THE APPEAL INCLUDED THE RESULTS IN THE FIRST PATIENT, WHICH THEY DID NOT HAVE AT THE TIME OF THE FIRST REQUEST. I JUST PUT IN THE REQUEST THINKING IF THEY APPROVED THE FIRST KID, THEN THEY WON'T NEED TO GO THROUGH THE WHOLE PROCESS. SO THIS JUST MAY BE A PROCESS THING; BUT AT LEAST AS OF TODAY, THEY'VE DENIED.

MS. LANSING: THERE SHOULD BE A PROCESS CERTAINLY OF PUBLIC OPINION TO MAKE SURE THAT THEY APPROVE IT.

DR. WAGNER: I DON'T WANT YOU TO THINK THAT THEY'VE DENIED DENIED FOR GOOD. IT MAY BE JUST DENIED FOR THE FIRST PASS.

CHAIRMAN LO: JOHN, THANKS VERY MUCH. THAT'S REALLY EXTRAORDINARY WORK. THANK YOU FOR PRESENTING TO US TODAY.

(APPLAUSE.)

CHAIRMAN LO: OKAY. KEVIN EGGAN IS GOING TO BE OUR NEXT SPEAKER. LAST SPRING KEVIN'S GROUP FROM HARVARD PUBLISHED VERY EXCITING WORK

SHOWING THAT IT WAS POSSIBLE TO DERIVE CORD STEM CELLS USING ANEUPLOID EMBRYOS, EMBRYOS THAT HAD AN EXTRA CHROMOSOME AND WERE NOT BEING IMPLANTED AND OTHERWISE WOULD BE DISCARDED. USING SOME VERY SORT OF IMAGINATIVE, SOPHISTICATED TECHNIQUES, KEVIN'S GROUP WAS ABLE TO TRANSFORM THOSE CELLS INTO A STEM CELL LINE.

HIS WORK IS ONE EXAMPLE OF A NUMBER OF INNOVATIVE WAYS TO TRY AND DEVELOP PLURIPOTENT STEM CELL LINES AND SORT OF TRY TO ADDRESS THE PROBLEM OF BOTH POLICY RESTRICTIONS AND ALSO PRACTICAL RESTRICTIONS IN TRYING TO RECRUIT WOMEN TO DONATE OOCYTES SPECIFICALLY FOR RESEARCH. SO I'VE ASKED KEVIN TO TALK ABOUT THE DEVELOPMENT OF INDUCED PLURIPOTENT STEM CELLS, STEM CELLS THAT YAMANAKA FIRST IN JAPAN AND THEN SUBSEQUENTLY ALSO THE GROUP AT THE WHITEHEAD INSTITUTE THAT RUDY JAENISCH SHOWED WAS POSSIBLE IN HUMANS TO TAKE A HUMAN SOMATIC CELL AND BY INSERTING FOUR TRANSLATIONAL FACTOR GENES CONVERT THOSE TO PLURIPOTENT CELLS.

MS. CHARO: JUST OUT OF LOYALTY, I HAVE TO SAY IT WAS ACTUALLY WISCONSIN, NOT THE WHITEHEAD, THAT PUBLISHED THE PAPER SIMULTANEOUSLY.

CHAIRMAN LO: SET THE RECORD STRAIGHT, I BELIEVE -- WE'LL PASS ON THAT ONE. KEVIN, GO AHEAD.

DR. EGGAN: SO I WON'T BELABOR THIS POINT TOO MUCH, BUT, OF COURSE, I THINK ONE OF THE MAJOR AIMS --

DR. ROWLEY: CAN YOU SPEAK LOUDER, KEVIN, PLEASE?

DR. EGGAN: CERTAINLY I CAN. I'M STILL KIND OF MESSING AROUND GETTING STARTED HERE. I WON'T BELABOR THE POINT, BUT, OF COURSE, ONE OF THE MAJOR GOALS IN THE FIELD RIGHT NOW IS TO TRY TO GENERATE PLURIPOTENT CELLS OR EMBRYONIC STEM CELL-LIKE CELLS WHICH HAVE THE GENOTYPES OF PATIENTS, AS YOU CAN SEE DIAGRAMED HERE IN THAT SLIDE. AND ESSENTIALLY ATTEMPTS AT THIS HAVE PRIMARILY FOCUSED IN THREE PARTICULAR AREAS. ONE, OF COURSE, WHICH WE'VE TALKED ABOUT OVER AND OVER IN THIS GROUP, IS SOMATIC CELL NUCLEAR TRANSPLANTATION. AND AT THE END I'M HAPPY TO COMMENT ON SOME WORK THAT WE'VE DONE, WHICH I THINK OPENS UP THE POOL OF MATERIAL THAT YOU COULD CONSIDER USING FOR HUMAN SOMATIC CELL NUCLEAR TRANSPLANTATION EXPERIMENTS.

I THINK THIS IS STILL AN EXCITING

TECHNOLOGY, ALTHOUGH IT MAY BECOME INCREASINGLY PASSE. BECAUSE AT THE MOMENT IT'S THE ONLY WAY TO GENERATE A BONA FIDE EMBRYONIC STEM CELL LINE WHICH HAS THE GENES OF THE ADULT DONOR CELL.

ANOTHER INTERESTING TECHNOLOGY, WHICH IS REALLY THE CONCEPTUAL BASIS FOR THE THIRD TECHNOLOGY WHICH I'LL TALK ABOUT, IS CELL FUSION. AND HERE WORK IN ASIM SURANI'S LAB ORIGINALLY IN MOUSE AND SOME WORK FROM MY OWN LAB IN HUMAN SHOWED THAT EMBRYONIC STEM CELLS THEMSELVES HAVE REPROGRAMMING ACTIVITIES THAT CAN TURN BACK THE CLOCK IN ADULT FIBROBLASTS. NOW, THAT'S WONDERFUL. THE PROBLEM WITH THIS TECHNIQUE IS THAT IT RESULTS IN A HYBRID CELL WHICH HAS THE GENOME OF BOTH THE EMBRYONIC STEM CELL AND THE ADULT FIBROBLAST IN IT. AND THE PROBLEM WITH THIS IS THAT, OF COURSE, THAT RENDERS IT USELESS FOR MANY OF THE APPLICATIONS THAT YOU'D LIKE TO PURSUE. BEYOND THAT, IT'S A BONA FIDE EMBRYONIC STEM CELL LINE.

NOW, REALIZING THAT THIS INDICATES THAT THERE ARE FACTORS WITHIN THOSE EMBRYONIC STEM CELLS WHICH MEDIATE THAT REPROGRAMMING, SHINYA YAMANAKA'S GROUP LAUNCHED INTO EFFORTS TO TRY TO IDENTIFY WHAT THOSE THINGS WERE, AND HE FOCUSED ON

GENES WHICH WERE EXPRESSED SPECIFICALLY IN EMBRYONIC STEM CELLS, BUT NOT ADULT CELLS. AND ESSENTIALLY THAT WORK RESULTED IN A LIST OF SPECIFIC FACTORS WHICH WERE CANDIDATE GENES WHICH MIGHT BE INVOLVED IN MEDIATING THAT PROCESS.

AND HE THEN EMBARKED ON QUITE A REMARKABLE APPROACH TO INTRODUCE EACH ONE OF THOSE GENES, MOST OF WHICH WERE TRANSCRIPTION FACTORS, INTO RECOMBINANTLY MODIFIED MOLONEY-BASED RETROVIRAL VECTORS. AND THEN LITERALLY FIRST IN POOLS CONTAINING A VARIETY OF THESE DIFFERENT GENES INTRODUCED BY RETROVIRAL TRANSDUCTION THOSE GENES INTO EMBRYONIC OR ADULT MOUSE FIBROBLASTS AT FIRST. QUITE REMARKABLY THAT RESULTED IN THE GENERATION OF EMBRYONIC STEM CELL-LIKE CELLS, WHICH HE TERMED INDUCED PLURIPOTENT CELLS BECAUSE, PARTICULARLY IN THE FIRST INCARNATION OF THESE CELLS, THEY HAD SEVERAL NOTABLE DIFFERENCES FROM EMBRYONIC STEM CELLS.

I WON'T BELABOR THAT POINT BECAUSE OVER TIME AND THROUGH SEVERAL ITERATIONS OF THIS WORK, WHICH DID ACTUALLY INCLUDE SOME WORK AT THE WHITEHEAD INSTITUTE AND HARVARD, AND MY COLLEAGUE, KONRAD HOCHEDLINGER'S LAB, REALLY THESE CELLS BY MOST CRITERIA ARE INDISTINGUISHABLE FROM EMBRYONIC

STEM CELLS.

SO THIS IS WHERE THINGS REALLY STOOD. I'LL BACK UP A SECOND AND I'LL JUST SAY IN THE END THIS COULD BE DONE WITH A COCKTAIL OF RETROVIRUSES WHICH ENCODED JUST FOUR GENES: KLF 4, OCT 4 AND MYC. WE CAN TALK MORE ABOUT WHAT THE DISCRETE FUNCTION OF THESE GENES ARE IF YOU LIKE, BUT I THINK THE TWO MOST IMPORTANT ARE THESE IN THE MIDDLE, SOX 2 AND OCT 4, WHICH ARE KEY REGULATORS OF MANY OF THE GENES IN EMBRYONIC STEM CELLS WHICH PROMOTE THEIR SELF-REMOVAL AND PROLIFERATION.

THIS FALL A SERIES OF PAPERS WERE PUBLISHED, ALL IN VERY QUICK SUCCESSION, BOTH FROM SHINYA'S GROUP AND ALSO FROM JAMIE THOMPSON'S GROUP AT THE UNIVERSITY OF WISCONSIN. GO BADGERS.

MS. CHARO: THANK YOU, KEVIN.

DR. EGGAN: AND REALLY THESE EXPERIMENTS BASICALLY FULFILLED THE PROMISE OF TRYING TO MOVE THIS TECHNOLOGY FROM ANIMAL MODELS AND INTO HUMAN CELLS.

AND THEN JUST A WEEK LATER, SHINYA'S LAB PUBLISHED A FOLLOW-UP PAPER, WHICH I'LL TALK ABOUT. SO I'M GOING TO GO THROUGH EACH OF THESE THREE, WHICH I FIND TO BE THE MOST SIGNIFICANT PAPERS, IN SOME DETAIL TO TALK ABOUT THE BENEFITS

AND THE DIFFERENCES IN THE APPROACHES THAT THEY USED.

SO FIRST, SHINYA'S *CELL* PAPER. ESSENTIALLY THIS REPRESENTS AN EXACT CARBON COPY OF WHAT WAS DONE IN THE MOUSE INTO HUMAN FIBROBLASTS. HE USED A VARIETY OF DIFFERENT ADULT CELLS, ADULT FIBROBLASTS, JOINT TISSUE, NEONATAL CELLS. THESE ARE THE TYPES OF ANONYMIZED CELLS FROM THE AMERICAN TYPE CULTURE COLLECTION, FOR INSTANCE, THAT WE APPROVED FOR USE IN THIS TYPE OF TECHNOLOGY RECENTLY.

THE EXACT SAME FOUR FACTORS THAT WERE USED IN MOUSE, THEIR HUMAN COUNTERPARTS WERE USED SUCCESSFULLY TO DO THIS. NOW, THE WAY THAT THIS WAS DONE WAS TO LITERALLY MAKE EXACTLY THE SAME TYPE OF VIRUSES THAT WERE USED BEFORE, WHICH ARE ACTUALLY MOUSE VIRUSES, AND INFECT THE HUMAN CELLS WITH YET A FIFTH VIRUS, WHICH ALLOWED THESE VIRUSES TO INFECT THOSE HUMAN CELLS. FOR THOSE OF YOU WHO FIND THAT CONFUSING, I CAN PROVIDE CLIFF NOTES LATER. SO THERE ARE ACTUALLY FIVE DIFFERENT VIRUSES WHICH WENT INTO THESE HUMAN FIBROBLASTS TO ELICIT THIS CHANGE.

NOW, HERE'S WHAT THIS LOOKS LIKE. WHEN THEY DO THIS, YOU START WITH A LAWN OF SLOWLY

DIVIDING FIBROBLASTS. IN THE COURSE OF A COUPLE OF WEEKS, MANY HUNDREDS OF THESE NONEMBRYONIC STEM CELL-LIKE COLONIES APPEAR. AND OUR EXPERIENCE IS THAT THESE HAVE A SUBSET OF THE GENES AND NOT ALL OF THE GENES. THESE ARE SORT OF WEEDS THAT GROW UP IN THE CULTURE THAT YOU HAVE TO AVOID. AND THEN HIDING AMIDST THE WEEDS ARE THE BURIED TREASURE, AND THAT BURIED TREASURE ARE VERY RARE HUMAN ES CELL-LIKE COLONIES THAT CAN BE FOUND AND PROPAGATED.

WHEN SHINYA'S LAB PROPAGATED THESE, WHAT HE FOUND WAS, AGAIN, THESE HUMAN EMBRYONIC STEM CELL-LIKE CELLS ARE REALLY RATHER INDISTINGUISHABLE FROM OTHER HUMAN EMBRYONIC STEM CELL LINES. SO THIS IS AN IMMUNOSTAINING ANTIBODY ANALYSIS FOR A VARIETY OF MARKERS WHICH ARE COMMONLY USED TO LOOK AT THE PLURIPOTENCY OF HUMAN EMBRYONIC STEM CELLS, SO SSA-3 AND 4, THOSE SORTS OF THINGS, VERY COMMON ASSAYS FOR ACTUALLY LOOKING AT WHETHER OR NOT THESE CELLS ARE LIKE EMBRYONIC STEM CELLS. THIS PANEL, WHICH I WON'T BELABOR, IS BASICALLY SHOWING THAT THESE CELLS EXPRESS MANY OF THE GENES WHICH ARE FOUND IN EMBRYONIC STEM CELL LINES AND, MAYBE MOST IMPORTANTLY, THESE SCATTERED DIAGRAMS HERE ARE WHOLE GENOME ANALYSIS OF

TRANSCRIPTION WITHIN THESE CELLS.

AND YOU CAN SEE HERE'S A COMPARISON OF THE IPS CELLS TO STARTING OUT DERMAL FIBROBLASTS. THE LARGER THE SCATTER AWAY FROM THE MIDLINE FOR EACH ONE OF THESE POINTS, THE BIGGER THE DIFFERENCE IN GENE EXPRESSION. SO YOU CAN SEE THERE'S A BIG SCATTER AWAY FROM THE MIDLINE HERE. AND THEN WHEN YOU ACTUALLY COMPARE THESE THINGS TO EMBRYONIC STEM CELLS, YOU CAN SEE THAT THE DATA TIGHTENS UP VERY CLOSE TO THE MIDLINE BECAUSE THE GENE EXPRESSION IS VERY SIMILAR.

THIS IS SORT OF ANALYSIS ACROSS THE ENTIRE GENOME ARGUING THAT THESE ARE A LOT LIKE EMBRYONIC STEM CELLS. MOST IMPORTANTLY -- BEFORE I GO ON, I'LL SAY ANOTHER IMPORTANT THING ABOUT THEIR PARTICULAR APPROACH, WHICH IS ACTUALLY A LITTLE BIT DIFFERENT FROM JAMIE THOMPSON'S APPROACH, IS THAT THESE VIRUSES THAT THEY USED ARE ACTUALLY SILENCED WHEN THE EXPERIMENT IS SUCCESSFUL, IF YOU WILL. SO THERE'S SOMETHING PECULIAR ABOUT THE WAY ADULT VERSUS EMBRYONIC CELLS HANDLE THESE RECOMBINANT RETROVIRUSES, AND I THINK THIS IS A KEY THING FOR PEOPLE TO UNDERSTAND. WHEN ADULT CELLS ARE INFECTED BY THESE OF TYPES OF MOLONEY-BASED RETROVIRAL

VECTORS, THOSE GENES WITHIN THEM ARE EXPRESSED AT A VERY HIGH LEVEL.

EMBRYONIC CELLS, FOR SOME REASON, HAVE VERY POTENT METHODOLOGIES FOR SILENCING THOSE GENES WITHIN THOSE VIRUSES. SO IT'S ACTUALLY A QUITE CLEVER APPROACH. YOU INFECT THE ADULT CELLS. THE GENES RESPONSIBLE FOR REPROGRAMMING ARE EXPRESSED AT A VERY HIGH LEVEL. WHEN YOU GET TO WHERE YOU WANT TO GO, THOSE INTRINSIC DEFENSE MECHANISMS ARE ACTIVATED, AND THE VIRAL GENES ARE SILENCED. THAT'S, OF COURSE, CRITICAL BECAUSE THEN WHAT YOU WANT IS FOR THOSE TO BE OFF SO THAT, AGAIN, THEY CAN GO ABOUT THEIR BUSINESS OF DIFFERENTIATING.

THAT'S A LONG-LASTING EPIGENETIC INHERITABLE CHANGE WITHIN THOSE CELLS. THAT SILENCING IS MEDIATED. SO ACTUALLY THE REASON THAT ALL OF THESE 123457, 12367, THESE ARE EMPTY THERE IS BECAUSE THE VIRUSES ARE NO LONGER EXPRESSED FOR EITHER MYC, KLF, OR SOX 2, OR THESE OTHER IN MOST CASES OCT 4 WITHIN THESE CELLS. YOU CAN COMPARE AND CONTRAST THAT TO THIS OPEN WHITE BOX, WHICH IS AN ANALYSIS OF VIRAL EXPRESSION WITHIN THE ADULT CELLS THAT ARE ORIGINALLY AFFECTED. SO INFECT THE ADULT CELLS, YOU GET A

LOT OF EXPRESSION, AND IN THE EMBRYONIC CELLS IT GOES OFF.

DR. TAYLOR: KEVIN, WHAT KIND OF DRIVES THEM TO REMOVE -- IF YOU TUNE DOWN THE EXPRESSION OF THE TRANSCRIPTION FACTORS THAT INDUCE STEMNESS, WHAT KEEPS THOSE GOING, OR IS IT JUST LOW LEVEL TRANSCRIPTION IS ALL THAT'S REQUIRED?

DR. EGGAN: THE ENDOGENOUS GENES COME ON THEMSELVES. SO BASICALLY WHAT HAPPENS IS YOU CAN THINK OF THIS AS SORT OF LIKE AN ENERGY DIAGRAM. YOU'RE IN ONE SORT OF META STABLE STATE. OVER HERE THERE'S ANOTHER ENERGY WELL, WHICH REPRESENTS THE EMBRYONIC STEM CELL STATE IN ANOTHER PLACE, AND WHAT THESE VIRUSES ARE DOING ARE PUSHING YOU OUT OF THAT ENERGY WELL UP OVER SOME MOUNTAIN INTO ANOTHER META STABLE STATE. ONCE YOU GET THERE, THEN THE ENDOGENOUS GENES TAKE OVER, AND THESE GENES ARE SILENCED, SO YOU NO LONGER NEED THEM ANYMORE.

IN FACT, I GLOSSED OVER IT. MUCH OF THIS ANALYSIS IS LOOKING AT THE ENDOGENOUS GENE'S EXPRESSION RATHER THAN EXPRESSION FROM THE RETROVIRUSES. AND THAT'S SOMETHING THAT THEY DISCOVERED IN THEIR MOUSE EXPERIMENTS AND ARE CONFIRMING HERE NOW IN HUMAN. THE VIRUSES ARE

EXPRESSED. THEY PUSH YOU IN THIS NEW DIRECTION. ONCE YOU GET THERE, THE VIRUSES ARE TURNED OFF BY GETTING THERE, AND THE ENDOGENOUS GENES CARRY ON.

MS. CHARO: JUST BEFORE YOU GET OFF THIS POINT, ONCE THE IPS CELL WITH ITS EMBRYONIC STEM CELL-LIKE CHARACTERISTICS BEGINS TO ITSELF BEGIN TO DIFFERENTIATE DOWN THE LINE OF SPECIALIZATION AND APPROACHES THE STATE OF WHAT WE COMMONLY ARE CALLING ADULT STEM CELLS, WHY IS IT THAT THOSE VIRAL GENES ARE NOT NOW REACTIVATED BECAUSE OF THE LOSS OF THE STEMNESS QUALITY OF THE CELL, OR DO WE NOT KNOW THAT YET?

DR. EGGAN: WELL, THE ANSWER IS THAT THEY CAN BE A VERY LOW FREQUENCY. AS YOU WILL SEE, THAT'S PROBLEMATIC, AND, IN FACT, IT IS PROBLEMATIC WITH THIS PARTICULAR TECHNICAL APPROACH WHICH IS USED. IN FACT, THERE IS BIOLOGICAL JUSTIFICATION FOR WHY THIS MECHANISM WOULD EXIST WITHIN US AND ALL MAMMALS. OUR GENOMES ARE LITERALLY LITTERED WITH INTRINSIC RETROVIRAL ELEMENTS THAT ARE VERY SIMILAR TO THESE. AND YOU HAVE TO KEEP THESE GUYS DOWN SO THEY DON'T DESTROY OUR GENOMES. IF THEY WERE ABLE TO ACTIVATE AND BE REVERSE TRANSCRIBED IN OUR OWN CELLS AND HOP ALL OVER THE GENOME, THEY'D BE

CONSTANTLY INSERTIONALLY MUTAGENIZING ALL OF OUR GENES, AND WE WOULDN'T BE HERE.

SO WITHIN THE EARLY EMBRYO AND THE CELLS, THE EARLY EMBRYO THAT GIVE RISE TO OUR GERM LINE, IT IS CRITICAL THAT THESE REMAIN SILENCED. IT IS LESS CRITICAL SO IN OUR ADULT SOMAS, WHICH ARE NOT GOING TO GO AND GIVE RISE TO OUR OFFSPRING. SO THE IDEA IS THAT THESE MECHANISMS ARE MORE RELAXED IN THOSE CELLS. AND, IN FACT, THOSE RETROVIRUSES THAT ARE INTRINSIC WITHIN US, AND THESE AS A RESULT ARE SOMETIMES ACTIVATED. IN THIS PARTICULAR INSTANCE, THAT HAS STRONG AND NEGATIVE CONSEQUENCES, WHICH WE'LL GET TO. DOES EVERYONE UNDERSTAND THAT?

THE BIOLOGY BEHIND THIS IS QUITE INTERESTING AND SOPHISTICATED, AND SOME WAS BY DESIGN AND SOME, I WOULD SAY, WAS BY REMARKABLY GOOD FORTUNE. NEVERTHELESS, THESE CELLS WHICH WERE GENERATED, THESE HUMAN EMBRYONIC STEM CELL-LIKE CELLS, THESE HUMAN IPS CELLS, CAN DIFFERENTIATE INTO A WIDE VARIETY OF CELL TYPES. SO THIS IS THE COMMON TYPE OF ANALYSIS THAT WOULD BE DONE BY ANYONE CHARACTERIZING A NEW HUMAN EMBRYONIC STEM CELL LINE.

YOU CAN TAKE THESE CELLS AND INJECT THEM

INTO IMMUNE COMPROMISED MICE WHERE THEY FORM TERATOMAS, AND WITHIN THOSE TERATOMAS YOU CAN FIND A VARIETY OF DIFFERENT CELLS FROM THE THREE PRIMARY EMBRYONIC GERM LAYERS, EPITHELIUM, MUSCLE, EPIDERMIS, ADIPOSE TISSUE, CARTILAGE. YOU CAN ALSO DIFFERENTIATE THESE IN EMBRYOID BODIES OR ADHERENT CULTURES AND FIND CELLS FROM THESE DIFFERENT DISTINCT LINEAGES, AND MAYBE, MOST IMPORTANTLY, IN SHINYA'S PAPER THEY ALSO DID A NICE EXPERIMENT WHERE THEY FOLLOWED ONE OF THE WELL-ESTABLISHED PROTOCOLS FOR MAKING DOPAMINE POSITIVE NEURONS. IT'S NOT ONE OF THE BEST PROTOCOLS FOR DOING THIS, BUT IT'S ONE THAT PEOPLE USE. AND THESE CELLS ARE, AT LEAST I WOULD SAY, TO SOME APPROXIMATION THE TYPE OF CELLS YOU'D WANT TO PUT BACK INTO A PARKINSON'S PATIENT.

THAT'S VERY A INTERESTING FINDING. SO THAT SUMMARIZES SHINYA'S RESULTS. CONTEMPORANEOUSLY, JAMIE THOMPSON, I THINK LARGELY INSPIRED, ALTHOUGH HE INSISTS NOT, BY SHINYA'S RESULTS, REPORTED IN *SCIENCE* ALSO THE GENERATION OF VERY SIMILAR CELLS. THERE ARE SOME SUBTLE DIFFERENCES WHICH ARE, I THINK, SIGNIFICANT. JUST BRIEFLY WORTH TALKING ABOUT.

ONE IS THAT HE USED A DIFFERENT COCKTAIL

OF GENES. AGAIN, SOX-2 AND OCT 4 ARE TWO GENES THAT ARE CENTRAL PLAYERS HERE, AND HE ALSO INSISTED THAT NANOG, WHICH IS ANOTHER TRANSCRIPTION FACTOR IMPORTANT IN MAINTENANCE OF EMBRYONIC STEM CELLS, WAS ALSO A CRITICAL PART OF HIS SUCCESS. AND OCCASIONALLY THEY ADDED OTHER GENES IN THEIR COCKTAIL WHICH AREN'T WORTH TALKING ABOUT BECAUSE THEY'RE NOT CRITICAL PLAYERS.

HE ONLY SUCCEEDED IN REPROGRAMMING NEONATAL AND FETAL FIBROBLASTS WITH THIS COCKTAIL, WHICH I THINK IS IMPORTANT MENTIONING, AND HE WAS NOT SUCCESSFUL IN REPROGRAMMING ADULT CELLS HERE.

LARGELY THE RESULTS ARE THE SAME. YOU START WITH A PLATE OF FIBROBLASTS AND YOU END UP WITH COLONIES OF CELLS THAT RESEMBLE HUMAN EMBRYONIC STEM CELLS. ONE NOTABLE DIFFERENCE IS THE TYPE OF VIRUS WHICH WAS USED IN THIS STUDY VERSUS SHINYA YAMANAKA'S STUDY. SO JAMIE'S LAB USED A DIFFERENT VIRAL VECTOR. IT'S A RECOMBINANT RETROVIRUS, BUT THIS TIME, INSTEAD OF BEING BASED ON AN INTRINSIC MOUSE VIRUS, IT'S BASED ON THE HIV VIRAL VECTOR. IT'S CALLED A LENTIVIRUS. ONE DIFFERENCE IS THAT THESE ARE NOT AS POTENTLY SILENCED IN EMBRYONIC STEM CELLS AS MOLONEY-BASED RETROVIRUSES. HERE BASICALLY THESE TALL BARS IN

THE IPS CELLS ARE SHOWING US THAT THOSE VIRUSES REMAIN EXPRESSED WITHIN THOSE CELLS.

AND SO ALTHOUGH THIS PROVES THE POINT, A CONSTITUTIVE EXPRESSION OF THESE VIRUSES IS SOMETHING TO TALK ABOUT BECAUSE IT COULD BE PROBLEMATIC FOR USING THESE CELLS FOR DOWNSTREAM APPLICATIONS. NEVERTHELESS, THEY ARE CAPABLE OF DIFFERENTIATING INTO ALL THE DIFFERENT CELL TYPES WE'D BE CONCERNED WITH, AT LEAST AT THE FIRST APPROXIMATION, LIKE EPITHELIUM, NEURAL TISSUE, CARTILAGE. I WON'T BELABOR THE POINT.

JUST AS SHINYA SHOWED, THEY EXPRESSED MANY OF THE ANTIGENS WHICH ARE FOUND IN EMBRYONIC STEM CELLS. THIS IS A FLOW CYTOMETRIC ANALYSIS INSTEAD OF THE MICROSCOPIC ANALYSIS, BUT THE RESULTS ARE THE SAME. THESE RED AND GREEN BARS BASICALLY SHOW US THAT THESE CELLS HAVE A GENE EXPRESSION PROFILE WHICH IS LIKE HUMAN EMBRYONIC STEM CELLS.

SO THEN JUST WHEN WE THOUGHT THINGS WOULD BE QUIET FOR A LITTLE WHILE, ONLY ONE WEEK LATER, PREDICTED OFTEN BY, AS IS OFTEN THE CASE, THE FINAL LINE IN HIS PREVIOUS PAPER, SHINYA PUBLISHES ANOTHER PAPER WHICH NOW SHOWS THAT, IN FACT, YOU CAN WITHDRAW MYC FROM THE COCKTAIL. AND

THIS IS AN IMPORTANT FINDING FOR A VARIETY OF REASONS, WHICH I'LL GO INTO. BUT BASICALLY AT A MUCH LOWER EFFICIENCY AND OVER A MUCH LONGER TIME SCALE, IT'S POSSIBLE JUST TO USE THESE THREE FACTORS: KLF 4, SOX 2, AND OCT 4 BOTH IN MICE TO MAKE MOUSE IPS CELLS, BUT ALSO IN HUMAN FIBROBLASTS TO MAKE HUMAN IPS CELLS. THIS IS FROM BOTH MOUSE EMBRYONIC FIBROBLASTS AND ADULT FIBROBLASTS AS WELL AS ADULT HUMAN CHEEK CELLS.

HERE THE MAIN RESULT, I'LL SUMMARIZE, IS THAT, UNLIKE PREVIOUS FINDINGS WITH ALL FOUR GENES, AT LEAST AT VERY SHORT TIME SCALES, THESE ANIMALS DON'T GET CANCER. ONE OF THE MAIN SORT OF CONCERNS ABOUT THE INITIAL RESULT IS THAT WHEN THESE MOUSE IPS CELLS WHICH CARRIED ALL FOUR FACTORS WERE PUT BACK INTO THE EMBRYO AND MICE WERE MADE, WITHIN ONLY ABOUT EIGHT WEEKS, THOSE ANIMALS STARTED TO SUCCUMB TO AGGRESSIVE TUMORS. AND THE REASON WHY THOSE MICE GOT CANCER WAS FOR THE REASON THAT I SORT OF PRELUDED BEFORE, WHICH IS THAT THOSE RECOMBINANT RETROVIRUSES IN A SMALL SUBSET OF CELLS BECOME REACTIVATED. AND WHEN IT'S THE MYC VIRUSES WHICH GET TURNED ON, MYC IS A VERY POTENT ONCOGENE. AND, IN FACT, THAT RESULTS IN TUMOR FORMATION AND THOSE ANIMALS DIE.

NOW, I'LL GET INTO THIS IN A LITTLE BIT MORE DETAIL, BUT GETTING RID OF MYC AT LEAST AMELIORATES THAT PROBLEM IN THE SHORT TERM. THAT'S IMPORTANT.

WHAT ARE THE PROBLEMS AND THE PROMISE WITH THIS TECHNIQUE? SO THE BIG PROBLEM WITH THIS TECHNIQUE, IF YOU THINK ABOUT USING IT THERAPEUTICALLY IN A HUMAN CONTEXT, IS FRANKLY JUST CANCER. THERE ARE TWO BIG CONCERNS ABOUT THE APPROACH AS YOU THINK ABOUT IT RIGHT NOW. FIRST OF ALL, THIS APPROACH PERMANENTLY MODIFIES THE HOST GENOME BECAUSE, FOR THOSE WHO AREN'T FAMILIAR WITH WHAT RETROVIRUSES DO, THEY ENTER INTO THE CELL, THEY'RE REVERSE TRANSCRIBED INTO DNA, AND THEN THEIR GENOME IS PERMANENTLY INTEGRATED INTO THE HOST GENOME. SO IT IS THERE FOREVER WITHIN THOSE CELLS. IT IS TRUE THAT THE REST OF THE GENOME IS EXACTLY LIKE THAT OF THE PATIENT IN PRINCIPLE, BUT IT HAS THESE GENETIC MODIFICATIONS. THOSE GENETIC MODIFICATIONS ARE PROBLEMATIC IN TWO PRINCIPAL WAYS.

FIRST OF ALL, THE MODIFICATIONS THAT ARE MADE TO MAKE THE TECHNIQUE WORK ARE PROBLEMATIC BECAUSE ALL FOUR OF THESE GENES HAVE BEEN IMPLICATED IN ONE WAY OR ANOTHER IN TUMOR

FORMATION. SO MYC IS SORT OF THE PROTOTYPICAL ONCOGENE, ONE OF THE MOST POTENT ONCOGENES THAT WE KNOW OF. SO IF IT'S TURNED ON, IT'S GOING TO CAUSE CANCER. WELL, WE'VE GOTTEN RID OF THAT ONE, AT LEAST FOR THE TIME BEING, SO THAT'S GOOD. ACTIVATION OF OCT 4 IN EPITHELIAL ISSUES IN ANIMALS CAUSES THEM TO EXPLODE INTO TUMORS IN JUST A VERY SHORT PERIOD OF TIME. IN FACT, OCT 4 CAN KILL MICE FASTER THAN MYC CAN. AND, AS I SAID, I THINK IT'S REALLY ONE OF THE CENTRAL PLAYERS IN THIS PROCESS, AND IT'S NOT GOING TO BE SOMETHING THAT CAN BE GOTTEN RID OF.

SOX 2 HAS ALSO BEEN IMPLICATED IN SOME CANCERS, AND KLF 4 INTERACTS AND MODULATES P-53 ACTIVITY, WHICH IS ONE OF THE CENTRAL TUMOR SUPPRESSOR GENES IN OUR GENOME.

MS. CHARO: SO THE SOX 2 AND THE OCT 4 WERE COMMON BETWEEN THE YAMANAKA AND THE THOMPSON LABORATORIES. BUT THE NANOG VERSUS THE KLF 4 WAS DIFFERENT. DOES THE NANOG HAVE ANY DIFFERENT CHARACTERISTICS WITH REGARD TO TUMOR FORMATION IN ITS INTERACTION WITH THE SOX 2 AND OCT 4?

DR. EGGAN: THAT HASN'T BEEN INVESTIGATED IN THE SAME CONTEXT THAT IT WOULD NEED TO BE INVESTIGATED AND FIND OUT. PEOPLE JUST

HAVEN'T LOOKED FOR THAT YET. I THINK THE ANSWER IS WE DON'T KNOW.

MS. CHARO: THERE'S STILL A LOT OF PERMUTATIONS TO CARRY OUT.

DR. EGGAN: YEAH. BASICALLY THE EXPERIMENTS THAT WERE DONE WITH OCT 4 WERE TO INDUCE ITS EXPRESSION AT HIGH LEVELS IN ADULT ANIMALS AND ASK WHAT THAT DID. AND THE ANSWER TO WHAT DID IS IT KILLS THEM WITHIN A WEEK, AND IT KILLS THEM BECAUSE THEY GET THESE AGGRESSIVE INTESTINAL TUMORS, WHICH ACTUALLY KEEP THEM FROM EATING BECAUSE THEY'RE SO AGGRESSIVE. THAT EXPERIMENT HASN'T BEEN DONE YET, AT LEAST NOT TO MY KNOWLEDGE, WITH NANOG. THAT'S PROBLEM NO. 1. THE GENES THAT YOU'RE USING ARE INTRINSICALLY RELATED TO CANCER.

THE OTHER PROBLEM IS THAT THE VIRAL VECTORS, WHICH, AS I DESCRIBED TO YOU, ARE A CRITICAL PART OF GETTING THE PROCESS TO WORK, AT LEAST AT THE MOMENT, ARE THEMSELVES CARCINOGENIC. MANY OF YOU WILL KNOW THAT THERE WAS A TIME IN THE DAYS OF GENE THERAPY WHEN WE WERE QUITE EXCITED BECAUSE KIDS WHO HAD SEVERE COMBINED IMMUNE DEFICIENCY THEN SUCCESSFULLY TREATED BY TRANSDUCING THEIR CELLS WITH RETROVIRUSES WHICH

RESCUED AN EXPRESSION OF A GENE THAT THEY WERE MISSING.

SADLY, MANY OF THOSE CHILDREN HAVE NOW SUCCUMBED TO LEUKEMIA, AND THE CAUSE OF THAT LEUKEMIA, THERE ARE EXPERTS IN THE ROOM WHO CAN SPEAK TO THIS BETTER THAN I CAN, AS UNDERSTAND IT, ARE THOUGHT TO BE CAUSED BY THE PROPENSITY OF THE VIRUSES WHICH ARE USED, WHICH ARE EXACTLY THE SAME VIRUSES USED HERE, TO INSERT INTO ONCOGENES.

SO TO SAY THAT IN A DIFFERENT WAY, THE VIRAL VECTORS THEMSELVES ARE INTRINSICALLY CANCER PROMOTING EVEN IF THEY WERE CARRYING NOTHING. SO THAT'S AN IMPORTANT THING TO SAY. THESE ARE TWO MAJOR HURDLES WHICH IN THIS INCARNATION, I BELIEVE, WOULD PREVENT THEM FROM EVER BEING USED IN THE CLINIC.

DR. KIESSLING: THAT'S EASIER TO UNDERSTAND, I THINK, IF YOU TALK ABOUT THE FACT THOSE VIRUSES INSERT THEMSELVES NEXT TO THE ONCOGENES, AND THE VIRUSES HAVE SO MANY COPIES OF PROMOTERS, THEY TURN THAT ONCOGENE ON INADVERTENTLY.

DR. EGGAN: THAT'S RIGHT. ANN IS CLARIFYING BEAUTIFULLY. SO IT TURNS OUT THAT THE VIRUSES THEMSELVES HAVE GENE EXPRESSION PROMOTING

ELEMENTS WITHIN THEM. WHEN THEY LAND NEAR THESE ONCOGENES, WHICH THEY HAVE A TENDENCY TO DO, WHICH COULD BE AN INTRINSIC PART OF THEIR OWN BIOLOGY, THEY PROMOTE THE EXPRESSION OF THOSE GENES, AND THAT RESULTS IN TUMOR FORMATION.

THOSE ARE ALL A BIG PROBLEM. THAT'S A CLEAR RED. NOW, THIS MAY OR MAY NOT BE SOMETHING THAT CAN BE GOTTEN AROUND BY OTHER APPROACHES. IN FACT, MANY OF YOU MAY HAVE SEEN A PRESS RELEASE WHICH HAS BEEN CIRCULATED BY A COMPANY IN SOUTHERN CALIFORNIA THIS WEEK CLAIMING THAT THEY'VE BEEN ABLE TO DO THIS WITHOUT PERMANENT GENETIC MODIFICATION OF THE CELLS. IT'S IN PRINCIPLE POSSIBLE; BUT, OF COURSE, LIKE MANY THINGS, IT MAY BE DIFFICULT TO ACHIEVE THIS.

SO I THINK A MAJOR FOCUS OF THE FIELD IS TO TRY TO USE THESE GENES AND THEIR ACTIVITIES TO PROMOTE REPROGRAMMING WITHOUT PERMANENTLY INTEGRATING THEM INTO THE GENOME OF THE TARGET CELLS. NO ONE HAS YET BEEN SUCCESSFUL IN DOING THAT. AND BEFORE THIS COULD EVER BE USED THERAPEUTICALLY, THAT WILL HAVE TO BE DONE, I BELIEVE.

ANOTHER MAJOR QUESTION IS, PARTICULARLY IN THE CONTEXT OF THIS SPECIFIC APPROACH, IS HOW

STABLE IS THIS REPROGRAMMED STATE? ALTHOUGH AT FIRST APPROXIMATION, THESE LOOK A LOT LIKE HUMAN EMBRYONIC STEM CELLS, A LOT MORE WORK HAS TO BE DONE TO FIGURE OUT WHETHER OR NOT THEY REALLY ARE.

THE OTHER PROBLEM IS EXACTLY THE ONE THAT WE DESCRIBED AND SO WELL, I THINK, DEMONSTRATED BY THE CANCER IN THESE ANIMALS WHERE MYC IS REACTIVATED. AND THAT IS THAT EVEN THOUGH THESE RETROVIRUSES ARE SILENCED, THEY CAN AT SOME REASONABLE FREQUENCY BE TURNED BACK ON AGAIN. WE NEED TO KNOW WHETHER OR NOT THAT IS A PROBLEM FOR DISEASE MODELING OR ANALYSIS OF THESE CELLS IN VITRO.

DR. TAYLOR: SO THERE ARE TECHNIQUES OF SORT OF TRANSIENTLY TRANSFECTING, INTRODUCING GENES INTO THE CELLS THAT WILL ULTIMATELY BE LOST, NOT THROUGH RETROVIRUS MECHANISMS, BUT OTHER MECHANISMS. AND YOU KIND OF INDICATED THAT ONCE YOU'VE INDUCED KIND OF AN EMBRYONIC STEM CELL STATE, THEY TURN ON THEIR OWN PROGRAM OF STEMNESS GENES. SO IT SEEMS TO ME THAT THIS IS SORT OF A PRESUMABLY READILY SURMOUNTABLE KIND OF A PROBLEM.

DO YOU HAVE A SENSE OF WHAT THAT PERIOD OF TIME IS THAT YOU HAVE TO INDUCE TO GET YOUR COLONIES TO GROW?

DR. EGGAN: THERE ARE TWO STUDIES THAT ARE JUST RECENTLY PUBLISHED WHICH SUGGEST, ALTHOUGH IT TAKES ABOUT THREE WEEKS TO GET ALL THE WAY THERE, THERE'S SORT OF A POINT OF NO RETURN BETWEEN ABOUT SEVEN AND TEN DAYS. AND I THINK THAT WORK IS ONGOING RIGHT NOW TRYING TO FIGURE OUT WHAT THE RIGHT BALANCE OF THESE FACTORS IS IN ORDER TO BE ABLE TO -- YOU WANT TO KNOW IN WHAT PROPORTION DO YOU NEED EXPRESSION OF THESE THINGS AND FOR HOW LONG SO THAT YOU MIGHT BE ABLE TO DO THIS. AND ESSENTIALLY THAT'S ACCOMPLISHED IN THIS RETROVIRAL APPROACH THROUGH A NUMBERS GAME WHERE YOU INFECT VERY HIGH TITERS OF THESE VIRUSES, WHICH IS ANOTHER PROBLEM. THIS CAN BE DONE, BUT IT IS NOT TECHNICALLY TRIVIAL, I CAN TELL YOU FROM OUR OWN EXPERIENCE, TO MAKE VIRUSES AT THE TITERS WHICH ARE REQUIRED TO PERFORM THIS APPROACH.

WE'VE BEEN ABLE TO DO IT, BUT IT'S NOT AN EASY THING. DON'T EXPECT THIS TO BE HAPPENING -- YOU CAN EXPECT EVERY LAB TO BE TRYING TO DO THIS RIGHT NOW BECAUSE THEY ARE, BUT IT'S NOT A TRIVIAL THING TO DO. SO I THINK PROGRESS IS STILL GOING TO BE A LITTLE BIT SLOW FOR THE TIME BEING.

OF COURSE, THE OTHER PROBLEM IN HUMAN

MORE THAN IN ANIMALS IS YOU GET THESE OTHER WEEDS WHICH OVERGROW. THESE CELLS THEMSELVES CONTAMINATE THE CULTURES AND ARE PROBLEMATIC FOR ANALYSIS AND POTENTIALLY DOWNSTREAM USE AS WELL. THAT'S OURS AND OTHERS' EXPERIENCE. OF COURSE, THE MAJOR ADVANTAGE OF THIS IS THAT ANYBODY CAN DO IT. ANYONE AT AN INSTITUTION WITH A COMMITTEE ON MICROBIOLOGICAL SAFETY, AN ESCRO, AND AN IRB CAN REALLY GET TO WORK ON, I THINK, THIS SORT OF THING RIGHT AWAY. IT'S JUST SIMPLY NOT LIMITED BY LOGISTICAL AND TECHNICAL LIMITATIONS OF SOMATIC CELL NUCLEAR TRANSPLANTATION, WHICH AS WE ALL KNOW IS A MAJOR ISSUE. IT'S ALSO SCALABLE, WHICH IS ALSO WONDERFUL.

SO YOU CAN IMAGINE, I THINK, IN VERY SHORT ORDER TRYING TO MAKE THESE TYPES OF CELLS FROM MANY DIFFERENT FLAVORS OF PATIENTS FOR DISEASE MODELING. MANY LABS ARE TRYING TO DO THAT, INCLUDING OUR OWN RIGHT NOW.

I HOPE THAT GIVES YOU A FLAVOR OF THE PROBLEMS AND PROMISE WITH THIS PARTICULAR TECHNIQUE. I DO THINK IT'S A REALLY WONDERFUL AND AMAZING ADVANCE. IT'S ONLY A MATTER OF TIME BEFORE SHINYA GOES TO STOCKHOLM. BUT AS A THERAPEUTIC APPROACH FOR CELL TRANSPLANTATION, I

THINK IT'S A NONSTARTER UNLESS THESE TECHNICAL RETROVIRUSES CAN BE OVERCOME. AND I DON'T THINK IT'S NECESSARILY A TRIVIAL THING TO OVERCOME IT BECAUSE OF THIS PECULIARITY OF THE VIRUSES BEING SILENCED WHEN YOU GET THERE. IT'S SORT OF LIKE YOU HAVE THE RIGHT DOSE THAT TRIES TO GET YOU TO WHERE YOU WANT TO GO, BUT THE CELLS THEMSELVES KNOW WHEN THEY'VE HAD ENOUGH, AND THEY TURN OFF THE GENES, AND THEY'RE NOT RELYING ON ANY SORT OF INTERVENTION FOR THAT.

IT COULD BE TOMORROW THAT PEOPLE WILL HAVE REPORTED DOING THIS, BUT I DON'T THINK THAT WE SHOULD -- I THINK, LIKE ANY, IT WILL REQUIRE A REAL SCIENTIFIC ADVANCE FOR THAT TO BE DONE. AS WE KNOW, THOSE ARE DIFFICULT TO PREDICT THE TIMING OF. I THINK THAT'S HOW I WOULD SAY IT.

DR. PETERS: KEVIN, DID YOU YOURSELF HAVE SOME EARLIER EXPERIMENTS WHICH YOU WERE TRYING TO REPROGRAM THE CYTOPLASM, NOT THE NUCLEUS, AND WITHOUT USING THESE AUXILIARY GENES?

DR. EGGAN: THIS WAS THE CELL FUSION APPROACH THAT I DESCRIBED TO YOU AT THE BEGINNING OF MY TALK. AND I THINK THAT STILL IS IN PRINCIPLE A WONDERFUL APPROACH, BUT NO ONE HAS BEEN ABLE TO CRACK THE PUZZLE OF HOW TO USE

CYTOPLASM FROM EMBRYONIC STEM CELLS TO DO THIS. ALL OF THE SUCCESSFUL APPROACHES THUS FAR HAVE ACTUALLY REQUIRED USING THE WHOLE EMBRYONIC STEM CELL, AND THAT INVARIABLY RESULTS IN THE FORMATION OF THESE HYBRID CELLS, WHICH THEMSELVES ARE EVEN MORE GENETICALLY MODIFIED BECAUSE THEY HAVE A WHOLE NOTHER PERSON'S GENES IN THEM THAN THESE VIRUSES.

SO FOR THAT REASON THOSE AREN'T GOING TO BE USEFUL, AND A LOT OF PEOPLE HAVE BEEN WORKING ON TRYING TO DO THAT, BUT NO ONE HAS BEEN SUCCESSFUL.

DR. ROWLEY: KEVIN, WHAT APPROACH ARE YOU TAKING RIGHT NOW?

DR. EGGAN: JANET, WE'RE REALLY STILL -- I'D SAY WE'RE TAKING A TWO-PRONGED APPROACH RIGHT NOW. FIRST OF ALL, WE'VE HAD SOME SUCCESS IN REPLICATING THIS IN HUMAN CELLS WITH AGAIN SLIGHT MODIFICATIONS TO THIS APPROACH, SO USING SIMILAR RETROVIRAL CONSTRUCTS TO SHINYA'S, USING MOLONEY-BASED RETROVIRUSES, BUT NOW ACTUALLY PACKAGING THEM IN A SYSTEM WHICH ALLOWS THEM TO DIRECT DIRECTLY HUMAN CELLS. AND WE'VE HAD SOME SUCCESS ACTUALLY GENERATING THESE CELLS DIRECTLY FROM PRIMARY PATIENT BIOPSIES. SO THAT'S

ENCOURAGING. I REALLY THINK THAT CAN BE DONE. IT'S NOT JUST WITH THESE, YOU KNOW, COMMONLY AVAILABLE "LONG CULTURE" PRIMARY CELL LINES. THIS CAN BE DONE. YOU CAN GO OUT, YOU CAN GET A BIOPSY FROM A PATIENT, YOU CAN TAKE IT BACK TO YOUR LAB, YOU CAN INFECT IT WITH THESE VIRUSES, AND YOU CAN MAKE THESE CELLS.

HOW THOSE CELLS WILL BEHAVE IN DISEASE MODELING APPLICATIONS, WE DON'T KNOW YET, BUT WE HAVE SOME REASONABLE ASSAYS NOW FOR ALS USING SORT OF RUN-OF-THE-MILL HUMAN EMBRYONIC STEM CELL LINES, AND WE'LL BE ABLE TO RUN THESE THINGS THROUGH NOW AND SEE HOW THEY COMPARE. SO THERE ARE ABOUT THREE PEOPLE IN MY LAB THAT WORK ON THAT NOW, AND THERE ARE STILL TWO PEOPLE IN MY LAB THAT WORK ON SOMATIC CELL NUCLEAR TRANSPLANTATION.

BERNIE TALKED ABOUT THIS WORK THAT WE HAD PUBLISHED ABOUT A YEAR AGO IN WHICH WE SHOWED THAT AT LEAST IN ANIMALS, IN THE MOUSE, YOU CAN USE FERTILIZED -- CELLS OF THE FERTILIZED EMBRYO RATHER THAN JUST OOCYTES TO DO REPROGRAMMING, AND WE'VE BEEN FOLLOWING UP THAT IN OTHER ANIMALS. IT WORKS BEAUTIFULLY IN RABBIT, FOR INSTANCE, AS WELL AS NOW WITH HUMAN DONATED MATERIAL.

AND WE HAVE HAD ACTUALLY A LOT OF --

WELL, A FAIR AMOUNT OF SUCCESS, I WOULD SAY, IN SOURCING FROZEN ZYGOTES FOR THOSE EXPERIMENTS. WE'VE HAD SEVERAL HUNDRED FROZEN ZYGOTES DONATED TO US NOW FOR THOSE EXPERIMENTS. AND THOSE ARE GOING FORWARD. AS IS OFTEN THE CASE, THINGS ARE NOT AS SIMPLE IN HUMAN EMBRYOLOGY, AS ANN AND JOSE AND OTHERS KNOW WELL, FOR THESE TYPES OF MANIPULATIONS AS THEY ARE IN HUMAN. I THINK IT'S REALLY A QUITE PROMISING APPROACH.

THAT BEING SAID, IF I HAD ACCESS TO UNFERTILIZED OOCYTES, THAT WOULD BE MY PREFERRED CHOICE OF MATERIAL. BUT AS MOST OF YOU HAVE HEARD ME SAY AT LEAST ONCE BEFORE, WE'VE NOW HAD A HUMAN SUBJECTS PROTOCOL IN MASSACHUSETTS WHERE EGG DONORS CAN'T BE COMPENSATED FOR THE LAST TWO YEARS. WE SPENT MORE THAN $100,000 ON ADVERTISING. WE'VE HAD ALMOST 300 CALLS NOW FROM WOMEN WHO ARE INTERESTED, BUT WE'VE HAD ONE DONOR. AND I THINK IN STATES WHERE THERE IS THIS CLEAR DOUBLE STANDARD BETWEEN WHAT A WOMAN CAN BE COMPENSATED FOR TO DO THE SAME THING FOR TWO DIFFERENT PURPOSES, YOU KNOW, THAT FOR WHICH SHE CANNOT BE COMPENSATED SHE WILL NOT DO. I THINK THAT'S SIMPLY SAID.

DR. CIBELLI: I JUST WANTED TO ASK A

SIMPLE QUESTION. YOU MADE A LOT OF -- THAT WAS A VERY CLEAR PRESENTATION, AT LEAST I HOPE EVERYBODY GOT IT. YOU MADE A LOT OF EMBRYONIC STEM CELLS BY NUCLEAR TRANSFERRING MICE, AND THEN YOU MADE ANIMALS FROM THEM, WHOLE ANIMALS. SO MY QUESTION IS HAVE ANY OF THOSE ANIMALS YOU HAVE PRODUCED HAVE EVER DEVELOPED CANCERS ABOVE THE NORMAL OBSERVED RATE OF CANCER IN MICE?

DR. EGGAN: THAT'S A GOOD QUESTION. NO. WE'VE HAD SOME OF THOSE ANIMALS ON FOR THEIR ENTIRE LIFE SPAN, TWO, THREE YEARS; AND FOR THOSE THAT HAVE BEEN GENERATED FROM NUCLEAR TRANSFER ES CELL LINES, WE'VE NEVER SEEN ANYTHING LIKE THIS. SO THERE'S NOTHING NEGATIVE ABOUT THE REPROGRAMMING PROCESS ITSELF. YOU KNOW, THE ONLY EXAMPLE OF THAT, OF ANYTHING BAD LIKE THAT EVER OCCURRING WAS THAT HANS SCHOLER'S LAB MADE SOME CLONED ANIMALS IN WHICH THEY SAW A KINKED TAIL PHENOTYPE WHICH WAS HERITABLE WHEN THEY MADE THOSE ANIMALS. WHEN THEY ACTUALLY WENT BACK AND LOOKED AT THE DONOR CELL POPULATION THAT THEY WERE USING, THAT MUTATION HAPPENED TO ARISE IN THE SOMATIC CELLS OF THAT INDIVIDUAL. SO, OF COURSE, THAT WAS A PERMANENT GENETIC CHANGE THAT HAPPENED JUST RANDOMLY, JUST LIKE IT WOULD IN ANY OF OUR CELLS,

SO THERE IS SOME RISK OF THAT, BUT THAT'S ONLY BEEN DETECTED ONE TIME IN THE MANY THOUSANDS AND THOUSANDS OF CLONED ANIMALS THAT HAVE BEEN GENERATED.

DR. TAYLOR: KEVIN, JUST TO KIND OF GET BACK TO THIS RETROVIRUS ISSUE, SO ARE LIPOSOMAL DELIVERY SYSTEMS JUST WAY TOO INEFFICIENT?

DR. EGGAN: YOU'RE DEFINITELY GOING THROUGH THE THOUGHT PROCESS THAT EVERYBODY ELSE IS. I KNOW MYSELF PERSONALLY OF GROUPS THAT ARE TRYING PARTICLE-BASED DELIVERY OF PROTEINS AND NUCLEIC ACIDS, ADENOVIRAL-BASED VECTORS WHICH ALLOW NONLONG-LASTING INTEGRATION INTO THE GENOME, BUT EXPOSURE FOR TWO TO THREE WEEKS. WE OURSELVES HAVE TRIED PSEUDORABIES VIRUS-BASED LIPOSOMAL VECTORS. PEOPLE HAVE TRIED SB-40 BASED LIPOSOMAL VECTORS. PEOPLE ARE JUST TRYING BULK TRANSVECTION OF DNA INTO CELLS.

PEOPLE WILL TRY ALL OF THESE THINGS AND ANYTHING THEY CAN IMAGINE FOR INTRODUCING THESE NUCLEIC ACIDS INTO CELLS TO TRY TO GET THIS TO WORK. IT WILL EITHER OR IT WILL NOT. AND IT MAY BE THAT WE COME TO UNDERSTAND THIS PROCESS MUCH BETTER, AND THEN IT WILL WORK.

I THINK THE FACT OF THE MATTER, THOUGH,

THAT IT IS UNDENIABLY TRUE THAT THIS IS A MUCH MORE MANIPULATABLE SYSTEM WHICH IS MUCH MORE, I GUESS I WOULD SAY, AMENABLE TO UNDERSTANDING IN THE WAY THAT MOST BIOLOGISTS THINK ABOUT UNDERSTANDING THINGS THAN NUCLEAR TRANSFER IS PER SE. IT STILL HAS CHALLENGES TO UNDERSTANDING BECAUSE, FOR INSTANCE, HERE YOU HAVE MANY MILLIONS OF CELLS OR HUNDREDS OF THOUSANDS OF CELLS, AND YOU INFECT THEM WITH THESE VIRUSES, AND ONLY A VERY SMALL NUMBER OF THEM, LIKE ONE OR TWO OR TEN, WILL END UP BEING THE THING THAT YOU WANT. AND IT'S OFTEN AN ENORMOUS CHALLENGE TO TRY TO SORT OUT, FIRST TO FIND THAT NEEDLE IN A HAYSTACK, AND THEN FIND OUT HOW THAT NEEDLE CAME TO BE OUT OF A PIECE OF STRAW, WHICH IS AT THE BEGINNING JUST LIKE THE SAME AS ALL THE OTHER PIECES OF STRAW IN THE HAYSTACK.

MS. CHARO: TWO QUESTIONS. ONE OF WHICH ACTUALLY FOLLOWS ON PERFECTLY FROM THIS. THAT IS, THOSE OF US WHO FOLLOW SCIENCE AT A POPULAR SCIENCE LEVEL KEEP READING ABOUT THESE ADVANCES IN SYNTHETIC BIOLOGY. AND I WAS WONDERING IF YOU MIGHT TALK TO WHETHER OR NOT THERE'S ANY SUGGESTION IN THAT WORLD THAT THERE MIGHT BE THE ABILITY TO CONSTRUCT AN ARTIFICIAL VIRUS THAT

DOESN'T POSE THESE KINDS OF THREATS AS A VECTOR.

AND THE SECOND QUESTION IS, REGARDLESS OF WHETHER ONE GETS OVER THIS PROBLEM WITH RETROVIRAL RISKS, THOSE WOULD SEEM TO BE RISKS THAT ARE RELEVANT TO THE USE OF THIS FOR CLINICAL CARE IN TERMS OF TISSUE TRANSPLANT. CAN YOU TALK ABOUT WHETHER THIS POSES ANY PROBLEM IN COMPLICATING THE USE OF THESE CELL LINES WHEN IT COMES TO STUDYING TISSUES THAT HAVE PARTICULAR DISEASE MUTATIONS OF INTEREST?

DR. EGGAN: SO I GUESS RIGHT NOW SYNTHETIC BIOLOGY IS A REALLY REMARKABLE FIELD, BUT IN ITS EARLIEST DAYS. SO YOU COULD THINK OF -- THIS IS SORT OF LIKE SOME OF THE MOST REMARKABLE -- THIS IS SORT OF -- THERE'S ALSO THIS THING CALLED SYSTEMS BIOLOGY, WHICH IS RELATED TO SYNTHETIC BIOLOGY. IN SYSTEMS BIOLOGY YOU COULD THINK ABOUT IT AS TRYING TO UNDERSTAND THE COMPLEX WIRING OF THE NETWORKS WHICH CONTROL CELL IDENTITY AND DECISIONS THAT CELLS MAKE. AND THIS INVOLVES, I THINK, TRYING TO UNDERSTAND SOME OF THE MORE INTERESTING SYSTEMS BIOLOGY WHICH IS OUT THERE. IT SORT OF SAYS HOW YOU CAN SHIFT FROM ONE NETWORK TO ANOTHER NETWORK BY PUSHING ON JUST A FEW NODES WITHIN THAT NETWORK, IF THAT MAKES SENSE.

SYNTHETIC BIOLOGY IS SO PRIMITIVE, THAT THEY'RE STILL TRYING TO FIGURE OUT HOW TO FLIP ON AND OFF THE LIGHT SWITCH RIGHT NOW. I DON'T THINK THAT FOR THE MOMENT THOSE ADVANCES ARE RELEVANT HERE, BUT VIRAL VECTORS, THAT FIELD ITSELF IS A VERY WELL-DEVELOPED ONE, AND SO PEOPLE ARE QUITE CLEVER. THERE ARE MANY DIFFERENT TYPES OF VIRAL VECTORS THAT PEOPLE WILL TRY.

ONE APPROACH WHICH HAS BEEN USED IS TO USE DIFFERENT VECTORS TO INTRODUCE THESE GENES, AND THEN ACTUALLY FLANK THOSE VECTORS WITH SITE-SPECIFIC RECOMBINASE SITES SO THAT SOME OF THEM CAN BE REMOVED POST HOC FROM THE GENOME. RUDOLPH JAENISCH'S LAB AT THE WHITEHEAD INSTITUTE CAN SUCCESSFULLY DO THAT FOR MYC FOR SOME OF THESE CELLS IN A MODEL AND ACTUALLY A CELL. I THINK THAT'S ALSO WORTH TALKING ABOUT TOO. SO THERE IS ONE PAPER PUBLISHED IN *SCIENCE* BY RUDOLPH JAENISCH'S LAB SHOWING THAT YOU CAN TAKE THESE IPS CELLS, DIFFERENTIATE THEM INTO BLOOD FORMING HEMATOPOETIC STEM CELLS, AND THEN TRANSPLANT THEM INTO A MOUSE MODEL OF SICKLE CELL DISEASE.

I REALLY WANT TO TALK ABOUT THIS PAPER BECAUSE IT WAS A HUGE SPLASH IN THE LAY PRESS. AND THERE ARE GREAT THINGS ABOUT IT, AND THERE ARE

BAD THINGS ABOUT IT, AND THERE ARE MISLEADING THINGS ABOUT IT. SO FIRST, THE GOOD THINGS ABOUT IT. IT SHOWS THAT YOU CAN WALK THROUGH ALL OF THESE STEPS, WHICH ARE ALL VERY SOPHISTICATED, AND IN PRINCIPLE THAT CAN BE DONE. AND, IN FACT, IT SHOWS IN THAT PAPER THIS APPROACH OF REMOVING MYC AFTER YOU GET THE CELLS SO THAT THE ANIMALS DON'T GET CANCER, AT LEAST A SHORT TIMEFRAME. I STILL THINK THERE IS A FRANK CONCERN THAT AS THESE MICE GET OLDER WITH THESE OTHER VIRUSES THERE, THAT THEY CAN STILL GET CANCER FROM EFFECTS OF THE OTHER GENES BEING ACTIVATED AT LATER TIMES.

THOSE, I THINK, ARE THE GOOD AND THE BAD THINGS ABOUT IT. THE MISLEADING THING ABOUT IT IS THAT THEY CHOSE THAT PARTICULAR DISEASE FOR A VERY GOOD REASON. AND THAT IS THAT THE METHODOLOGY THAT THEY USED FOR DIFFERENTIATING THOSE CELLS INTO HEMATOPOETIC STEM CELLS ALLOWS THEM TO DIFFERENTIATE VERY WELL DOWN THE MYLOID LINEAGE, BUT IT DOES NOT ALLOW THEM TO BECOME LYMPHOCYTES.

SO ESSENTIALLY IT'S TRUE THAT THEY USED THIS APPROACH TO CURE THE SICKLE CELL DISEASE IN THOSE ANIMALS, BUT THEY GAVE THEM SEVERE COMBINED IMMUNE DEFICIENCY. I'VE GIVEN RUDOLPH A VERY HARD TIME ABOUT THAT. THIS COULD BE LEVELED AT THE

SAME TREATMENT FOR EMBRYONIC STEM CELLS, BUT I THINK IT UNDERSCORES THE IMPORTANCE OF BEING FRANK ABOUT WHAT YOU'RE DOING HERE, AND I THINK THAT'S PROBLEMATIC. SO I HOPE THAT ANSWERS BOTH OF YOUR QUESTIONS.

DISEASE MODELING. THE DISEASE MODELING, I THINK ONLY TIME WILL TELL. I THINK MY GUT FEELING IS, YES, THAT THIS WILL BE USEFUL. AND I CAN SAY THAT'S TRUE BECAUSE I FEEL STRONG ENOUGH ABOUT IT THAT WE'RE INVESTED IN TRYING TO DO IT. BUT I DON'T THINK WE CAN KNOW UNTIL WE ACTUALLY DO THE EXPERIMENTS AND FIND OUT. THE GOOD NEWS IS NOW THAT THERE ARE A VARIETY OF HUMAN EMBRYONIC STEM CELL LINES THAT HAVE BEEN DERIVED EITHER THROUGH GENETIC MODIFICATION OR THROUGH DERIVATION FROM PREIMPLANTATION GENETIC DIAGNOSED EMBRYOS WHICH CARRY DISEASE GENES, AND WE CAN MAKE DIRECT COMPARISONS WITH THOSE, AND WE CAN FIND OUT JUST WHAT NEEDS TO BE DONE. AS LONG AS I HAVE THE BULLY PULPIT, I WOULD SAY THAT CIRM SHOULD FUND THAT TYPE OF RESEARCH.

DR. OLDEN: I MAY HAVE GOTTEN LOST. THESE FOUR GENES THAT ARE TRANSFECTED, ARE THEY NEEDED TO PROPAGATE THE CELLS TO EXPAND THE CELLS IN VITRO, OR ARE THEY NEEDED FOR THE SUBSEQUENT

DIFFERENTIATION PROCESS OR BOTH?

DR. EGGAN: NO. IN FACT, IT IS THOUGHT THAT THEY WERE NEEDED FOR EITHER OF THOSE PROCESSES. AND, IN FACT, IT MAY BE THAT THEIR CONTINUED EXPRESSION WOULD, INDEED, INTERFERE WITH THESE PROCESSES. WHAT THEY ARE NEEDED IS TO GO FROM THAT STARTING ADULT STATE BACK.

DR. OLDEN: DEDIFFERENTIATION.

DR. EGGAN: THAT'S RIGHT. ONCE YOU'RE THERE, YOU WANT THEM TO GO AWAY.

DR. OLDEN: MY QUESTION IS WHY CAN'T YOU KNOCK THEM OUT AFTER YOU GOT WHAT YOU WANT BEFORE YOU USE THEM IN THE TRANSPLANTATION?

DR. EGGAN: THAT'S A GOOD QUESTION. AND THAT'S SOMETHING THAT MANY OF THE REVIEWERS IN SHINYA'S ORIGINAL PAPER ASKED ABOUT. HE GAVE A VERY REASONABLE ANSWER, WHICH I THINK IS TRUE, AND THAT IS IT HAPPENS TO BE THAT WHEN YOU ACTUALLY LOOK AT THE CELLS AT THE END OF THE DAY AND YOU USE HOW MANY OF THESE VIRUSES ACTUALLY GOT IN THERE, WHICH VIRUSES ARE THERE, YOU FIND THAT VIRUSES WHICH ENCODE THESE FOUR DIFFERENT GENES ARE PRESENT IN THE GENOME, AND THEY ARE PRESENT IN VARYING COPY NUMBERS. AND THE COPY NUMBERS VARY DEPENDING ON THE GENE WHICH IS THERE.

AND ROUGHLY SPEAKING, I THINK CURRENT THINKING IS THAT IT'S ABOUT FIVE COPIES OF OCT 4, ABOUT FIVE COPIES OF MYC, SEVERAL COPIES, TWO OR THREE, OF KLF 4, AND ONE OF SOX 2 FOR WHATEVER REASON.

AND IF YOU WERE TO USE ESTABLISHED TECHNOLOGIES FOR RECOMBINING THESE THINGS OUT OF THE GENOME, YOU WOULD -- BECAUSE THERE WOULD BE SO MANY OF THOSE THINGS RANDOMLY ASSORTED THROUGHOUT THE GENOME, YOU WOULD ACTUALLY LEAD TO RECOMBINATION EVENTS AND GENETIC CATASTROPHES BETWEEN CHROMOSOMES, WHICH MAKE IT IMPOSSIBLE TO PERFORM. THE ONLY WAY TO DO THAT IS PROBABLY TO COME UP WITH SOME SYSTEM WHICH COULD BE USED TO, IF YOU NEEDED TO MODIFY THE GENOME, PUT THEM ALL AT THE SAME PLACE FOR SOME LENGTH OF TIME AND THEN TAKE THEM OUT OF AFTERWARDS. I THINK THOSE SORTS THINGS MIGHT COME FROM A BETTER UNDERSTANDING OF THE PROCESS. I DON'T WANT TO BELABOR THE POINT TOO MUCH.

DR. TAYLOR: KEVIN, I APOLOGIZE FOR BELABORING IT. SO ANOTHER ISSUE IS DO YOU THINK THAT THE ONCOGENIC POTENTIAL OF RETROVIRAL DELIVERY SYSTEMS IS GOING TO KIND OF SHUT DOWN EVERYTHING? I CAN IMAGINE IN A DISEASE LIKE

PARKINSON'S, FOR INSTANCE, SOMEBODY WOULD -- SORT OF PARKINSON'S DISEASE OR DISEASES THAT AFFECT SORT OF OLDER INDIVIDUALS, ONE MIGHT ACTUALLY CONSIDER TAKING ON THE RISK OF ULTIMATE ONCOGENIC POTENTIAL AND JUST DECIDING THAT THE NEXT FIVE TO TEN YEARS OF QUALITY OF LIFE MIGHT ACTUALLY BE WORTH TAKING THAT RISK. IS IT THAT A NO-GO TYPE OF --

DR. EGGAN: HERE'S AN AREA WHERE, YOU KNOW, I'M A MOLECULAR CELL BIOLOGIST, SO I CAN TELL YOU ALL ABOUT THE BIOLOGICAL DANGERS, BUT I WOULD BE HESITANT TO READ THE MIND OF THE FDA. AND SO I PROBABLY LOOK TO JOHN FOR SOME THOUGHTS ON THAT. DO YOU HAVE ANY PERSPECTIVE ON THAT? YOUR GUESS. YOUR GUESS IS AS GOOD AS OURS.

CHAIRMAN LO: ARE THERE ANY AUDIENCE QUESTIONS, COMMENTS? KEVIN, THANKS VERY MUCH FOR A VERY CLEAR AND LOGICAL AND VERY HELPFUL PRESENTATION.

WHY DON'T WE TAKE A 15-MINUTE BREAK AND THEN COME BACK, AND I'LL HAVE ALAN TROUNSON ADDRESS US THEN. FIFTEEN MINUTES.

(A RECESS WAS TAKEN.)

CHAIRMAN LO: WHY DON'T WE RECONVENE. ALAN TROUNSON IS GOING TO SPEAK TO US.

I ASKED ALAN TO DO SEVERAL THINGS. FIRST TO SORT OF SHARE WITH US HIS VISION REALLY FOR CIRM. HE COMES WITH DIFFERENT PERSPECTIVES, SOME FRESH IDEAS. I THINK IT'S REALLY IMPORTANT FOR US TO KNOW WHERE HE SEES THE FIELD AND CIRM IN PARTICULAR BEING HEADED. AND HE HAS A PARTICULAR ISSUE OR SEVERAL PARTICULAR ISSUES HE WANTED TO BRING TO OUR ATTENTION AND ASK US TO DELIBERATE ON AND HELP CIRM WITH.

ALAN, WE ARE DELIGHTED TO HAVE YOU, AND THANK YOU FOR COMING AND LOOKING FORWARD TO HEARING WHAT YOU HAVE.

DR. TROUNSON: THANKS, BERNIE. AND THIS IS MY FIRST WORKING GROUP WITH THIS GROUP. SO PLEASE, YOU KNOW, I DON'T HAVE A HISTORY HERE, SO I DON'T GO BACK REMEMBERING EVERYTHING THAT YOU'VE BEEN THROUGH, WHICH IS AN ENORMOUS AMOUNT OF WORK, AND I UNDERSTAND THAT. SO IF I SAY SOMETHING WHICH IS OBVIOUS THAT YOU'VE ALREADY BEEN THROUGH IT, YOU CAN REMIND ME THAT THAT'S ALREADY HAPPENED.

AS I KNOW, THE PEOPLE ON THIS PROGRAM HAVE DONE AN ENORMOUS AMOUNT OF WORK IN THIS AREA. MY INTEREST CLEARLY IS THE MISSION, AND THAT'S WHAT WE'RE ABOUT, DELIVERING TREATMENTS TO THE

PATIENTS. AND THAT'S THE PRIMARY ACTIVITY. IT'S EASY TO UNDERSTAND, AND THAT'S WHERE WE GOT TO GO.

SO I THINK THE TWO TALKS THIS MORNING WERE REALLY TERRIFIC. AND JOHN RAISES THE ISSUE ABOUT THE FACT THAT HOW BURNING IT IS FOR PATIENTS; AND, OF COURSE, THEY'RE WILLING TO TAKE AN INCREDIBLE AMOUNT OF RISK TO GET TO A BETTER OUTCOME. AND EVERYBODY UNDERSTANDS THAT. AND THERE WILL BE MORE, AND I HOPE THERE ACTUALLY ARE, MORE STUDIES LIKE THAT, AND I HOPE THEY'RE ALL REALLY SUCCESSFUL.

BUT BEHIND THAT COMES, YOU KNOW, A LOT OF HEAVY-WEIGHT SCIENCE. AND KEVIN HAS GIVEN YOU A GOOD INTRODUCTION, SO I DON'T NEED TO EMBELLISH WHAT HE SAID IN ANY WAY. IT'S CLEAR AT THE MOMENT THAT INDUCED PLURIPOTENTIAL CELLS ARE NOT THE PANACEA FOR EMBRYONIC STEM CELLS. AND WE'RE ALL IN AGREEMENT IN THE AGENCIES THAT I KNOW AND PROBABLY DISAGREE WITH THE PRESIDENT OVER THAT MATTER AND MEMBERS OF HIS ADMINISTRATION.

SO GIVEN THAT, WE REMAIN INTERESTED IN ALL THESE AREAS. AND WE HAVE RFA'S OUT AT THE PRESENT TIME AND HAVE RECEIVED APPLICATIONS. FOR EXAMPLE, IN THE AREAS OF NEW PLURIPOTENTIAL STEM CELL LINES, THAT IS, NEW METHODS FOR DERIVING

THEM, I THINK THERE WAS 66 LETTERS OF INTEREST -- APPLICATIONS. THERE WAS A LARGE NUMBER OF APPLICATIONS IN THIS AREA. SOME OF THEM DEALT WITH INDUCED PLURIPOTENTIALITY, BUT OTHERS HAVE DEALT WITH OTHER AREAS OF RESEARCH, INCLUDING 10 PERCENT, AROUND 10 PERCENT OR MAYBE A LITTLE MORE OF THOSE WHO WISH TO ACCESS HUMAN EGGS FOR PARTHENOGENETIC EMBRYONIC STEM CELLS FOR NUCLEAR TRANSFER.

SO WE HAVE IN FRONT OF US, IN RECEIPT OF, AND WE HAVE TO TAKE TO A WORKING GROUP GRANT APPLICATIONS THAT INCLUDE ACCESSING HUMAN EGGS. NOW, THIS IS A MATTER THAT IS FACING US RIGHT NOW.

AS I READ IT, THE RECOMMENDATIONS AND THE DECISIONS COMING FROM THIS GROUP IN TERMS OF ACCESSING HUMAN EGGS, THAT IT IS EXTREMELY DIFFICULT TO DO THAT IN THE STATE OF CALIFORNIA WITH CIRM FUNDING. WITHOUT THE FUNDING, YOU COULD CERTAINLY DO IT. WITH CIRM FUNDING, I READ IT TO BE EXTREMELY DIFFICULT TO IMPOSSIBLE.

THE REASONS ARE, AND YOU NEED TO CORRECT ME AT SOME POINT ABOUT THIS OR PROVIDE SOME CLARIFICATION, IS THAT YOU CANNOT ACCESS SPARE EMBRYOS FROM WOMEN/COUPLES UNDERGOING REPRODUCTIVE PROCESSES BECAUSE I THINK THE ARGUMENT WAS PLACED

AT SOME POINT, ERRONEOUSLY IN MY VIEW, IS THAT ABOVE -- YOU KNOW, IF YOU TAKE ANY NUMBER OF EGGS FROM A POOL OF EGGS THAT A PATIENT IS ABLE TO PRODUCE AT ANY ONE TIME, YOU WOULD LIMIT HER REPRODUCTIVE CAPACITY OR THE COUPLE'S CAPACITY TO HAVE A CHILD. I THINK THAT'S AN ERRONEOUS ARGUMENT AND PERHAPS WE CAN TEST THAT OUT.

I HAVE A NUMBER OF REVIEWS JUST BY LOOKING LAST NIGHT AT THE LITERATURE FROM THE U.S., FROM SWEDEN, AND FROM THE UK THAT ALL VERY SOLIDLY SUPPORT THE MAINTENANCE OF HIGH PREGNANCY RATES AND OUTCOMES WITH SINGLE EMBRYOS. NOW, YOU DON'T NEED 10 OR YOU DON'T NEED 15 OR YOU DON'T NEED 20 EGGS TO DERIVE A QUALITY EMBRYO.

MS. LANSING: I HAVE A CORRECTION OR I'M WRONG. THAT'S WHY I WANT TO ASK. THE WAY I UNDERSTOOD IT, AND THAT DOESN'T MEAN I'M RIGHT.

DR. ROWLEY: I CAN'T HEAR A THING.

MS. LANSING: JANET, THE WAY THAT I UNDERSTOOD IT, AND I HOPE I SAY THIS RIGHT, AND MAYBE I'M WRONG, IS THAT IF A WOMAN HAD DECIDED TO DONATE HER EGGS, SHE COULD IF SHE HAD NOT RECEIVED MONEY FOR IT. IF SHE HAD EXTRA EGGS, THAT SHE COULD. AM I WRONG?

MR. SHEEHY: THAT'S ALWAYS BEEN MY

UNDERSTANDING AS LONG AS IT DIDN'T INTERFERE WITH HER REPRODUCTIVE --

MS. LANSING: BUT THAT HER WAS CHOICE.

MR. SHEEHY: YEAH. SO SHE --

MR. LANSING: IN OTHER WORDS, IF SHE HAD 20 AND SHE SAID I'M DONE, HERE ARE TEN, THAT WAS HER CHOICE.

MR. SHEEHY: YEAH. WE FERTILIZED TEN EMBRYOS, WE'RE IMPLANTING ONE OR TWO OR THREE, I'M FREEZING THREE OR FOUR OR FIVE. I DON'T SEE -- I DON'T THINK THAT WE'VE MADE A RULE THAT MAKES THAT IMPOSSIBLE.

MS. LANSING: I ACTUALLY THINK WE SAID SHE COULD AS LONG AS SHE HADN'T RECEIVED MONEY FOR IT.

DR. PETERS: AS LONG AS SHE ACKNOWLEDGES THAT THESE WILL GO FOR RESEARCH.

MS. LANSING: YES.

DR. TROUNSON: WELL, I THINK THERE NEEDS TO BE SOME CLARITY ON THAT BECAUSE I DRILLED GEOFF LOMAX ON THIS, AND THAT WAS NOT THE READOUT THAT I GOT.

MR. KLEIN: I THINK, ALAN, THE CONFUSION IS OVER THE QUESTION OF WHETHER THE WOMAN CAN RECEIVE REIMBURSEMENT FOR PART OF HER IVF COSTS,

AND THAT IS THE ISSUE.

DR. TROUNSON: I THINK THAT IS AN ISSUE. WE COULD SAY, AT LEAST IN THEORY, THAT IF IT WAS PERMISSIBLE THAT A WOMAN WHO'S GOING THROUGH IVF WHO HAD, LET'S SAY, 15 EGGS AND WAS PREPARED TO DONATE FIVE OR WHATEVER NUMBER BECAUSE SHE AND HER CLINICIAN FELT THAT THAT WASN'T GOING TO DECREASE HER CHANCE OF HAVING A CHILD FROM THE PROCEDURE, THEY COULD DONATE THAT WITHOUT ANY INDUCEMENT, JUST REALLY BECAUSE IT'S AVAILABLE TO DO.

WHETHER THAT CAN -- WHETHER THAT ACTUALLY WILL HAPPEN IS CLEARLY ANOTHER THING. AND AT LEAST IN MY DISCUSSIONS WITH THE CLINICIANS THAT I KNOW THAT IT'S PROBABLY PRETTY UNLIKELY TO GET MANY EGGS. YOU MAY GET ON SOME OCCASIONS SOME EGGS, AND CLEARLY THERE ARE OTHER PEOPLE IN THIS ROOM WHO HAVE BEEN IN THIS BUSINESS. SO IT IS POSSIBLE, IF WE GET THAT CLARIFIED, THAT THEY COULD DONATE IF THEY AGREED AND THEIR CLINICIAN AGREED THAT IT WAS NOT GOING TO BE AN IMPEDIMENT TO THEIR OUTCOME OF THEIR TREATMENT.

I THINK WHAT HAPPENED IN THE UK, FOR EXAMPLE, AND IT'S ONE PLACE WHERE I KNOW THAT THAT WAS TESTED OUT, WAS THAT THEY DIDN'T GET MANY OR ANY EGGS. SO THAT'S WHY THEY INTRODUCED THE EGG

SHARING PROCEDURES WHERE AT LEAST PART OF THEIR TREATMENT WAS BEING PAID FOR BY WHATEVER AGENCY WAS APPROPRIATE IN ORDER TO BE ABLE TO ACCESS SOME OF THEIR EGGS. SO THAT, IN FACT, THERE IS SOME INDUCEMENT TO DO THAT BECAUSE IF YOU TURN IT OVER TO THIS COUNTRY, THE COSTS OF IVF ARE VERY CONSIDERABLE HERE. AND SO IF YOU PREPARED -- IF YOU ARE PREPARED TO DO THAT, THEN YOU MAYBE GET YOUR TREATMENT AT A CHEAPER RATE.

SO LET'S FOLLOW THIS THROUGH. THE OTHER SCENARIO WHERE YOU COULD ACCESS OOCYTES WOULD BE FROM PATIENTS WHO ARE WILLING TO DONATE THEM DIRECTLY FOR RESEARCH, SO THEY WEREN'T PART OF ANY REPRODUCTIVE PROCEDURE. SO THIS WOULD BE PEOPLE WHO ARE DRIVEN BECAUSE THEY MAY HAVE RELATIVES WHO HAVE DISORDERS OR DISEASES WHICH THEY THINK THAT, IF THEY PROVIDED EGGS, COULD ASSIST IN THE RESEARCH. AND I THINK KEVIN EGGAN, AMONGST MANY OTHER PEOPLE, HAVE SHOWN THAT THIS BASICALLY DOESN'T WORK BECAUSE THERE'S A CERTAIN -- THESE PROCEDURES ARE DEMANDING, THEY ENTAIL SOME RISK BECAUSE YOU'RE GETTING FERTILITY DRUGS, ETC., AND WOMEN ARE NOT PREPARED TO GO THROUGH THOSE PROCEDURES WITHOUT SOME FORM OF COMPENSATION.

NOW, THE COMPENSATION MAY BE IN SOME WAY

THE TRAM TICKET OR THE TAXI RIDE THAT GETS THEM TO THE HOSPITAL AND SOME PAYMENT FOR TIME, BUT THERE IS A CERTAIN MINIMUM AND IN MANY WAYS THE CONSTRUCTION OF THE COMPENSATION FOR THEIR TIME BECOMES, IN FACT, THE COMPENSATION FOR THE PROCEDURE.

NOW, SO I THINK IT'S ONLY IN -- IT'S GOING TO BE AN EXTREMELY LIMITED OPPORTUNITY BECAUSE THAT LAST SCENARIO, I UNDERSTAND, IS NOT LEGALLY POSSIBLE UNDER THE RULES THAT HAVE BEEN CREATED FOR --

MR. KLEIN: ALAN, ACTUALLY UNDER THE EXISTING RULES -- AND MAYBE, BERNIE LO, YOU SHOULD ADDRESS THESE RULES OR GEOFF SHOULD.

MR. SHEEHY: I JUST WANT TO SAY WE HAVE A STATE LAW, 1260, SB 1260, THAT HAS BEEN PASSED BY THE LEGISLATURE AND SIGNED BY THE GOVERNOR THAT EXPRESSLY PROHIBITS COMPENSATION FOR EGG DONATION. YOU KNOW, WHETHER IT'S A DISCOUNT ON IVF OR WHAT HAVE YOU, A DISCOUNT ON IVF IS VALUABLE CONSIDERATION THAT IN MY MIND PRESENTS COMPENSATION.

NOTWITHSTANDING THE LEGAL RAMIFICATIONS, I THINK WE WOULD NEED TO HAVE A FAIRLY LENGTHY DISCUSSION WITHIN THIS WORKING GROUP AND HEAR FROM

OUR ETHICISTS AS TO WHETHER OR NOT THAT MIGHT CREATE AN UNDUE INDUCEMENT TO -- THAT TYPE OF COMPENSATION MIGHT BE AN UNDUE INDUCEMENT AND CROSS SOME ETHICAL BRIGHT LINES.

I CAN IMAGINE SCENARIOS WHERE WOMEN ARE ENCOURAGED TO PUT THEMSELVES AT GREATER RISK FOR THE HYPEROVULATION SYNDROME BECAUSE THEY TAKE MORE DRUGS TO PRODUCE MORE EGGS BECAUSE THEY'RE GOING TO GET A CHEAPER IVF PROCEDURE AND --

DR. TROUNSON: CAN I ADDRESS THAT BECAUSE I FIND IN THE SENSE THAT I THINK YOU NEED TO BE VERY CAREFUL WHAT YOU SAY HERE BECAUSE THE CLINICIANS WHO WORK WITH THESE PATIENTS WORK WITH THOSE PATIENTS ON THE BASIS THAT THEY NEED TO GET A SAFE AND EFFECTIVE OUTCOME FOR THEIR PATIENTS. SO I THINK IF YOU HAVE THAT IN MIND, YOU NEED TO BE CAREFUL THAT YOU'RE NOT SAYING SOMETHING ABOUT THE REPRODUCTIVE INDUSTRY THAT IS, IN FACT, NOT TRUE. BECAUSE I ACTUALLY DON'T KNOW OF ANY CASE WHERE A CLINICIAN WOULD GIVE A PATIENT MORE DRUG TREATMENT THAN WOULD BE SAFE OR EFFECTIVE IN GETTING THE OUTCOME.

SO I THINK WHILE IT NEEDS TO BE PUT IN A VERY CAREFUL WAY THOSE THINGS BECAUSE I THINK THE CLINICIANS IN THIS BUSINESS ARE VERY CAREFUL AND

THEY WORK CLOSELY WITH THEIR PATIENTS, AND I THINK WE NEED TO BE VERY CAREFUL THAT WE DON'T GET BETWEEN THEM, THE CLINICIANS AND THEIR PATIENTS, IN PROVIDING A PROPER TREATMENT AND OUTCOME FOR THOSE PEOPLE.

MR. SHEEHY: THERE ARE BAD ACTORS IN EVERY FIELD. WE HAVE THE SHAW EXAMPLE OF A DOCTOR, IVF CLINICIAN, WHO VIOLATED ETHICAL STANDARDS. YOU KNOW, IN GENERAL, I THINK MOST PEOPLE DO ACT TO THE BENEFIT OF THEIR PATIENTS, BUT THERE ARE EXCEPTIONS TO THAT RULE. I JUST HAVE A PROBLEM --

MR. KLEIN: JEFF, FIRST OF ALL, YOU RAISED A FACTUAL ISSUE, AND LET'S TRY AND DEAL WITH THE FACTUAL ISSUE BECAUSE I THINK, AND THIS COMMITTEE SHOULD GO BACK AND DO THE RESEARCH, THAT WHEN 1260 PASSED, IT WAS SPECIFICALLY NOT TO APPLY TO OUR AGENCY. BUT NEVERTHELESS, WE HAVE A POLICY ON THE BOOKS THAT I'D LIKE GEOFF -- I'D ASK GEOFF OR BERNIE LO TO CLARIFY, THAT I BELIEVE THAT POLICY STATES THAT PEOPLE CAN GET REIMBURSED FOR THEIR EXPENSES, REIMBURSED FOR THEIR TIME. THAT'S NOT CONSIDERED COMPENSATION. THAT'S CONSIDERED A REIMBURSEMENT. IS THAT A CORRECT STATEMENT?

MR. SHEEHY: WE HAD A VERY LENGTHY

DISCUSSION OVER WHAT WOULD BE APPROPRIATE COMPENSATION.

CHAIRMAN LO: ALAN, MAY WE INTERRUPT YOUR PRESENTATION AND TRY AND CLARIFY?

MS. LANSING: BECAUSE IT WILL HELP YOU BECAUSE THERE'S SO MUCH SINCE WE TALKED.

DR. TROUNSON: BECAUSE IT'S VERY -- WHAT I NEED TO INSTRUCT THE INSTITUTE IS REALLY WHAT IS ALLOWABLE. AND SO WHEN IT COMES TO ACCESSING THIS IMPORTANT MATERIAL, THAT WE EITHER SAY, LOOK, SORRY, RESEARCHERS, YOU CAN'T DO THAT, OR, YES, IT'S ALLOWABLE UNDER THESE CONDITIONS.

MS. LANSING: ALAN, YOU NEED CLARITY. TO BE HONEST WITH YOU, WHEN WE TALKED ON THE PHONE, I DIDN'T HAVE THE CLARITY AND STILL DON'T. LET'S GET IT.

CHAIRMAN LO: LET ME FIRST ASK GEOFF AND ALTA TO CLARIFY WHAT THE CURRENT MES REGULATIONS SAY, AND THEN ALSO TO TRY AND ASK FOR SOME CLARIFICATION ON SB 1260. GEOFF, YOU WANT TO GO FIRST AND THEN ALTA.

DR. LOMAX: SURE. THANK YOU, BERNIE. I THINK ONE OF THE RESOURCES EVERYONE HAS AVAILABLE IS THE REGULATIONS, WHICH ARE THE YELLOW COPY. THERE'S A FEW WHITE VERSIONS FLOATING AROUND. ON

PAGE 1, SECTION 100020, I WOULD REFER YOU TO THE DEFINITION OF PERMISSIBLE EXPENSE, WHICH IS 100020(H), AND I WILL READ THAT FOR THE RECORD. PERMISSIBLE EXPENSES MEANS NECESSARY AND REASONABLE COSTS DIRECTLY INCURRED AS A RESULT OF DONATION OR PARTICIPATION IN RESEARCH ACTIVITIES. PERMISSIBLE EXPENSES MAY INCLUDE, BUT ARE NOT LIMITED TO COSTS ASSOCIATED WITH TRAVEL, HOUSING, CHILDCARE, MEDICAL CARE, HEALTH INSURANCE, AND ACTUAL LOST WAGES. SO THAT'S THE OPERATIONAL SORT OF LISTING OF COSTS THAT CAN BE PAID FOR OR COMPENSATED FOR.

IF YOU THEN TURN TO SECTION 100095, WHICH IS, I THINK, ANOTHER. IT'S ON PAGE 6 OF THE YELLOW DOCUMENT, LEFT-HAND SIDE. THERE'S A SET OF CONDITIONS WHICH DESCRIBE FUNDED RESEARCH INVOLVING PROCUREMENT OF OOCYTES. AND THERE'S AN INITIAL A AND B, INCLUDES A SET OF -- B IS WHERE THE LANGUAGE REGARDING OPTIMAL REPRODUCTIVE SUCCESS APPEARS. THE PROCUREMENT AND DISPOSITION FOR RESEARCH PURPOSES OF OOCYTES INITIALLY PROVIDED FOR REPRODUCTIVE USE, EITHER FOR USE BY THE DONOR OR ANOTHER WOMAN, SHALL NOT KNOWINGLY COMPROMISE THE OPTIMAL REPRODUCTIVE SUCCESS OF THE WOMAN IN INFERTILITY TREATMENT.

SO, AGAIN, I THINK WHAT THE WORKING GROUP IN THE COMMENTS PREVIOUSLY ACCURATELY REFLECTED WAS THAT IF THERE WERE SURPLUS EGGS AND THE WOMAN DETERMINED THEY WERE NOT REQUIRED FOR REPRODUCTIVE SUCCESS, THEY COULD BE DONATED TO RESEARCH. IT GOES ON IN POINT 2 TO SAY THE WOMAN IN INFERTILITY TREATMENT MAKES A DETERMINATION SHE DOES NOT WANT OR NEED THE OOCYTES FOR HER OWN REPRODUCTIVE SUCCESS. THOSE TWO POINTS OF THE REGULATIONS, FIRST, DESCRIBE WHAT ARE ALLOWABLE IN TERMS OF PAYMENT. AND THE SECTIONS I REFERRED IN 95 DESCRIBE THE CONDITIONS FOR WHICH THE OOCYTES MAY BE DONATED WITH REGARD TO KIND OF THE REPRODUCTIVE ENTERPRISE, IF YOU WILL. IS THAT HELPFUL?

MS. CHARO: I'M SORRY. THAT WAS MY UNDERSTANDING AS WELL. A WOMAN CAN BE REIMBURSED FOR HER OUT-OF-POCKET COSTS, BUT CANNOT BE GIVEN ANY FUNDS ABOVE AND BEYOND THAT. AND THAT EGG SHARING WAS FINE SO LONG AS IT DID NOT AFFECT HOW THE PROCEDURE WAS DONE FOR HER OWN REPRODUCTIVE PURPOSES.

SO THE QUESTION, BERNIE, IS WHETHER IT'S APPROPRIATE NOW, OR SHOULD I WAIT TILL THE END TO TALK A LITTLE BIT MORE GENERALLY ABOUT WHAT ALAN

IS PRESENTING HERE?

CHAIRMAN LO: WHY DON'T WE FIRST LET ALAN FINISH HIS PRESENTATION.

DR. KIESSLING: THIS IS SOMETHING THAT PROBABLY, ALAN, YOU'RE NOT FAMILIAR WITH BECAUSE ONE OF THE REASONS, ONE OF THE BASES FOR THESE GUIDELINES THAT WE CAME UP WITH WAS WE HAD A VERY HEATED DEBATE. AND ALTA REMINDED US THAT OUR COUNTRY HAS VERY WELL-ESTABLISHED STANDARDS FOR KIDNEY DONATION. SO SHE LOOKED UP THE GUIDELINES FOR KIDNEY DONATION FOR WHICH YOU ALSO CANNOT BE COMPENSATED, BUT YOU CAN BE REIMBURSED FOR LOST WAGES.

SO WHAT WE PUT IN OUR GUIDELINES ESSENTIALLY MIMICKED WHAT OUR NATIONAL STANDARD IS FOR DONATING KIDNEYS.

DR. TROUNSON: WELL, I THINK THAT'S PERFECTLY REASONABLE. WHAT HAPPENED IS IT IS A VERY DIFFERENT SITUATION BECAUSE IF YOU'RE DONATING A KIDNEY, IT'S USUALLY FOR SURVIVAL OF A FAMILY MEMBER OR SOMEBODY YOU KNOW. IT'S ABOUT SURVIVAL. THIS IS ABOUT RESEARCH. AND SO THE BENEFITS SPECIFICALLY CAN'T NECESSARILY BE GUARANTEED FOR WHATEVER YOU ARE GOING TO DO. IT'S GOING TO GO TO RESEARCH, AND IT MAY NOT HAVE AN

IMPACT.

DR. KIESSLING: THE POINT WAS THAT YOU CAN REIMBURSE THESE PEOPLE FOR THEIR LOST WAGES, AND THAT WAS WHAT WE WERE REALLY TRYING TO DO.

DR. TROUNSON: OKAY.

MS. CHARO: I WON'T GO INTO THE LONGER SET OF CONCERNS I'VE GOT ABOUT HOW WE DISCUSS THIS ISSUE, BUT IT MAY BE WORTH NOTING THAT, AT LEAST TO MY KNOWLEDGE, AND I'M HAPPY TO BE CORRECTED, THE EFFORTS TO RECRUIT WOMEN HAVE NOT NECESSARILY EXPLORED ALL OF THE MOST PROMISING AVENUES. I KNOW THAT HARVARD ADVERTISED WIDELY, AND I KNOW THAT AT LEAST KEVIN INFORMALLY TURNED ME DOWN WHEN I VOLUNTEERED, TELLING ME I WAS WAY TOO OLD. BUT TO MY KNOWLEDGE, THE PATIENT DISEASE GROUPS HAVE NOT YET EVER VOLUNTEERED TO TAKE ON THE TASK OF SURVEYING THEIR OWN MEMBERS TO SEE WHETHER OR NOT THOSE MEMBERS OR THEIR OWN FAMILIES WOULD WANT TO BE CONTACTED ABOUT BEING POTENTIAL DONORS, WHICH IS THE WAY TO CATCH PEOPLE WHO COME CLOSER TO WHAT YOU WERE SUGGESTING IN THE KIDNEY CONTEXT. IT COMES CLOSER TO CATCHING PEOPLE FOR WHOM IT IS MORE PERSONAL AND MORE ASSOCIATED WITH SOMETHING THAT IS LIFESAVING OR SERIOUSLY HEALTH PROMOTING THAN THE TRUE ANONYMOUS DONOR TO ANONYMOUS

RESEARCH. SO WE HAVEN'T COMPLETELY EXPLORED ALL THE OPTIONS FOR THIS VERY ALTRUISTIC MODEL FOR DONATION.

DR. TROUNSON: THAT MAY WELL BE TRUE, BUT THOSE PEOPLE THROUGH PATIENT ADVOCATES HERE AND OTHER PLACES ARE VERY WELL INFORMED OF WHAT'S POSSIBLE, BUT THEY'RE NOT COMING FORWARD IN ANY WAY TO WANT TO DO THAT. SO WHETHER THEY DO OR THEY DON'T HASN'T POSSIBLY BEEN ABSOLUTELY TESTED OUT.

I THINK WHEN YOU SAY YOU'RE GOING TO BE COMPENSATED FOR YOUR LOSS OF SALARIES, THAT IS, IN FACT, NO COMPENSATION FOR THE PROCEDURE. SO ALL YOU'RE DOING IS PAYING FOR YOUR TIME OFF WORK, WHICH YOU WOULD HAVE GOT ANYWAY, RIGHT? SO ESSENTIALLY THERE'S NO --

MS. CHARO: IT'S A NO LOSS, NO GAIN MODEL.

DR. TROUNSON: SO THERE'S NO REASON WHY SOMEONE WOULD WANT TO DO IT ABOVE AND BEYOND THAT THEY FELT IT WAS IMPORTANT FOR WHATEVER REASON. SO WHAT WE'RE SAYING, I THINK, IS NOT DIFFERENT TO THAT. IN FACT, YOU KNOW, AND I THINK IN MY OWN VIEW, AND I DON'T WANT TO COLOR THIS DISCUSSION TOO MUCH BECAUSE ALL I WANT TO DO IS BE ABLE TO

TAKE WHATEVER THE DECISION IS AND MAKE SURE IN MANAGEMENT WE'RE GOING TO CLARIFY WHAT WE CAN DO FOR THESE PROJECTS. SO THAT'S MY ONLY REALLY IMPORTANT THING I WANT TO SAY.

BUT THE SENSE OF, YOU KNOW, IF YOU'RE GOING THROUGH A PROCEDURE, AT LEAST IN MY COUNTRY IF THERE WAS AN INTERNAL CATHETERIZATION, YOU WOULD ACTUALLY BE PAID SOME COMPENSATION FOR THAT. THERE WAS A PAIN AND SUFFERING ASSOCIATED WITH THAT AND A CERTAIN RISK OF INFECTION. SO YOU ACTUALLY DO GET PAID SOME COMPENSATION FOR THAT. I WOULD HAVE THOUGHT THAT MIGHT BE ACTUALLY CLOSER TO THE DONATION OF EGGS.

NOW, WHETHER THAT'S RIGHT OR WRONG IN THIS SITUATION IN THIS STATE IS SOMETHING THAT YOU NEED TO DECIDE.

CHAIRMAN LO: OBVIOUSLY WE'RE GOING TO HAVE A VERY IMPORTANT DISCUSSION. I WANT TO GIVE ALAN A CHANCE TO MAKE HIS PRESENTATION. WE'LL HAVE LOTS OF TIME. IN FACT, THAT'S WHAT A LOT OF OUR AFTERNOON IS GOING TO BE IS SORT OF STARTING TO THINK ABOUT THESE ISSUES. ALAN.

DR. TROUNSON: SO COME BACK TO WHAT'S IMPORTANT ABOUT THE RESEARCH, AND THERE'S AN UPSIDE AND THERE'S A DOWNSIDE. LET'S TAKE THE

DOWNSIDE. THE EVIDENCE AT THE PRESENT TIME FOR MAKING AN EMBRYONIC STEM CELL LINE FROM NUCLEAR TRANSFER IN ANIMALS, INCLUDING MONKEYS, IS THAT IT'S GOING TO TAKE SOMETHING LIKE 100, 150, PERHAPS EVEN 200 EGGS IN EACH CASE TO MAKE AN EMBRYONIC STEM CELL LINE. IT IS CERTAINLY NOT ARGUABLY LESS THAN A HUNDRED AT THE PRESENT TIME. THE ANIMAL EXPERIMENTS WOULD INDICATE THAT YOU ARE PROBABLY GOING TO NEED AROUND 100 EGGS TO MAKE AN EMBRYONIC STEM CELL LINE.

NOW, WHAT THAT MIGHT SAY, BECAUSE ACCESSING THOSE NUMBER OF EGGS IS NO TRIVIAL MATTER, NO MATTER WHAT THE OPPORTUNITIES ARE. IN THAT CIRCUMSTANCE THE DEMAND FOR THE OOCYTES MAY BE WAY BEYOND WHAT WE CAN POSSIBLY DELIVER IN AN OUTCOME. AND IT MAY TAKE US FIVE YEARS TO DO THAT. IF WE GAVE A THREE-YEAR GRANT, THAT WOULD BE NONSENSE BECAUSE THE CHANCE OF DERIVING A CELL LINE MIGHT BE EXTREMELY LOW. I THINK IT'S VERY IMPORTANT TO BE ABLE TO DERIVE DISEASE-SPECIFIC STEM CELL LINES, PARTICULARLY FOR COMPLEX DISEASES, WHICH WE STILL DON'T REALLY UNDERSTAND THAT WELL BECAUSE YOU TAKE THE CELLS BACK TO A NAIVE STATE. AND THEN IF YOU CAN ACTUALLY THEN SEE OR DEMONSTRATE THE PHENOTYPE OCCURRING IN THE

LABORATORY, YOU HAVE A VERY POWERFUL MODEL TO INTERROGATE THE ONSET OF THE DISEASE.

I THINK ARGUABLY THERE'S A GOOD CASE FOR DOING IT, BUT IT'S EXTREMELY DIFFICULT TO COMPREHEND HOW YOU ARE GOING TO OBTAIN THAT MANY EGGS TO DO THIS. PERHAPS EXPERIMENTS IN ANIMALS WILL SHOW THAT IT CAN GET MUCH MORE EFFICIENT, BUT THERE HASN'T BEEN A REAL CHANGE IN EFFICIENCY, AS I JUDGE IT, AT THE PRESENT TIME.

THE UPSIDE FOR EGG DONATION IS THAT IT SEEMS THAT IT'S A LOT MORE EFFICIENT TO DERIVE PARTHENOGENETIC EMBRYONIC STEM CELLS AND THAT YOU DON'T NEED HUNDREDS OF EGGS TO DO THAT. YOU PROBABLY NEED 10, 10 EGGS TO DERIVE AN EMBRYONIC STEM CELL LINE, PERHAPS EVEN LESS. AND A NUMBER OF GROUPS AROUND THE WORLD ARE DERIVING THESE CELL LINES, AND THESE CELL LINES WILL BE TRANSPLANT COMPATIBLE FOR THE WOMEN WHO ACTUALLY DONATE THEM. SO YOU CAN ACTUALLY, IF YOU THINK ABOUT IT, YOU COULD CONSTRUCT A BANK OF CELLS WHICH WOULD COVER A NUMBER OF SCENARIOS FOR TRANSPLANTATION BY THIS METHOD BECAUSE YOU COULD HAVE EMBRYONIC STEM CELLS THAT ARE A VIRTUAL MATCH ACROSS THE SPACE, AT LEAST MATCHING A PROPORTION OF THE COMMUNITY.

I THINK THERE'S SOME INTEREST IN THE

GRANTS THAT WE'RE RECEIVING. A MORE COMPLEX SCENARIO, BUT ONE WHICH I TAKE FROM SOME UNPUBLISHED DATA THAT I'VE BEEN MADE AWARE OF, IS THAT YOU CAN ALSO DERIVE WHAT THEY CALL ANDROGENETIC ES CELL LINES. THESE ARE WHERE YOU ACTUALLY REPLACE THE NUCLEUS WITH A MALE COMPONENT SO THAT YOU CAN GET A MALE-DERIVED EMBRYONIC STEM CELL LINE.

INTERESTING, THESE CELL LINES APPEAR TO HAVE, AGAIN, THE PROPERTIES OF EMBRYONIC STEM CELL LINES, ALTHOUGH I THINK AT THIS STAGE THEY HAVEN'T BEEN ADEQUATELY SCREENED AND INTERROGATED FOR THEIR REAL VALUE IN DETERMINING HOW WELL THEY FUNCTION WHEN THEY'RE TRANSPLANTED INTO ANIMAL MODELS AS YET, BUT THE WORLD IS ALIVE WITH THESE AREAS OF RESEARCH. AND I THINK WE HAVE GOT SOME OF THOSE KIND OF APPLICATIONS IN THE PORTFOLIO.

SO IT THEN BECOMES, ON ONE HAND, THE NUCLEAR TRANSFER MAYBE IS NOT SUCH A DRIVER BECAUSE IT'S GOING TO BE SO HARD TO GET THE NUMBER OF EGGS WE REQUIRE. AND ON THE OTHER HAND, IN THE AREA OF PARTHENOGENESIS AND ANDROGENETIC STEM CELL LINES, THERE MIGHT BE A MUCH MORE PRACTICAL REASON TO TRY AND ACCESS THOSE NUMBER OF EGGS.

SO ON ONE SIDE WE'VE GOT INTERESTING

SCIENTIFIC OPPORTUNITIES, AND ON THE OTHER SIDE WE NEED TO BE EITHER PRACTICAL AND ENABLING TO DO THIS, OR WE NEED TO BE ABLE TO SAY, LOOK, YOU KNOW, WE'RE UNCOMFORTABLE ABOUT IT, AND THIS IS WHERE THE ETHICAL LINE IS. SO LET'S NOT DO THOSE STUDIES. LET'S PUT THEM OFF TO SOME OTHER TIME OR LET THEM BE DONE SOMEWHERE ELSE. THEY MAY WELL BE DONE SOMEWHERE ELSE.

SO I THINK THAT'S WHAT THE ISSUE IS. I HOPE I'VE EXPLAINED AT LEAST THE PRIMARY DRIVERS OF THE RESEARCH. THAT'S WHY WE'VE COME BECAUSE WE HAVE THESE APPLICATIONS SITTING IN OUR PORTFOLIO WHICH WE'RE QUESTIONING ABOUT HOW DO WE MOVE FORWARD ON THIS, OR DO WE SORT OF TAKE THEM OFF THE TABLE AND LET THE OTHER ONES PROCEED. I THINK IT'S IMPORTANT FOR YOU TO UNDERSTAND THAT IT'S REAL-TIME NOW. WE HAVE TO ACTUALLY KNOW EXACTLY WHAT IS APPROPRIATE TO DO.

DR. PETERS: I'D LIKE TO OFFER A COMMENT AND A QUESTION.

CHAIRMAN LO: BEFORE YOU DO THAT, COULD I JUST ASK ALAN A CLARIFICATION QUESTION. ALAN, JUST TO BE CLEAR, YOU'RE ASKING THAT WE, THE SWG, CONSIDER OR RECONSIDER, I GUESS, THE POSSIBILITY OF ALLOWING CIRM TO FUND DERIVATION OF STEM CELL

LINES USING FRESH OOCYTES, TO OBTAIN THOSE FRESH OOCYTES THROUGH A SHARING ARRANGEMENT WHEREBY A WOMAN IN IVF WOULD SHARE SOME OF HER OOCYTES THAT SHE DOES NOT NEED FOR HER REPRODUCTIVE GOALS WITH RESEARCHERS, BUT WHICH IS ALREADY PERMITTED, AS WE CLARIFIED, BUT THE CHANGE YOU'RE ASKING US TO CONSIDER IS TO ALLOW SOME COMPENSATION FOR THE WOMAN'S IVF COSTS FOR THOSE OOCYTES DONATED TO RESEARCH.

DR. TROUNSON: BERNIE, I'M ASKING FOR CLARIFICATION. I THINK, YOU KNOW, WHAT YOU DECIDE, I THINK, IS YOUR DECISION. I THINK WHATEVER IT NEEDS TO BE, IF YOU DECIDE THAT EGGS ARE AVAILABLE, YOU NEED TO DECIDE WHETHER IT'S PRACTICAL OR NOT. THAT'S THE PRIMARY PROBLEM. IF IT'S IMPRACTICAL, AS KEVIN KNOWS, IT DOESN'T WORK. IT DOESN'T HAPPEN. SO WE SPEND A LOT OF SCIENTISTS' AND PEOPLE'S ENERGY ON SOMETHING THAT CAN'T BE DONE. THAT'S NOT A VERY GOOD RETURN FOR WHAT WE WANT TO DO FOR THE MISSION.

MR. KLEIN: I THINK, BERNIE, YOU MEAN HE'S SPECIFICALLY ADDRESSING REIMBURSEMENT OF A PART OF THOSE COSTS, NOT COMPENSATION. IT'S REIMBURSING A PORTION OF THOSE COSTS.

CHAIRMAN LO: MY UNDERSTANDING IS THAT'S

ONE OF THE -- THERE'S AN EMBEDDED SET OF ISSUES, ONE OF WHICH WOULD BE SPECIFICALLY, GIVEN THE LACK OF RESPONSE TO DATE FROM ASKING WOMEN TO DONATE WITHOUT ANY COMPENSATION LIKE THAT, TO RECONSIDER THE IDEA OF ALLOWING PARTIAL COMPENSATION OF IVF COSTS.

MS. LANSING: WELL, I'M NOW A LITTLE CONFUSED. SO I WANT TO SAY IT BACK AS A PATIENT ADVOCATE TO MAKE SURE I UNDERSTAND IT. YOU WANT CLARIFICATION, WHICH WE THOUGHT WE HAD, THAT IF A PATIENT IS UNDERGOING REPRODUCTIVE THERAPY AND DECIDES TO DONATE SOME OF HER EGGS, WE THINK AS A GROUP THAT SHE HAS THE RIGHT TO DO SO. IF THAT'S NOT CLEAR IN OUR YELLOW SHEET, WE WANT TO MAKE THAT CLEAR.

WHAT WE ALSO AGREED ON IN OUR GROUP, I JUST WANT TO BE SURE, IS THAT SHE COULD NOT BE PAID FOR THIS. WHAT I THINK YOU'RE SAYING, BUT I WANT TO QUESTION IT FOR A SECOND, IS THAT IF YOU DO THAT, WOMEN WON'T GO. AND I WILL SAY THAT IT IS QUITE DIFFERENT TO BE ASKED TO DONATE YOUR EGGS FOR SCIENTIFIC RESEARCH AND NOT BE PAID AS TO SAY THAT YOU WANT A CHILD AND YOU ARE GOING THROUGH REPRODUCTIVE THERAPY TO HAVE THAT CHILD AND YOU HAVE EXCESS EGGS.

I WOULD LIKE TO SAY THAT I THINK VERY FEW, IF ANY, WOMEN WHO WANT A CHILD ARE LOOKING TO BE PAID TO GO THROUGH REPRODUCTIVE THERAPY. SO IT'S TWO DISTINCT ISSUES.

NOW, IF I WANT TO GO TO THE THIRD ISSUE, WHICH I THINK YOU'RE ALSO PUTTING ON THE TABLE, IS FORGET REPRODUCTIVE THERAPY. LET'S GO INTO DONATING YOUR EGGS FOR RESEARCH. THEN I THINK WHAT YOU'RE BOTH SAYING IS YOU DO NOT BELIEVE THAT WOMEN WILL DO THAT UNLESS THEY'RE PAID; IS THAT CORRECT?

MR. KLEIN: FROM A LEGAL POINT OF VIEW, I'M VERY CONCERNED WITH THE USE OF WORDS HERE. I DON'T KNOW ANYONE THAT'S SUGGESTING YOU MAKE A $10,000 PAYMENT TO SOMEBODY. IF SOMEBODY HAS REAL COST, AND THEY CAN DOCUMENT THOSE COSTS, AND THEY CAN GET REIMBURSED FOR PART OF THOSE COSTS. WHAT'S BEING ADDRESSED HERE IS REIMBURSEMENT FOR PART OF THE COST, NOT A $20,000 PAYMENT TO SOMEONE.

MS. LANSING: WE HAVE THAT. WE ALREADY HAVE THAT.

MR. SHEEHY: THAT REIMBURSEMENT IS COMPENSATION. JUST BECAUSE YOU CALL IT REIMBURSEMENT, IT'S COMPENSATION.

I ALSO -- CAN I JUST -- I HAVE A PROBLEM BECAUSE I HAVEN'T SEEN ANY EVIDENCE. WE HAVE PEOPLE WHO HAVE SUBMITTED APPLICATIONS KNOWING THE RULES UNDER WHICH WE'RE OPERATING. AND WE LEFT A LOT OF THESE RESPONSIBILITIES TO THE INSTITUTIONS TO FIGURE OUT HOW TO IMPLEMENT THESE RULES. IF THEY DID NOT THINK THAT THEY COULD GET THE EGGS, THEY SHOULD NOT HAVE SUBMITTED THE APPLICATIONS.

THEY HAVE SUBMITTED APPLICATIONS, SO THEY MUST BELIEVE THAT THEY CAN GET THE EGGS. NOW, I AGREE THAT THE HARVARD CASE IS IN FRONT OF US, BUT FOR US TO GO AND UNWIND THIS BEFORE WE'VE HAD EVIDENCE OF FAILURE, IT SEEMS TO ME, YOU KNOW, TO BE AN INAPPROPRIATE PROCESS ON THE FACE OF IT.

CHAIRMAN LO: ALAN, YOU'VE TRIGGERED DISCUSSION. IS THAT OKAY?

MS. LANSING: CAN WE JUST HAVE CLARITY FOR A SECOND? GEOFF, JUST GET CLARITY.

DR. LOMAX: SO THE QUESTION THAT SHERRY HAD ASKED WAS IT'S THE QUESTION OF WITHIN PERMISSIBLE EXPENSES, EXPENSES ASSOCIATED WITH FERTILITY TREATMENT ARE NOT PERMISSIBLE EXPENSES. SO THE IDEA OF SORT OF UNDERWRITING THE COST OF FERTILITY TREATMENT ARE NOT IN THE DEFINITION OF PERMISSIBLE EXPENSES, NOR WERE THEY CONTEMPLATED

BY THE WORKING GROUP WHEN THIS DEFINITION WAS CRAFTED.

IT'S ALL EXPENSES ASSOCIATED, ALL OUT-OF-POCKET EXPENSES ASSOCIATED WITH A RESEARCH ONLY DONATION WERE INTENDED TO BE CAPTURED UNDER THIS DEFINITION OF PERMISSIBLE EXPENSES; IS THAT CORRECT?

MS. LANSING: IF YOU MISSED WORK OR YOU HAD TO TAKE A CAB OR WHATEVER IT IS.

DR. TROUNSON: I WOULD SAY TO SHERRY THAT THE ONLY THING I THINK I DISAGREE WITH WHAT YOU SAID IS THAT THERE ARE PATIENTS WHO WILL NOT COME THROUGH THE IVF, YOU KNOW, AT A FREQUENT RATE OR AT ALL BECAUSE THE COSTS ARE TOO HIGH. IF THERE WAS A SHARED COST, THAT THEY WOULD. AND THAT'S THE EXPERIENCE IN THE UK. IN AUSTRALIA IT'S NOT BECAUSE THE GOVERNMENT PAYS FOR ALL TREATMENT, SO IT'S NOT AN ISSUE. BUT HERE AND THE UK'S EXPERIENCE WAS THEY COULDN'T GET A PATIENT TO DONATE EGGS FROM LEFT-OVER IVF PROCEDURES IN ANY AMOUNT, VERY, VERY FEW EGGS, UNLESS THEY DID THIS SHARING PROCEDURE. SO I'M NOT SUGGESTING THAT'S THE SAME HERE, BUT ONE OF THE DRIVERS IS THAT THE PROCEDURE IS EXPENSIVE.

DR. PETERS: IF WE'RE DONE WITH THE

COMPENSATION, I'D LIKE TO GO ON TO THE NUCLEAR TRANSFER.

DR. EGGAN: WE'RE NOT REMOTELY DONE.

CHAIRMAN LO: THIS IS GOING TO BE A VERY IMPORTANT AND COMPLEX DISCUSSION. LET'S TRY AND STAY ON THE COMPENSATION, TED, AND MAKE SURE WE COME TO THE SCNT. I HAVE ALTA, KEVIN, AND THEN JEFF AGAIN, AND PROBABLY OTHERS AS WELL.

MS. CHARO: SO FIRST, ALAN, LET ME PRECEDE MY COMMENTS BY SAYING THAT I AM ACTUALLY QUITE SYMPATHETIC TO YOUR POINT OF VIEW AND THE FRUSTRATION AT THE DIFFICULTY OF OBTAINING EGGS, AND I'M VERY SYMPATHETIC WITH THE ARGUMENT THAT ORDINARY SUBJECTS OF HUMAN SUBJECTS RESEARCH ARE, IN FACT, PAID. I'M NOT GOING TO USE THE WORD "COMPENSATION" BECAUSE WE'RE ALL CONFUSING WHICH WE MEAN BY IT. THEY ARE PAID. THEY'RE INCENTIVIZED TO PARTICIPATE. AND I ALSO UNDERSTAND THAT WOMEN WHO GIVE EGGS FOR REPRODUCTIVE PURPOSES ARE PAID HOWEVER IT'S CALLED.

SO I'M SYMPATHETIC, BUT I ALSO RECOGNIZE THAT THERE HAVE BEEN SOME CONSTRAINTS ALONG THE WAY WHICH MAKE ME VERY NERVOUS ABOUT OPENING UP THIS CAN OF WORMS BEYOND A CLARIFICATION THAT

STEMS FROM ACTUALLY GETTING, AND I'VE GOT IN FRONT OF ME AND CAN'T FIND IT, THE SECTION IN PROP 71 THAT SPECIFIES THE NO PAYMENT.

THE COMPROMISE IS THIS. WE HAD A SITUATION IN WHICH WE HAD WILDLY DIVERGENT OPINIONS ABOUT WHETHER CLONING RESEARCH SHOULD EVEN BE LEGAL IN THE UNITED STATES. AND THERE ARE STILL PEOPLE WHO ARE UNHAPPY AT THE THOUGHT THAT UNDER ANY CIRCUMSTANCES, WITH OR WITHOUT MONEY, THAT A WOMAN COULD GIVE EGGS TO RESEARCH. AND THERE ARE OTHERS WHO WOULD TAKE A VERY LIBERTARIAN STANCE AND LET PEOPLE PAY WHATEVER THEY WANT. AND THE COMPROMISE THAT WAS STRUCK, WHICH IS THIS ALTRUISM MODEL IN WHICH PEOPLE HAVE A NO BENEFIT, NO HARM, FINANCIALLY SPEAKING, KIND OF OUTCOME WAS ONE THAT ACTUALLY ALLOWED THIS TO MOVE FORWARD.

AND, INDEED, PROP 71, WHICH ITSELF HAD THIS WRITTEN IN TO SOME EXTENT AS A POLITICAL MATTER, DROVE THE NATIONAL ACADEMY GUIDELINES WHICH FELT LIKE THEY WERE ALREADY BASICALLY HAVING TO FOLLOW THE CALIFORNIA LEAD ON THE ALTRUISTIC MODEL HERE.

DR. TROUNSON: I DON'T THINK IT DRIVES IT FORWARD. THAT'S THE PROBLEM.

MS. CHARO: I UNDERSTAND, ALAN. LET ME

TRY TO GET THE THOUGHT OUT THOUGH. WE HAD THIS COMPROMISE, AND NOW WE'RE IN A SITUATION, I THINK, WHERE IT'S PARTICULARLY TOUCHY TO TRY AND REVISIT THE COMPROMISE, PUTTING ASIDE WHETHER OR NOT IT'S EVEN LEGALLY POSSIBLE GIVEN THE LANGUAGE OF PROP 71. BECAUSE, IF ANYTHING, THE EXISTENCE OF DISEASE-SPECIFIC LINES FROM PGD, THE PROMISE OF DISEASE-SPECIFIC LINES FROM IPS HAVE ALREADY RAISED IN THE CONGRESS, IN THE STATE LEGISLATURES, AND IN THE PUBLIC DISCOURSE THE SUGGESTION THAT SCNT IS NO LONGER NEEDED AT ALL. AND THEN THE NEXT STEP HAS BEEN THAT IT SHOULD BE CRIMINALIZED, WHICH SETS A VERY DANGEROUS PRECEDENT IN THE WORLD OF SCIENCE IN WHICH WE CRIMINALIZE THINGS SIMPLY BECAUSE THEY ARE NOT MANIFESTLY NECESSARY.

IN THE STATE LAWS THAT HAVE BEEN PROPOSED, WE ALSO SEE THAT EXTENDED TO PARTHENOGENESIS AND ANDROGENESIS, WHICH YOU YOURSELF HAVE IDENTIFIED AS POTENTIALLY USEFUL TECHNIQUES. WHAT I FEAR IS THAT IF WE UPSET WHAT HAD BEEN THIS VERY DELICATE COMPROMISE TO LET EVERYBODY TRY TO MOVE FORWARD, EVEN IF IT IS INCREMENTALLY SLOW WITH GREAT DIFFICULTY, THAT WHAT WE'RE OPENING UP IS THE POSSIBILITY OF SPLINTERING THESE GROUPS THAT CAME TOGETHER, AT

LEAST SOMEWHAT, AND INVITING REALLY QUITE DRACONIAN RESPONSES ACROSS A WIDE RANGE OF SCIENTIFIC AREAS.

THANK YOU FOR LETTING ME GIVE MY IMPASSIONED SPEECH.

DR. EGGAN: NOW IT'S MY TURN FOR MY IMPASSIONED SPEECH. JEFF, I CAN'T SAY ANY MORE CLEARLY THAN WE'VE DONE THE EXPERIMENT. THE EXPERIMENT WAS A FAILURE. WE ALREADY KNOW THE ANSWER TO THIS QUESTION. WE'VE TRIED TO SEEK THE ANSWER TO YOUR QUESTION FOR TWO YEARS NOW. IT'S BEEN MORE THAN TWO YEARS SINCE I WAS APPROVED BY HARVARD'S IRB AND ESCRO, WESTERN IRB, COLUMBIA UNIVERSITY'S IRB AND ESCRO TO TRY TO HAVE WOMEN DONATE OOCYTES OUT OF THE GOODNESS OF THEIR HEART FOR OUR EXPERIMENTS. I HAVE SPENT COUNTLESS HOURS STOMPING AROUND TO DIFFERENT DISEASE ADVOCACY GROUPS, TEA CIRCLES, KNITTING CIRCLES, TRYING TO FIND ANYONE AND EVERYONE WHO WOULD DONATE THEIR OOCYTES FOR OUR EXPERIMENTS, EVEN OUT OF THE GOODNESS OF THEIR HEART BECAUSE THEY HAD SOMEONE THAT THEY CARED ABOUT WHO WAS AFFECTED BY THESE DISEASES THAT WE MIGHT IN THE VERY LONG TERM PROVIDE HOPE FOR.

WE SPENT MORE THAN $100,000 IN

ADVERTISING IN THE *BOSTON GLOBE*, IN THE *BOSTON HERALD*, IN THE BOSTON AREA PAPERS, IN THE SUBURBS OF BOSTON. WE HAVE LITERALLY PURSUED EVERY OPTION. WE'VE PURSUED TRYING TO RECRUIT DONORS FROM OTHER PARTS OF THE UNITED STATES TO COME TO BOSTON TO DONATE THEIR OOCYTES FOR RESEARCH. THIS WILL NOT WORK. IN A COUNTRY WHERE WOMEN KNOW THAT THEY CAN BE COMPENSATED FOR DOING THE EXACT SAME THING, THEY SIMPLY WILL NOT, AND IN THE FACE OF THE DIFFICULTIES, I SHOULD ADD, IT'S NOT LIKE THEY'RE NOT DOING IT SOLELY BECAUSE OF THE MONEY, THEY'RE DOING IT BECAUSE OF THE MONEY AND BECAUSE IT'S A VERY DIFFICULT THING TO DO OOCYTE DONATION. AND THOSE TWO THINGS COLLABORATE TOGETHER TO CREATE AN ENVIRONMENT IN WHICH WOMEN WILL NOT DO THIS IN A MEANINGFUL WAY WHICH WILL ALLOW THE RESEARCH TO GO FORWARD.

I REALLY CAN'T SAY ANY MORE SIMPLY THAN THAT. I THINK IT'S CLEAR. SO I THINK TO SAY THAT WE DON'T KNOW THE ANSWER TO THAT, TO SAY THAT WE NEED MORE TIME TO FIND OUT WHAT THE ANSWER TO THAT IS IS SIMPLY NOT THE CASE. SO I THINK THAT'S THE FIRST ISSUE.

AND THEN I WANT TO SPECIFICALLY ADDRESS ALTA'S POINT. AND I THINK THIS IS A DIFFICULT

ISSUE, AND I THINK WHAT YOU'RE SAYING IS RIGHT. THE QUESTION IS WHAT TO DO ABOUT THAT BECAUSE IN A SENSE THIS COMPROMISE THAT WE HAVE IS AKIN TO PROTECTING THE COWS FROM THE INDIANS BY SETTING THEM FREE OUT INTO THE MOUNTAINS AND LETTING THEM RUN AWAY. IT'S TRUE, YOU PROTECT IT BY ENSURING THAT IT CAN'T HAPPEN. AND, OF COURSE, THAT WASN'T WHAT ANYONE IMAGINED WHEN WE REACHED THIS COMPROMISE AT THE BEGINNING.

I GUESS FROM MY POINT OF VIEW, IT'S A COMPLICATED ISSUE BECAUSE WE SHOULD, YOU KNOW, I BELIEVE, AND IT CERTAINLY, AS I UNDERSTAND IT, FEDERAL POLICY THAT WE SHOULD COMPENSATE WOMEN FOR THEIR TIME AND THEIR EFFORT AND THE PAIN THAT THEY GO THROUGH OR THAT ANY HUMAN SUBJECT GOES THROUGH IN THE COURSE OF AN EXPERIMENT. SO I STILL STRUGGLE TO UNDERSTAND WHY THESE WOMEN SHOULDN'T BE COMPENSATED FOR THOSE THINGS BECAUSE COMPENSATION FOR THOSE THINGS IS WHAT'S REQUIRED TO MAKE THEM WHOLE AFTER PARTICIPATING IN THE EXPERIMENT. IT'S NOT JUST OUT-OF-POCKET EXPENSES, AS I UNDERSTAND IT.

SO I GUESS, YOU KNOW, FROM SITTING WHERE I'M SITTING, WHICH WAS NOT DIRECTLY IN THE ROOM, IT SEEMS TO ME THAT AT THE TIME, I AGREE, IT WAS A

VERY REASONABLE COMPROMISE TO SAY WE NEED TO GIVE UP COMPENSATION BECAUSE WE CAN'T AFFORD TO BE ASSAILED BOTH FROM THE RIGHT AND THE LEFT ON THIS POSITION, BUT NOW WE KNOW THAT THAT COMPROMISE POSITION IS A FAILURE. SO WHAT DO WE DO ABOUT THAT? I THINK THE FACT OF THE MATTER IS THAT IT MIGHT AS WELL BE AGAINST THE LAW IF WE CAN'T DO IT. THAT'S ONE SORT OF NULL HYPOTHESIS FOR YEARS. SO HOW TO PROCEED IN THE FACE OF THAT, I AGREE, IT'S RISKY; BUT IF WE DON'T TAKE THE RISK, THEN THE OUTCOME WILL BE THE SAME AS IF WE TAKE THE RISK AND THE FUTURE THAT YOU PREDICT COMES TRUE.

CHAIRMAN LO: WE HAVE A NUMBER OF PEOPLE WHO WANT TO SPEAK. I HAD JEFF SHEEHY AND BOB KLEIN. SHERRY HAD A QUESTION FOR KEVIN FIRST.

MS. LANSING: I WANT A CLARIFICATION. I UNDERSTAND WHAT YOU ARE SAYING, BUT ARE YOU SAYING, THIS IS MY IGNORANCE AS A LAYPERSON, REPRODUCTIVE THERAPY AND THERE'S ADDITIONAL EGGS LEFT OVER, ARE YOU TELLING ME THAT A WOMAN WON'T DONATE HER EGGS? WHAT'S THE COST TO HER? THEY'RE ALREADY THERE.

DR. EGGAN: BECAUSE THE FACT OF THE MATTER IS THAT THERE ARE VERY FEW IVF DOCTORS THAT WILL ADVISE A WOMAN TO DO THIS. LET ME PUT THIS

INTO PERSPECTIVE. WHEN A WOMAN UNDERGOES ASSISTED REPRODUCTION, A CERTAIN NUMBER OF OOCYTES ARE GENERATED. SOMETIMES THERE ARE SITUATIONS WHERE WILDLY TOO MANY OOCYTES ARE GENERATED. THOSE ARE VERY RARE. AND, IN FACT, THOSE ARE VERY RARE AND ASSOCIATED WITH THE MOST DANGEROUS OUTCOMES IN OVARIAN HYPERSTIMULATION SYNDROME.

SO TO SINGLE OUT THOSE WOMEN AS POTENTIAL DONORS IS PROBLEMATIC BECAUSE IT COULD LEAD TO A SITUATION IN WHICH DOCTORS ARE ENCOURAGED TO PURSUE THAT OUTCOME, WHICH I THINK IS PROBLEMATIC. YOU WOULD WANT TO AVOID THIS.

MS. LANSING: WHAT ABOUT IF YOU'VE ALREADY HAD YOUR CHILDREN AND THE EGGS ARE STILL THERE?

DR. EGGAN: THAT SITUATION DOES NOT EXIST BECAUSE THERE IS NO, AT LEAST AT THE MOMENT, REPRODUCIBLE IN A MEANINGFUL WAY TO PRESERVE UNFERTILIZED OOCYTES FOR IN VITRO EXPERIMENTS. THERE ARE NO EXTRA UNFERTILIZED EGGS ROUTINELY HANGING AROUND IN IN VITRO FERTILIZATION CLINICS, PERIOD.

DR. KIESSLING: DID YOU HAVE A PROTOCOL FOR THAT THOUGH? I DON'T THINK YOU HAD.

DR. EGGAN: FOR?

DR. KIESSLING: FOR SUPERNUMERARY EGGS FROM A FERTILITY CLINIC.

DR. EGGAN: SUPERNUMERARY FROZEN EGGS.

DR. KIESSLING: UNFERTILIZED EGGS.

DR. EGGAN: NO. WHAT WE HAVE PURSUED IS -- THE MOST COMMON SUPERNUMERARY CLINICAL OOCYTES IN FERTILIZATION CLINICS ARE THOSE THAT ARE SO-CALLED FAILED-TO-FERTILIZE OOCYTES. MANY PEOPLE HAVE PURSUED THIS. THIS IS AN AVENUE OF RESEARCH WHICH HAS NOT BEEN SUCCESSFUL.

DR. KIESSLING: THE ANSWER TO SHERRY'S QUESTION IS THAT HARVARD REALLY DOESN'T HAVE THAT EXPERIENCE.

DR. EGGAN: NO, BUT THE ANSWER TO THAT QUESTION IS, ANN, IT'S TRUE THAT WE DIDN'T BOTHER TO PUT TOGETHER THAT HUMAN SUBJECTS PROTOCOL WHICH WOULD HAVE ENTAILED MANY HUNDREDS OF HOURS BECAUSE INSTEAD WE WENT AND WE BEAT THE BUSHES TO FIND OUT WHETHER OR NOT THAT THING EXISTED. AND THE ANSWER IS THAT WHEN EGGS ARE RETRIEVED, THEY ARE ALL MIXED. AS YOU KNOW, THEY'RE ALL MIXED WITH SPERM. AND THERE ARE NO -- THERE WOULD BE NO RESPONSIBILE IVF DOCTOR WHO WOULDN'T TAKE EVERY SINGLE EGG FROM THAT PATIENT AND MIX IT WITH SPERM IN THE ATTEMPT TO MAKE FERTILIZED EMBRYOS FROM THOSE.

DR. TROUNSON: AND THERE'S NO OPPORTUNITY AT THAT TIME TO INTERVENE BECAUSE, YOU KNOW, THE PATIENTS ARE UNDER ANESTHETICS. IT'S NOT AN APPROPRIATE TIME TO DISCUSS THAT MATTER.

DR. KIESSLING: I UNDERSTAND. IT'S JUST THAT THAT HASN'T BEEN DONE IN MASSACHUSETTS.

CHAIRMAN LO: JEFF AND THEN BOB KLEIN.

MR. SHEEHY: I WANT TO COME BACK TO ONE OF ALTA'S POINTS, WHICH IS ONE OF THE THINGS THAT I HOPED WE'D HAVE A DISCUSSION OF ONE OF THE THINGS I THOUGHT WAS VERY GOOD ABOUT KEVIN'S PRESENTATION. FOR ME, WHEN HE WALKED IN TODAY, I WASN'T SOMEONE WHO WAS CONVINCED THAT WE EVEN NEEDED TO DO SCNT. FOR THE GENERAL PUBLIC, AND I THINK I'M ON THE HIGHER END OF THE GENERAL PUBLIC, IPS SEEMS TO HAVE SUPPLANTED THE NEED FOR SCNT. THERE HAS NOT BEEN A ROBUST SCIENTIFIC DISCUSSION IN THE LAY PRESS ABOUT WHY WE EVEN NEED SCNT.

IN A LOT OF WAYS, THE COMPROMISE THAT -- ALTA IS VERY CORRECT. WE HAD THIS VERY CAREFULLY CRAFTED COMPROMISE THAT TOOK CARE OF AN ISSUE THAT PEOPLE WERE VERY SQUEAMISH ABOUT, AND WE ACTUALLY ARE STARTING OFF BEHIND. WE HAVE TO GO BACK AND SAY WE ACTUALLY NEED TO DO SCNT. AND I DO THINK AT SOME POINT IN THIS PROCESS, IF WE ARE GOING TO

GO DOWN THE ROAD OF SUGGESTING THAT WE NEED COMPENSATION, WE NEED TO DO A COUPLE OF THINGS. WE NEED TO CLEARLY STATE WHY WE NEED TO DO SCNT. WE ALSO NEED TO HAVE A ROBUST EVIDENCE BASE OF WHY WE ARE NOT SUCCEEDING WITHOUT COMPENSATION.

WE DO HAVE THE HARVARD EXPERIMENT. AND I'M VERY SYMPATHETIC TO THAT, BUT, YOU KNOW, I'M NOT COMFORTABLE WITH US AS AN AGENCY ANTICIPATING PROBLEMS ON BEHALF OF OUR GRANTEES THAT THEY HAVEN'T COME TO US WITH ALREADY. AND WE'VE KIND OF SAID, WELL, YOU'RE NOT GOING TO GET ANY EGGS EVEN THOUGH YOU SUBMITTED THESE APPLICATIONS. SO WE'RE GOING TO START RELAXING OUR RULES IN ADVANCE OF YOU HAVING PRESENTED PROBLEMS TO US IN FULFILLING THE GRANT THAT YOU SUBMITTED TO US, ASSUMING THAT YOU COULD GET -- I DON'T KNOW HOW THEY'RE GOING TO GET THEM. I HAVE NO IDEA. I KNOW THAT THEY'RE GOING TO OBTAIN THEM ACCORDING TO OUR ETHICAL STANDARDS. I FEEL CONFIDENT OF THAT.

BUT BEFORE WE GO AND SAY WE'RE GOING TO RELAX OUR STANDARDS BECAUSE WE DON'T THINK YOU CAN DO WHAT YOU SAID YOU COULD DO WHEN YOU SUBMITTED THAT APPLICATION, I'M JUST VERY TROUBLED BY THAT ON THE FACE OF IT.

AND I JUST COME BACK TO THE LAST TIME WE MET IN THIS HOTEL, WE WERE ACTUALLY DISCUSSING WHAT ARE THE MEDICAL RISKS OF DOING THIS PROCEDURE FOR RESEARCH ALONE, AND WE HAVEN'T EVEN REALLY NAILED THAT DOWN. I MEAN WE REALLY DON'T KNOW WHAT THE MEDICAL RISKS TO WOMEN ARE. I REMEMBER DR. OLDEN TALKING ABOUT FROM BEING AT NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH. YOU KNOW, IF YOU LOOKED AT WHAT WE CONSIDERED A RISK FOR CANCER, WHICH WAS ONE OR TWO IN A MILLION, AND WE HAVE A RISK OF ONE OR TWO IN A THOUSAND IN THIS INSTANCE, WE HAVEN'T REALLY THOUGHT ABOUT THIS. AND I THINK ON SOME LEVEL WE'RE LOOKING AT A BALANCE HERE. WHENEVER YOU DO THINGS LIKE THIS, I THINK YOU ETHICISTS KIND OF BALANCE THESE THINGS OUT. WHEN WE STARTED OUT, SCNT WAS THE ONLY WAY TO GET DISEASE-SPECIFIC CELL LINES. THAT IS NOT NECESSARILY TRUE.

WE STILL HAVE THE SAME RISK ON THIS END THAT WE'RE TRYING TO QUANTIFY AND UNDERSTAND AND ASSESS. AND, YOU KNOW, I THINK FOR MYSELF I THINK THIS SHOULD BE A TOPIC THAT WE DISCUSS AND THAT WE TAKE UP AND WE MONITOR. SOME OF THESE GRANTS, I'M CERTAIN, ARE GOING TO GET APPROVED, I HOPE. I'M HOPING IT'S GOOD SCIENCE. BUT THAT WE MONITOR, WE

FIND OUT WHAT THEIR SUCCESS IS. IF THEY'RE HAVING PROBLEMS, YOU KNOW, AT THE SAME TIME WE REALLY DO TRY TO NAIL DOWN THE MEDICAL RISK, WE START LOOKING AT COMPENSATION ISSUES, AND THINK ABOUT WHAT'S REASONABLE, WE EDUCATE THE PUBLIC ABOUT THE NEED FOR SCNT.

I DO THINK THAT WE WILL HAVE TO REQUEST THAT THE LEGISLATURE CHANGE 1260 IRREGARDLESS OF WHAT WE CAN DO UNDER PROP 71 OR NOT. I'M NOT AT ALL COMFORTABLE IN SAYING THAT WE HAVE A CARVE-OUT FROM WHAT EVERYBODY ELSE IN THE STATE CAN DO. A LAW THAT'S BEEN PASSED BY LEGISLATURE AND SIGNED BY THE GOVERNOR KIND OF BEATS WHAT WAS A LITTLE SLEIGHT OF HAND IN PROPOSITION 71 THAT WAS APPROVED BY THE VOTERS BECAUSE THE VOTERS THOUGHT THERE WASN'T GOING TO BE COMPENSATION FOR EGG DONORS WHEN THEY VOTED FOR IT, AND THEY DIDN'T KNOW WE WERE GOING TO GO BACK AND CHANGE IT. AND SO IN THAT CONTEXT I THINK THIS IS AN ISSUE THAT WOULD BE APPROPRIATE FOR US TO STUDY.

MR. KLEIN: WELL, I'M IN A REASONABLY GOOD POSITION, JEFF, TO DISCUSS THE ISSUE OF WHAT WAS PRESENTED TO THE VOTERS. AND --

MR. SHEEHY: I WAS YOUR AVERAGE VOTER, BOB. I WAS NOT ONE OF THESE PEOPLE THAT WAS

WAVING THE STEM CELL FLAG. I CAN TELL YOU THAT IF WE WERE GOING TO GO OUT AND SPEND $3 BILLION BUYING EGGS FROM WOMEN, I WOULDN'T HAVE VOTED FOR IT.

MR. KLEIN: CERTAINLY I WOULDN'T HAVE VOTED FOR IT EITHER, SO WE AGREE. BUT THE KEY HERE IS MEDICAL REIMBURSEMENT WAS CLEARLY CONTEMPLATED. I HAVE GONE TO JAMES HARRISON AND DISCUSSED THIS ISSUE WITH HIM. AND SPECIFICALLY 1260, I'VE JUST ASKED JAMES HARRISON, AND HE HAS E-MAILED IT TO ME, SPECIFICALLY SAYS THAT IT IS NOT INTENDED TO AMEND PROPOSITION 71 ON THIS ISSUE.

SO I DON'T THINK 1260 IS; NEVERTHELESS, I'M IN HEATED AGREEMENT WITH YOU, JEFF, ON YOUR FUNDAMENTAL CONCEPT HERE, WHICH IS THAT IN ORDER TO ADDRESS WHAT IS BEING PROPOSED HERE, WE NEED A ROBUST SET OF DATA. WE NEED TO DO OUR INQUIRY IN CALIFORNIA. WE NEED TO SEE WHETHER IT'S FRUSTRATING OUR INVESTIGATORS. WE NEED TO, AS YOU SAY, SPECIFICALLY WRITE A JUSTIFICATION OF SCNT BECAUSE I'M ONE OF THOSE WHO BELIEVE FROM A LAY PERSPECTIVE, READING A NUMBER OF SCIENTIFIC PAPERS, THAT THERE ARE ALREADY HUGE PROBLEMS IN IPS AND WE'LL BE YEARS BEFORE WE KNOW WHAT THE

STABILITY OF THESE IPS LINES ARE.

SO I THINK IT'S VERY IMPORTANT TO CONCURRENTLY PROCEED WITH SCNT, BUT WE HAVE AN EDUCATION JOB TO DO, A DOCUMENTATION JOB TO DO, AND AN INFORMATIONAL JOB TO DO BEFORE, I THINK, WE CAN MEANINGFULLY TAKE ACTION ON THIS. SO I'M IN HEATED AGREEMENT WITH YOU ON WHAT WE NEED TO DO TO MEET THE BURDEN OF PROOF HERE IN MEETING OUR MISSION, WHICH IS, IN FACT, WHAT THE VOTERS ASKED US TO DO.

SO WHAT'S IMPORTANT HERE IS THAT WE'VE HAD A SERIOUS ISSUE BEEN PUT BEFORE US BY THE PRESIDENT. WE HAVE INDEPENDENT COLLABORATION OF THAT BY AN EMINENT MEMBER OF OUR PANEL WHO EXHAUSTIVELY TRIED DIFFERENT APPROACHES AT HARVARD. I THINK IT MERITS MAKING THIS A PRIORITY FOR ASSIGNING STAFF AND MEMBERS OF THE PANEL TO INVESTIGATE AND REPORT BACK TO THIS PANEL ON THIS SUBJECT SO WE CAN MEET YOUR CRITERIA FOR A SERIOUS REEXAMINATION OF THIS ISSUE.

I DON'T THINK WE'RE IN A POSITION TO MAKE DECISIONS TODAY, BUT I DO THINK IT'S A VERY SERIOUS QUESTION. AND I JUST DON'T WANT TO FORECLOSE AN OPTION THAT APPEARS IN ENGLAND, AND I JUST SAT THROUGH A FULL DAY OF ABOUT 15 NATIONS

GOING THROUGH THEIR ETHICS PAPER AND A DISCUSSION OF WHAT WAS GOING ON IN ENGLAND WITH THIS ISSUE AND OTHER EUROPEAN COUNTRIES WHERE THEY'VE HAD SOME VERY GOOD EXPERIENCE. NOT THAT THAT SHOULD BE CONTROLLING, BUT IT SHOULD BE BEFORE US AS EVIDENCE FOR US TO THOUGHTFULLY CONSIDER. THAT'S ALL I'M ASKING FOR IS WE HAVE A SERIOUS ISSUE BEING BROUGHT TO US. LET US THOUGHTFULLY FOLLOW YOUR DIRECTION AND HAVE A ROBUST AND THOUGHTFUL DISCUSSION.

CHAIRMAN LO: JOHN, KEVIN, SANDRA CARSON.

DR. WAGNER: SO I WANT TO MAKE A FEW POINTS. ONE IS THAT CERTAINLY WE CAN COME UP WITH REASONS WHY SCNT NEEDS TO BE PURSUED. YOU MENTIONED THAT CERTAINLY WE HAVE EXCESS EMBRYOS THAT ARE FROM PGD IVF WITH DISEASES, BUT THAT ONLY COUNTS FOR THOSE WITH KNOWN GENETIC DISEASES. FOR EXAMPLE, SICKLE CELL FANCONI, THOSE DISEASES, YES, YOU'RE RIGHT. THERE ARE EMBRYOS THAT EXIST TODAY THAT COULD BE USED FOR DEVELOPING NEW CELL LINES FOR THERAPIES.

ON THE OTHER HAND, THAT DOESN'T HELP YOU WITH OTHER DISEASES LIKE DIABETES AND ALZHEIMER'S AND THINGS THAT YOU COULD DEVELOP CELL LINES TO

STUDY THOSE DISEASES, BUT YOU DON'T HAVE A GENETIC MARKER THAT NECESSARILY WILL ALLOW YOU TO DO PGD SUCH THAT YOU WILL BE ABLE TO PREDICT WHAT'S GOING TO HAPPEN. SO IT HELPS YOU FORM SOME DISEASES, BUT IT WON'T HELP YOU FOR OTHER DISEASES. THIS ALSO DOESN'T GET AROUND THE ISSUE OF IF YOU DO, AS WE DISCUSSED SCNT ORIGINALLY, IF YOU WANTED TO HAVE THAT, THEN, SPECIFIC CELL LINES THAT WERE DEVELOPED WITH SPECIFIC HLA TYPES TO HOPEFULLY MINIMIZE THE IMMUNE RESPONSE TO THESE CELL POPULATIONS, CERTAINLY SCNT CERTAINLY OFFERS ADVANTAGES THAT WE OTHERWISE DON'T HAVE.

SECOND POINT WAS IS THAT YOU TALK ABOUT WHAT DO WE KNOW ABOUT THE MEDICAL RISKS ASSOCIATED WITH IVF? THAT REALLY IS QUITE WELL DESCRIBED, AND PERHAPS WHAT WE NEED TO DO IS COME BACK AND HAVE THOSE PEOPLE COME BACK AND MAYBE DIFFERENT PEOPLE COME BACK TO TELL US THAT. THERE'S BEEN MANY, MANY IVF PROCEDURES PERFORMED. AND ALTHOUGH THE DATA MAY NOT HAVE BEEN COLLECTED EXACTLY THE WAY WE WOULD HAVE LIKED IT TO HAVE BEEN COLLECTED, THERE IS STILL CONSIDERABLE EVIDENCE TO BE ABLE TO TELL US WHAT THE TRUE RISKS ARE TO THESE OOCYTE DONORS.

THE LAST THING THAT I WANT TO MAKE A

POINT OF SAYING WAS IT'S KIND OF BOTHERSOME TO ME BECAUSE THERE'S OTHER EXAMPLES OF THIS. THAT IS THAT WE SHOULD -- I THINK IF WE BELIEVE THAT -- IF YOU WANT TO COLLECT THE DATA TO DETERMINE -- TO VERIFY THE HARVARD EXPERIENCE, SO WE SHOULD WORK OUT THE SCENARIOS IN ADVANCE. EITHER THE HARVARD DATA IS REPRESENTATIVE OF THE CALIFORNIA OR ELSEWHERE DATA OR IT WILL BE DIFFERENT. IT WILL BE THAT THEY'RE WRONG AND THAT, IN FACT, IT WAS ONLY THEIR LIMITED EXPERIENCE THAT WAS UNIQUELY DIFFERENT. BUT LET'S THEN CONSIDER THE POSSIBILITY THAT THEIR DATA WAS REPRODUCIBLE. THEN WHAT?

WHERE I THINK YOU WERE GOING, AND I DON'T WANT TO PUT WORDS IN YOUR MOUTH, BUT THEN YOU'RE SAYING LET'S VERIFY THAT DATA, AND THEN AT THAT POINT WE CAN THEN REASSESS WHETHER OR NOT, QUOTE, WE RELAX THE STANDARDS. THAT SEEMS TO BE A BIT BOTHERSOME BECAUSE THEN YOU'RE SAYING RELAXING STANDARDS. SO EITHER IT'S RIGHT OR IT'S NOT RIGHT TO DO.

AND SO I WOULD SAY THAT IF AT LEAST YOU ARE GOING TO PURSUE THAT, WHICH I'M VERY MUCH ALL FOR COLLECTING MORE DATA, AND I'VE SAID THIS BEFORE, AT LEAST LET'S COLLECT THE DATA SO THAT WE

CAN THEN MAKE A MORE EDUCATED DECISION IN THE FUTURE. WE SHOULD ALSO PLAN ON KNOWING WHAT WOULD THAT DATA SHOW US, AND HOW WOULD THAT IMPACT OUR DECISION, BUT DO THAT IN ADVANCE BEFORE YOU EVEN KNOW WHAT THE DATA TELLS US. I DON'T WANT TO GET TO THE POINT OF SPENDING THE NEXT TWO YEARS COLLECTING DATA AND STILL BE NO FURTHER AHEAD BECAUSE AT THE END OF THE DAY, THE PUBLIC STILL SAYS, NO, WE'RE NOT GOING TO ALLOW COMPENSATION. SO NO MATTER WHAT THE DATA SAYS, IT DOESN'T MATTER.

MR. SHEEHY: COULD I JUST RESPOND?

CHAIRMAN LO: I WANT TO TRY AND DISTINGUISH. THE DECISION WE HAVE BEFORE US TODAY IS DO WE PUT THIS ON OUR AGENDA AS A HIGH PRIORITY ISSUE FOR THE SWG OVER THE COMING YEAR TO REEXAMINE IT, RETHINK IT, AND RESOLVE SOME ISSUES? WHAT I DON'T WANT TO DO RIGHT NOW, IF IT'S OKAY, IS SORT OF GET INTO THE SUBSTANCE, WHICH WE'RE ALREADY STARTING TO GET INTO, BECAUSE I THINK WE'RE NOT GOING TO SETTLE TODAY, I DON'T THINK, AS BOB AND OTHERS HAVE SAID, THIS ISSUE. I THINK WHAT WE CAN DO, IF WE DECIDE THIS IS GOING TO BE A PRIORITY, TO THEN DEVELOP A WORKING PLAN FOR WHAT KIND OF INFORMATION WE WANT TO GATHER, WHO WE NEED

TO HEAR FROM, SORT OF DEVELOP IDEAS ON THESE IMPORTANT POINTS THAT HAVE BEEN RAISED.

I DON'T WANT -- I WANT TO TRY AND GET US TO LUNCH AT A REASONABLE TIME, SO I WANT TO ASK THOSE OF YOU ARE GOING TO SPEAK TO REALLY FOCUS RIGHT NOW ON SHOULD THIS BE SOMETHING ON THE SWG AGENDA. WE'LL COME BACK TO IT THIS AFTERNOON TO TALK ABOUT, IF WE PASS THAT THRESHOLD TEST, WHAT DO WE NEED TO DO. I THOUGHT WHAT JOHN SAID AND WHAT BOB SAID ARE ALREADY GIVING US IDEAS. GEOFF IS ALREADY WRITING DOWN AS TO HOW WE WOULD GO ABOUT DOING THAT, BUT I THINK WE FIRST NEED TO DECIDE SHORTLY AFTER LUNCH WHETHER THIS WILL BE A HIGH PRIORITY. WITH THAT TWIST IN MIND --

DR. EGGAN: I'LL TAKE MY TURN IN LINE TO SAY THAT, OF COURSE, YES, I DO FEEL LIKE THIS SHOULD BE A MAJOR PRIORITY FOR US. BUT I AGREE THAT IF WE AGREE TO TAKE UP THIS QUESTION, I THINK WE SHOULD TRY TO FREE OURSELVES FROM THESE PRAGMATIC QUESTIONS OF WHETHER OR NOT IPS TECHNOLOGY MIGHT BE BETTER OR MIGHT WORK OR MIGHT SOLVE OUR PROBLEMS AND, INSTEAD, APPROACH IT FROM THE POINT OF VIEW OF THAT THERE ARE SOME SCIENTISTS WHO BELIEVE THIS SHOULD BE DONE, AND THERE ARE SOME SCIENTISTS IN CALIFORNIA THAT

BELIEVE IT SHOULD BE DONE; THEREFORE, IT IS RELATIVELY IMPORTANT TO US TO CONSIDER THE QUESTION OF HOW BEST IT CAN BE DONE AND WHETHER OR NOT IT IS ETHICALLY SOUND FOR THEM TO DO IT IN VARIOUS WAYS.

AN IMPORTANT QUESTION THAT I HAVE IS IF WE'RE GOING TO DO THAT, THEN I THINK WE AS A GROUP SHOULD GO BACK TO THE BEGINNING AND DO THAT AND NOT BE ENCUMBERED BY THE STRUCTURE OF EXISTING CALIFORNIA STATE LAW OR REGULATIONS THAT WE'VE ALREADY FORMED INTO ADMINISTRATIVE LAW HERE, BUT TRY TO DECIDE AMONGST OURSELVES WHAT'S RIGHT. AND THEN BASED ON WHAT'S RIGHT, TRY TO MAKE A DECISION ABOUT WHAT WE CAN DO WITHIN THE CONSTRAINTS OF LAW.

THERE MAY BE THAT THERE'S NOTHING THAT CAN BE DONE ABOUT THAT, AND WE HAVE TO RETREAT TO SOME POSITION WHICH IS MANAGEABLE WHICH IS CLOSEST TO WHAT WE THINK IS RIGHT. BUT THAT'S WHAT I WOULD SUBMIT RESPECTFULLY.

CHAIRMAN LO: I'M GOING TO ASK SANDRA CARSON, WHO'S BEEN VERY PATIENT. SANDRA, I DON'T THINK WE FORMALLY INTRODUCED YOU. SHE'S A PROFESSOR OF OBSTETRICS, GYNECOLOGY, AND REPRODUCTIVE SCIENCES AT BROWN UNIVERSITY WHERE

SHE CHAIRS THE DEPARTMENT. SHE AND ROB TAYLOR CO-CHAIRED A WORKING GROUP THAT CIRM COMMISSIONED THAT WE'LL HEAR FROM THIS AFTERNOON. SANDRA, I'M GOING TO LET YOU JUMP IN, AND YOU'LL BE THE FIRST OF THE PUBLIC COMMENTS. IS THIS SOMETHING WE SHOULD BE ADDRESSING?

DR. CARSON: THANK YOU. AS THIS HAS GONE ON, MY LIST HAS GOTTEN LONGER. I WANT TO MAKE FIVE VERY INCHOATE POINTS AND GIVE YOU SOME INFORMATION OF SOME HISTORY THAT PERHAPS YOU DON'T KNOW.

FIRST OF ALL, I RECRUITED MY FIRST EGG DONOR IN 1988, SO I HAVE BEEN DOING THIS FOR A WHILE. I CAN TELL YOU THAT IN MY PRACTICE, I'VE BEEN DOING IN VITRO FERTILIZATION SINCE 1983. AND THE MOST WONDERFUL PART OF IVF IS DEALING WITH THESE EGG DONORS BECAUSE THEY TRULY ARE WOMEN WHO WANT TO SHARE THEIR FERTILITY WITH SOMEONE ELSE.

IN 1988 WE RECRUITED A HOST OF EGG DONORS FOR RESEARCH IN MEMPHIS; BUT IN DOING SO, WE DID COMPENSATE THEM FOR THEIR TIME. IT IS POSSIBLE, WE HAD A FEW DONORS RETURN THEIR COMPENSATION, BUT THOSE WERE FEW AND FAR BETWEEN. BUT I CAN TELL YOU THAT WHEN WOMEN ARE GIVEN A CHANCE TO DO SOMETHING FOR OTHER WOMEN, THEY COME

TO BAT AND THEY DO IT, AND IT'S WONDERFUL, AND IT'S JUST A GREAT -- I'M PRIVILEGED TO BE A PART OF THAT PROCESS.

BUT HAVING SAID THAT, IT'S KIND OF UNFAIR, I THINK, TO NOT GIVE THEM SOMETHING BACK. I'M NOT SAYING COERCE THEM. IN FACT, MEN HAVE BEEN GIVING THEIR SPERM TO OTHER INFERTILE COUPLES FOR FAR LONGER THAN WOMEN HAVE BEEN GIVING THEIR EGGS. IN FACT, THE AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE, AND I'M A PAST PRESIDENT OF THAT SOCIETY, ACTUALLY CAME UP WITH THE EGG DONOR GUIDELINES, TAKING THE DONOR SPERM COMPENSATION. SO THEY TOOK AN AVERAGE TIME THAT IT TOOK TO DONATE SPERM AND CONSIDERED THE REIMBURSEMENT FOR THAT SPERM. AND THEN, TRULY THIS IS WHAT HAPPENED, AND THEN TOOK THE TIME THAT IT TOOK WOMEN TO BE INVOLVED IN THE DONOR EGG PROCESS AND CAME UP WITH THE FEE FOR REIMBURSEMENT.

AND THE AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE HAS GUIDELINES, AND THEY CONSIDER A REIMBURSEMENT BETWEEN 3,000 AND $5,000, BASED ON THIS GUIDELINE, TO BE COMMENSURATE WITH THAT MEN ARE REIMBURSED TO GIVE THEIR SPERM.

HAVING SAID THAT, WE ALSO HAVE IN SOCIETY A NUMBER OF MODELS WHERE WOMEN RISK THEIR

LIVES, LIKE IN IRAQ, AND ARE PAID, LIKE THE STUNT PEOPLE IN HOLLYWOOD WHO ARE PAID TO RISK THEIR LIVES AND REALLY GET HURT AND ARE PAID. AND NOW WE'RE JUST SAYING THAT WOMEN CAN SHARE THEIR FERTILITY, ONE, OR, TWO, SHARE THEIR EGGS AND NOT EVEN SHARE THEIR FERTILITY FOR WOMEN IN SCIENCE IN GENERAL.

AND I WOULD URGE YOU AGAIN TO RECONSIDER NOT PAYING FOR EGGS, BUT PAYING FOR TIME AND EFFORT IN AN EFFORT THAT REALLY COULD BE QUITE SIGNIFICANT.

AND IN TERMS OF THIS SCNT ISSUE, THERE ARE LOTS OF OTHER REASONS THAT WOMEN CAN DONATE THEIR EGGS TO RESEARCH. I AGREE THAT THAT'S ANOTHER ISSUE THAT YOU ALL HAVE TO THINK ABOUT. BUT WE'RE LOOKING AT MICRO-RNA RIGHT NOW IN EGGS WHEN THEY ARE FERTILIZED AND TURNED INTO EMBRYOS. AND WOMEN ARE BEING ASKED TO DONATE EGGS FOR THIS TYPE OF RESEARCH AS WELL.

YA'LL ARE LEADING THE COUNTRY IN TERMS OF DONOR PROTECTION, EGG DONOR PROTECTION FOR RESEARCH, AND NOT ONLY STEM CELL RESEARCH, BUT JUST HOW WE TAKE CARE OF WOMEN WHO WANT TO DO THIS AND HOW THE OVERSIGHT THAT WE HAVE -- I'LL BE DISCUSSING A LITTLE BIT MORE ABOUT THE SAFETY OF

HOW WE CAN REALLY MINIMIZE THESE RISKS -- BUT EVERYBODY'S EYES ARE GOING TO BE ON YOU. SO PLEASE DON'T -- THERE ARE OTHER REASONS TO HAVE WOMEN DONATE EGGS FOR RESEARCH, SO PLEASE DON'T SAY NO JUST BECAUSE YOU MIGHT NOT CHOOSE TO DO IT FOR SCNT.

AND, FINALLY, I ALSO WONDER WHETHER THE INVESTIGATORS WHO PROVIDED THE APPLICATIONS WEREN'T THINKING THE WAY WE THINK IN ASRM IN THAT REASONABLE COMPENSATION FOR PARTICIPATION SHOULD BE MONETARILY REIMBURSED OR REWARDED, AND THAT MAY BE HOW THEY WERE THINKING AS WELL. AGAIN, I DON'T THINK THAT WOMEN NEED A LOT OF MONEY, BUT I DO THINK THEY NEED TO BE REIMBURSED FOR THEIR TIME AND EFFORT. THANKS.

CHAIRMAN LO: ARE THERE OTHER PEOPLE FROM THE PUBLIC WHO WANT TO COMMENT?

DR. PETERS: WE'VE PINCHED ME OUT OF LINE. I YIELDED OUT OF COURTESY. AND NOW THE CONVERSATION HAS GONE WAY BEYOND, SO DO YOU WANT TO HEAR WHAT I HAVE TO SAY?

CHAIRMAN LO: CERTAINLY.

DR. PETERS: I'D LIKE TO TALK ABOUT WHAT ALAN SAID. WHERE DID ALAN GO? THIS IS NOT WORKING OUT VERY WELL. ALAN, I WANT TO PICK UP ON

THE NUCLEAR TRANSFER ISSUE. EVERYBODY ELSE HAS GOT THEIR TWO CENTS WORTH IN.

THE RATIO OF MAYBE ONE SUCCESS OUT OF A HUNDRED THAT YOU WERE TALKING ABOUT IS THE FIGURE THAT IAN WILMOT WAS USING TOWARDS THE END OF HIS PERIOD AT THE ROSLIN INSTITUTE WHEN IT CAME TO SHEEP CLONING, ETC. AND IAN HAD AN ETHICS COMMITTEE THAT JUDGED THAT IF WE WERE TO DO THAT AT THAT RATIO WITH HUMAN EMBRYOS, THEY FELT THAT THAT WOULD BE IMMORAL. AND THE GROUND WAS THAT IT WOULD BE DISRESPECTFUL TO THOSE UNUSED EMBRYOS -- DESTROYED EMBRYOS.

WHAT I THOUGHT YOU MIGHT BE SAYING IS THAT IF WE GO THE ROUTE OF NUCLEAR TRANSFER, AND IF WE HAVE THE SAME RATIO OF SUCCESS TO FAILURE, THAT THEN WE WOULD NEED A LARGE NUMBER OF HUMAN OOCYTES. WHAT WE DON'T KNOW YET IS WHETHER OR NOT THAT'S TRUE. UNTIL WE GET A CONFIRMED PROCEDURE FOR NUCLEAR TRANSFER WITH HUMAN EMBRYOS, WE ACTUALLY DON'T KNOW WHETHER THE RATIO WOULD BE ONE OUT OF A HUNDRED OR MAYBE IT WOULD BE MUCH MORE EFFICIENT.

IT IS A TOPIC THAT WE PROBABLY WOULD NEED TO DISCUSS HERE, I THINK, WHEN THAT COMES UP. SO IN SOME WAYS, I WOULDN'T WANT THIS CONCERN TO

JUSTIFY A DECISION TO COMPENSATE WOMEN ON THE GROUNDS THAT WE WANTED TO PURSUE NUCLEAR TRANSFER.

MY SECOND IS THAT I'M STRONGLY IN FAVOR OF ENCOURAGING RESEARCHERS TO EXPERIMENT WITH NUCLEAR TRANSFER, AND I'M HOPING WE'LL GET TO DISCUSS SECTION 100080 WHERE WE TALK ABOUT ACCEPTABLE DERIVATION, (3)(A), WHICH READS HERE, "THE DERIVATION DID NOT RESULT FROM THE TRANSFER OF SOMATIC CELL NUCLEUS INTO A HUMAN OOCYTE."

I BROUGHT THIS UP AT THE LAST MEETING, BUT I WOULD REALLY LIKE TO HAVE OUR LABORATORY SCIENTISTS COMMENT ON THIS. DOES THIS MEAN YOU'RE PROSCRIBED FROM ENGAGING IN THOSE KINDS OF EXPERIMENTS? AND IF THAT'S REALLY WHAT THE IMPACT IS, THEN I WANT TO SAY WHY? AND I KNOW THERE'S -- I KNOW THAT THE NAS HAD TALKED THIS ONE THROUGH. I'D LIKE TO KNOW WHAT HAPPENED THERE AND WHETHER THAT SHOULD APPLY TO US AND WHETHER WE SHOULD AGREE WITH EXISTING PRECEDENTS ON THAT BECAUSE I WOULD LIKE TO SEE EXPERIMENTS IN NUCLEAR TRANSFER GO AHEAD, AND I DON'T THINK IPS OR SOME OF THESE OTHER PLACES WHERE WE MIGHT HAVE SOME HOPES ARE GOING TO ELIMINATE THE VALUE OF THAT LINE OF RESEARCH. THOSE ARE MY COMMENTS.

DR. TROUNSON: THANK YOU. IT'S VERY

DIFFICULT TO ADDRESS WHAT THE SITUATION MAY BE IF WE ARE ABLE TO ENGAGE SIGNIFICANTLY IN THIS AREA. IF WE'RE ONLY GOING TO GET FOUR EGGS A YEAR, THAT'S NOT REALLY VERY SIGNIFICANT. SO I THINK THE PURPOSE OF ME PUTTING THESE ISSUES TO YOU IS, ONE, IT'S A PRACTICAL MATTER, AND REALLY SHOULD WE FUND WORK WHERE IT'S UNLIKELY THAT YOU COULD ACCESS THE KIND OF NUMBER WHICH WOULD ENABLE THE SCIENCE TO PROGRESS?

AND I HAVE -- IF THERE'S ANY DECISION TO PUT IT OFF, I THINK I'LL CERTAINLY INSTRUCT THE STAFF TO INTERROGATE THOSE APPLICATIONS BECAUSE I SUSPECT THEY ARE PREDICATED ON PROVIDING SOME WHATEVER, SOME MONEY WHICH MAY NOT BE CLEARLY RECEIPTABLE IN ORDER TO DO THAT. BUT WHILE I HAVEN'T -- YOU KNOW, I DON'T EXACTLY KNOW THAT, I SUSPECT THAT'S THE ONLY WAY IT WILL HAPPEN.

THE ONLY THING THAT I CAN ADD TO IT IS THAT THE WORK IN SAN DIEGO DONE OUTSIDE CIRM SHOWED THAT YOU COULD GET REASONABLE NUMBERS OF HUMAN BLASTOCYSTS. WHAT'S A REASONABLE NUMBER? THEY GOT HUMAN BLASTOCYSTS, WHICH TECHNICALLY I KNOW THE SCIENTISTS WHO DID THAT WORK BECAUSE IT WORKED IN MY LAB, AND SO HE'S A VERY, VERY SKILLED OPERATOR. AND SO YOU WOULD HAVE TO TAKE THE VERY

SKILLED OPERATORS, I THINK, TO PROGRESS IN THIS AREA. AND THEN THEY NEED -- THOSE SKILLED OPERATORS, YOU KNOW, NEED ENOUGH MATERIAL TO WORK ON.

I DON'T KNOW IF IT'S GOING TO BE BETTER THAN ONE IN A HUNDRED. ONE WOULD ALWAYS HOPE THAT WAS THE CASE, BUT GENERALLY ANIMAL EXPERIMENTS GIVE YOU A FAIRLY STRONG POINTER TO WHAT'S LIKELY TO HAPPEN IN THE HUMAN. SO THE SITUATION, I THINK, HERE IS THAT I THINK IT'S A WORTHWHILE DISCUSSION TO HAVE, AND IT'S WORTHWHILE TO CHALLENGE THAT, YOU KNOW, WHATEVER THE REASONS FOR DECIDING ON THE CURRENT POLICY. IF IT'S GENUINELY IMPRACTICAL, WE NEED TO EITHER REVISIT IT, TAKE IT THAT IT'S STILL COMPLETELY ETHICALLY REASONABLE, OR MAKE AN ADJUSTMENT THAT ALLOWS SOME ACCESS TO THE SCIENCE MOVING FORWARD.

CHAIRMAN LO: I WANT TO ASK TWO FOLLOW-UP QUESTIONS. FIRST, CAN YOU GIVE US THE REFERENCE TO THE SECTION YOU READ BECAUSE GEOFF AND I ARE HAVING TROUBLE FINDING IT?

DR. PETERS: PAGE 2.

MS. CHARO: IT'S THE WHITE PAGES. IT'S THE REVISIONS.

DR. TAYLOR: GEOFF, I THINK IT'S THE

SAME THING I SENT YOU TWO DAYS AGO.

CHAIRMAN LO: I THINK WE'VE GOT IT.

MR. KLEIN: WHAT'S THE SECTION? I COULDN'T FIND IT EITHER.

DR. PETERS: 100080 UNDER ACCEPTABLY DERIVED MATERIALS, (3)(A), SECTION 2.

DR. LOMAX: I UNDERSTAND THE QUESTION. LET ME TRY TO PROVIDE A QUICK CLARIFICATION. KEEP IN MIND THAT THESE REVISIONS WERE INTENDED TO ALLOW THE USE OF ANONYMIZED TISSUES FOR DERIVATION RESEARCH. WHAT THAT PROVISION IS EXPLICITLY SAYING IS YOU CAN USE THOSE -- WHAT THE REGULATION ALLOWS IS YOU CAN USE IT FOR REPROGRAMMING, BUT YOU CAN'T TAKE AN ANONYMOUS SAMPLE TISSUE AND THEN PERFORM AN SCNT EXPERIMENT ON ANONYMOUS TISSUE BECAUSE FOR SCNT, WE WANT TO MAKE SURE OUR HEIGHTENED CONSENT OF ALL DONORS WOULD APPLY.

DR. PETERS: IT'S NOT A GENERIC PROSCRIPTION.

DR. LOMAX: IT'S NOT A GENERIC REQUIREMENT. IT'S A SPECIFIC REQUIREMENT TO ANONYMIZE TISSUE. IS THAT CLEAR?

DR. TAYLOR: I HAD THE SAME QUESTION ACTUALLY A COUPLE DAYS AGO. I DON'T THINK IT'S THAT CLEAR IN THE GUIDELINES, FRANKLY, BECAUSE I

HAD -- WHEN I WAS READING THROUGH THEM A FEW DAYS AGO, I HAD EXACTLY THE SAME QUESTION.

CHAIRMAN LO: IF TWO MEMBERS OF THE COMMITTEE DIDN'T UNDERSTAND, THERE MAY BE A NEED FOR A TECHNICAL REVISION. I'M GOING TO PUSH HERE A LITTLE BIT BECAUSE I THINK WE'LL ALL DO BETTER WITH A LITTLE LUNCH UNDER OUR BELTS.

TED, AM I TO INFER FROM WHAT YOU SAID THAT YOU WOULD FAVOR THE SWG ADDRESSING THIS ISSUE OF RELOOKING AT THE CONDITIONS OF OOCYTE DONATION FOR SCNT AND ELSEWHERE?

DR. PETERS: YES. I HAD MEANT TO SAY THAT. SORRY.

CHAIRMAN LO: YOU DID. I'M GOING TO ASK FOR PUBLIC COMMENTS AND THEN TRY AND HAVE LUNCH, AND WE'RE GOING TO COME BACK TO THIS AFTER LUNCH.

MR. REED: DON REED. TWO POINTS. ONE, IT'S MY UNDERSTANDING THAT SCIENTISTS ARE NOW WORKING TO DEVELOP A WAY TO DO SCNT WITH BLASTOCYSTS AND NOT ONLY EGGS ALONE.

SECONDLY, A STUDY WAS RECENTLY DONE WHICH CONTRADICTS THE PREVIOUS THOUGHT THAT PEOPLE WOULD NOT BE WILLING TO DONATE EGGS. THE FIGURE THEY USED TO GIVE WAS ONLY 3 PERCENT WOULD DONATE EGGS. AND THE RESEARCH DONE BY RESEARCH U.S.A.

SAID THAT WHEN TOLD THAT THERE WAS AN OPPORTUNITY TO DONATE UNUSED BLASTOCYSTS, 60 PERCENT OF DONOR COUPLES SAID THEY WOULD BE WILLING TO DONATE BLASTOCYSTS.

I WONDER IF IT MIGHT NOT BE WORTHWHILE JUST TO SEND A FLIER OUT TO EVERY IN VITRO FERTILITY CLINIC IN CALIFORNIA AND ASK THEM TO INFORM THEIR DONORS THAT THERE IS A GREAT NEED FOR BLASTOCYSTS, AND THAT WHAT IS LEFT-OVER TISSUE TO THEM MIGHT BE LIFESAVING FOR OTHER PEOPLE.

CHAIRMAN LO: THANK YOU. OTHER PUBLIC COMMENT?

DR. EGGAN: SO I KNOW OF NO ONE THAT'S TRYING TO DO NUCLEAR TRANSPLANTATION INTO BLASTOCYST STAGE EMBRYOS. BUT CERTAINLY OUR WORK SUGGESTS THAT SOME MATERIAL WHICH IS THROWN AWAY IN IVF CLINICS, THAT IS TO SAY, FERTILIZED ZYGOTES WHICH ARE SOMETIMES, BUT RARELY, FROZEN PERHAPS MAYBE BLASTOMERES IN FROZEN CLEAVAGE STAGE EMBRYOS WHICH ARE ROUTINELY DISCARDED IN IVF CLINICS MIGHT BE SUITABLE RECIPIENTS CELLS FOR SOMATIC CELL NUCLEAR TRANSPLANTATION.

AGAIN, THAT'S VERY EARLY RESEARCH WHICH HAS ONLY BEEN DONE IN MOUSE AND HAS NOT BEEN VALIDATED IN MANY OTHER SPECIES IN THE SAME WAY

THAT SOMATIC CELL NUCLEAR TRANSPLANTATION INTO OOCYTES HAS BEEN, BUT IT CERTAINLY DOES SAY THAT IS IN PRINCIPLE VALUABLE MATERIAL FOR SOMATIC CELL NUCLEAR TRANSFER EXPERIMENTS. AND PEOPLE SHOULD BE ENCOURAGED, I THINK, FROM MY OPINION, TO DEVELOP HUMAN SUBJECTS PROTOCOLS TO ALLOW THEM TO ACCESS THAT MATERIAL IN CALIFORNIA, AND PEOPLE SHOULD BE TOLD IT COULD BE VALUABLE. THAT MUCH IS TRUE.

DR. TAYLOR: JUST AN ASIDE, CLINICALLY THAT MATERIAL IS BECOMING MORE AND MORE AVAILABLE AS WE FREEZE MORE TWO-CELL STAGE EMBRYOS. THOSE SPECIMENS MIGHT BE AROUND IF THAT REALLY TURNS OUT TO BE FEASIBLE.

MS. FOGEL: HI. I'M SUSAN FOGEL. I'M WITH THE PRO CHOICE ALLIANCE, RESPONSIBLE RESEARCH. I WANT TO MAKE FIRST ONE JUST VERY GENERAL COMMENT, WHICH THIS IS A VERY SUBSTANTIVE CONVERSATION. AS A MEMBER OF THE PUBLIC, IT'S REALLY DISTRESSING THAT NOTHING INDICATING THIS KIND OF DISCUSSION WAS ON THE AGENDA. THERE WERE NO MATERIALS ON THE WEBSITE UNTIL MIDDAY YESTERDAY. AND THERE ARE A LOT OF PEOPLE WHO WOULD BE VERY INTERESTED IN THIS. AND I APPRECIATE THAT YOU HAVE EXEMPTED YOURSELVES FROM

OPEN MEETING RULES, BUT I JUST THINK IT'S APPALLING THAT THERE WAS NO INDICATION THAT WE WERE GOING TO BE ENGAGED IN THIS KIND OF CONVERSATION.

MY MORE SPECIFIC POINT IS I'M ACTUALLY RATHER DISTRESSED THAT YOU EVEN WANT TO PUT THIS ISSUE ON THE TABLE. I'M TOTALLY FOR RESEARCH. AND I WAS ONE OF THE PEOPLE WHO WORKED ON SB 1260. I'M ONE OF THE PEOPLE WHO HAVE BEEN ASKING YOU TO COLLECT DATA, BUT TO REOPEN A CONVERSATION ABOUT COMPENSATION, AND I REALLY DON'T WANT TO PARSE WORDS, WOMEN GET -- A COUPLE OR A WOMAN, A PERSON GETS A DISCOUNT IN IVF, IT'S COMPENSATION. TIME AND EFFORT, IT'S -- YOU'RE PAYING FOR EGGS. AND TO PRETEND YOU'RE NOT PAYING FOR EGGS BY USING THIS OTHER KIND OF LANGUAGE, LET'S TALK ABOUT WHAT IT IS IF WE ARE GOING TO HAVE A FRANK CONVERSATION ABOUT IT.

NOT PAYING WOMEN FOR THEIR EGGS, PUTTING IN THOSE KINDS OF PROTECTIONS AGAINST EXPLOITING WOMEN WAS THE KEY ISSUE IN THE CAMPAIGN. I KNOW BECAUSE I WAS ON LOTS OF DEBATE PANELS. IT WAS AN IMPORTANT ISSUE IN THE CAMPAIGN. IT'S BEEN AN IMPORTANT ISSUE AS YOU'VE BEEN MOVING FORWARD, IT'S A VERY IMPORTANT ISSUE IN THE LEGISLATURE,

AND I JUST THINK IT SHOULD BE OFF THE TABLE.
THANK YOU.
MR. REYNOLDS: JESSE REYNOLDS FROM THE CENTER FOR GENETICS IN SOCIETY. I'D LIKE TO JUST THROW OUT A COUPLE OF POINTS FOR CONSIDERATION. ONE IS THAT THIS -- I THINK IT'S CLEAR THAT THE DEBATE HERE SHOULDN'T BE ABOUT WHETHER COMPENSATION IS PERMITTED OR NOT, THAT'S CLEARLY PROHIBITED BY THE LANGUAGE OF PROPOSITION 71, BUT EXACTLY WHETHER THIS WOULD QUALIFY AS COMPENSATION OR REIMBURSEMENT.
AND ONE WAY IN WHICH I THINK THAT EGG SHARING STRIKES ME AS CLEARLY A FORM OF COMPENSATION IS THAT IT DOES SERVE AS A FORM OF INDUCEMENT. THERE WOULD BE WOMEN WHO WOULD BE PROVIDING EGGS FOR MULTIPLE PURPOSES, RESEARCH AND FOR FERTILITY PURPOSES, WHO WOULD NOT BE DOING THAT IN THE ABSENCE OF SUCH AN EGG SHARING PROGRAM. THAT STRIKES ME AS A FINANCIAL INDUCEMENT.
SECOND, WHERE I THINK I'LL DISAGREE WITH DR. EGGAN IS THAT I THINK IT IS IMPORTANT TO CONSIDER IN THE BALANCE OF CURRENT SCIENTIFIC EVIDENCE, CURRENT UNDERSTANDING OF THE POTENTIAL OF IPS, AS WELL AS THE DIFFICULTIES THAT SCNT HAS

FACED OVER THE LAST TEN YEARS OR SO, NOT JUST FROM A MORAL OR ETHICAL PERSPECTIVE, BUT AS WELL FROM A PRAGMATIC PERSPECTIVE ABOUT WHAT TYPE OF POLITICAL DISCUSSION WOULD RESULT FROM SUCH A PROPOSAL. THANK YOU.

CHAIRMAN LO: THANK YOU.

MR. KLEIN: I WOULD JUST LIKE TO SAY THAT IT'S MY UNDERSTANDING OF THE DISCUSSION TODAY IT'S TO SET AN AGENDA OF WHAT THE PRIORITIES ARE GOING TO BE. SO IT'S IMPORTANT TO NOTE FOR THE PUBLIC THAT WHAT I'VE BEEN TALKING ABOUT AND CERTAINLY WHAT JEFF HAS BEEN TALKING ABOUT IS A FULLY INFORMED DISCUSSION BEFORE THERE'S ANY DECISIONS BEING MADE, GETTING THE FACTS ON THE TABLE, LOOKING AT IT THOUGHTFULLY AND THOROUGHLY, GETTING CALIFORNIA EVIDENCE ON THE TABLE IN A FULL DISCUSSION WITH MATERIALS THAT WILL HAVE BEEN DEVELOPED AT THAT POINT FROM THAT RESEARCH AND COLLECTION OF DATA WITH EVERYONE HAVING NOTICE, WITH EVERYONE HAVING THE ABILITY TO PARTICIPATE IN THAT DISCUSSION.

SO I THINK THIS DISCUSSION TODAY IS MERELY TO FIGURE OUT WHAT IS GOING TO BE STUDIED.

MS. LANSING: I'M VERY MUCH FOR EVERYONE PUTTING, AS WE ALL KNOW, ANY AGENDA OR ANY

QUESTIONS THAT THEY HAVE ON THE TABLE. BUT WHEN WE COME BACK FROM LUNCH, AND I KNOW WE'RE GOING TO BREAK FOR LUNCH, I THINK IT IS IMPORTANT THAT AS WE DECIDE WHAT TO PRIORITIZE, WE DECIDE WHAT WE CAN ACTUALLY DO SOMETHING ABOUT AND THAT WE NOT SPEND, YOU KNOW, TWO WEEKS, LET ALONE A YEAR, AND THEN COME BACK TO SOMETHING THAT WE ACTUALLY CAN'T DEAL WITH, WHICH IS WHY I WANT A REAL CLARIFICATION. I THINK DR. TROUNSON WAS CONFUSED, AND IT TURNS OUT I WAS CONFUSED, AND IT TURNS OUT A LOT OF US WERE, SO IF NOTHING ELSE, I'D LIKE TO LEAVE WITH CLARIFICATION.

BUT FROM WHAT I UNDERSTAND, THERE IS A LAW THAT WE PASSED REGARDING CERTAIN THINGS. THIS IS WHAT I'M HEARING HERE. IN ORDER TO GET IT CHANGED WHEN YOU GO TO COMPENSATION, WE WOULD HAVE TO GO TO THE LEGISLATURE. IF THAT'S NOT TRUE, THEN I'M GETTING WRONG INFORMATION FROM GEOFF.

I ALSO WANT TO SAY THAT -- I'M NOT SUGGESTING THAT THIS SHOULDN'T BE ONE OF OUR ISSUES. I'M JUST TRYING TO PUT IT IN CONTEXT BECAUSE WE HAVE A LOT OF ISSUES THAT WE COULD BE DEALING WITH.

I ALSO WANT TO SAY THAT SOMETIMES THINGS ARE PREMATURE. MAYBE WE DON'T HAVE ENOUGH

EVIDENCE SINCE WE'RE JUST BEGINNING THIS TO ACTUALLY MAKE THE DECISION. AND SO IT'S NOT JUST EVIDENCE IN OTHER STATES. IT'S WHAT'S ACTUALLY GOING TO HAPPEN IN THIS STATE THAT PASSED THE $3 BILLION REFERENDUM, WHICH IS UNHEARD OF, AND IT'S THE NATURE OF THIS STATE THAT I QUESTION WHETHER WE'RE GOING TO HAVE ENOUGH INFORMATION TO MAKE AN INFORMED DECISION. I DON'T KNOW THE ANSWER TO THAT; BUT WHEN WE COME BACK AFTER LUNCH, AS WE EVALUATE THE VERY MANY THINGS THAT WE CAN TAKE ON AS OUR NEXT STRATEGIC INITIATIVE, WE SHOULD QUESTION THE LAW AND THE TIMING.

DR. PETERS: I'D LIKE UNDERSCORE THE FIRST OF SHERRY'S TWO POINTS, BERNIE. MAYBE WHEN WE OPEN THIS DISCUSSION, WE CAN ASK BOB AND THE TWO JEFFS TO INTERPRET PROPOSITION 71 SO WE KNOW WHAT THE PARAMETERS ARE, AND THEN WE CAN TRY TO HAVE AN EFFICIENT RATHER THAN AN INEFFICIENT DISCUSSION.

MR. SHEEHY: THERE'S TWO DIFFERENT, THERE'S PROPOSITION 71, AND BOB IS THE EXPERT ON THAT, AND THEN THERE'S SB 1260. AND SB 1260 EXPRESSLY PROHIBITS COMPENSATION. A LOT OF PEOPLE BELIEVE PROP 71 PROHIBITS COMPENSATION, BUT THE AUTHOR SUGGESTS THAT -- SAYS THAT THAT'S NOT

NECESSARILY ALWAYS TRUE.

I DO HAVE A PROBLEM, EVEN THOUGH APPARENTLY PROP 71 IS NOT GOVERNED BY STATE LAW IN THIS AREA, TO KIND OF OVERTURNING A PROPERLY PASSED STATE LAW JUST BECAUSE PROP 71 WAS WRITTEN IN A WAY TO MAKE THE STATE LAW NOT APPLY TO IT. I THINK THAT'S --

MR. KLEIN: BERNIE, I THINK THAT, AS A POINT OF ORDER, DEMANDS AN ANSWER. 1260 SPECIFICALLY SAYS IT IS NOT INTENDED TO AMEND PROPOSITION 71. IT SPECIFICALLY IN ITS TEXT SAYS THAT. I'LL GIVE YOU A COPY OF IT. SO IT WAS DISCUSSED AT THE TIME THIS WAS NOT INTENDED TO CHANGE PROPOSITION 71.

IN ADDITION, WHAT I AM TRYING TO GET A DISCUSSION ON IS MEDICAL REIMBURSEMENT, NOT COMPENSATION, MEDICAL REIMBURSEMENT FOR PART OF THE IVF COSTS. AND THE MEDICAL REIMBURSEMENT IS SOMETHING THAT WAS DISCUSSED TIME AND TIME AGAIN IN THE DISCUSSION OF PROPOSITION 71. BUT I'M NOT ASKING THAT WE CONCLUDE THOSE ISSUES HERE TODAY. I'M NOT -- I AM, AS I SAID BEFORE, IN ROBUST AGREEMENT WITH YOU. WE NEED FACT-FINDING. WE NEED TO BE SENSITIVE TO THE INFORMATION. WE NEED TO -- I'M JUST ASKING WE LOOK AT THIS ISSUE WITH

ALL OF THE FACTS WITH THE CALIFORNIA EXPERIENCE AND WITH ETHICAL INPUT TO THAT DISCUSSION AND FULL PUBLIC DISCUSSION.

CHAIRMAN LO: OKAY. WE HAVE A LOT TO COME BACK TO AFTER LUNCH, BUT LET'S ADJOURN FOR -- HOW LONG CAN WE TAKE -- 45 MINUTES, WHICH WOULD BRING US BACK HERE AT 1:30. SEE YOU LATER.

(A RECESS WAS TAKEN.)

CHAIRMAN LO: LET'S RECONVENE. I WAS ASKED TO REMIND PEOPLE THAT WHEN WE SPEAK TO MAKE SURE WE PRESS THOSE RED BUTTONS BECAUSE OTHERWISE BOTH THE TRANSCRIPTIONIST, AND IF JANET IS STILL ON THE PHONE, CAN'T HERE.

WHAT I'D LIKE TO DO NOW IS, FIRST, TURN TO SANDRA CARSON AND ROB TAYLOR, WHO CO-CHAIRED OUR ADVISORY PANEL THAT WE COMMISSIONED A NUMBER OF MONTHS AGO TO DEVELOP GUIDELINES FOR OOCYTE DONATION FOR STEM CELL RESEARCH. SO IN A SENSE THEY ASSUMED THAT THE DISCUSSION THIS MORNING -- THEY ASSUMED THERE WOULD BE WOMEN COMING IN TO DONATE OOCYTES SPECIFICALLY FOR RESEARCH, AND WE ASKED THEM TO ADDRESS THE QUESTION OF, IN THE LIGHT OF THE NATIONAL ACADEMY OF SCIENCES REPORT THAT CIRM SPONSORED, TALKING ABOUT MEDICAL RISKS AND OBVIOUSLY THE CONCERN AMONG THE PUBLIC ABOUT

RISKS TO WOMEN UNDERGOING RESEARCH SOLELY FOR OOCYTE DONATION SOLELY FOR RESEARCH PURPOSES, WE ASKED SANDRA AND ROB TO CO-CHAIR THIS EXPERT PANEL TO SORT OF SET GUIDELINES FOR HOW TO MAKE THOSE DONATIONS SAFELY.

AFTER WE HEAR FROM SANDRA AND ROB, WE'LL HAVE SOME TIME TO ASK QUESTIONS, THEN I WOULD LIKE TO GO BACK TO SORT OF ISSUES FROM THIS MORNING. UNFORTUNATELY JOHN WAGNER HAD TO LEAVE, BUT I THINK HIS TALK RAISED A LOT OF ISSUES THAT WE MAY WANT TO ADDRESS AS A STANDARDS WORKING GROUP IN TERMS OF ETHICAL AND POLICY ISSUES, REGULATORY ISSUES REGARDING PHASE I CLINICAL TRIALS INVOLVING STEM CELLS. I WANT TO MAKE SURE WE THINK THROUGH THAT AS WE'RE GOING THROUGH OUR SORT OF PRIORITIZATION FOR WHAT WE WANT TO DO THIS YEAR.

FIRST LET ME THANK SANDRA AND ROB AND THEIR COMMITTEE FOR WHAT I THINK IS A TERRIFIC REPORT, OBVIOUSLY A LOT OF HARD WORK. THEY PUT IT TOGETHER IN ADMIRABLE FASHION, AND I ACTUALLY THINK THIS WILL BE QUITE USEFUL AND HAVE A MAJOR IMPACT. SANDRA, THANKS FOR FLYING OUT HERE AS WELL.

DR. CARSON: THANKS. IT'S REALLY A PLEASURE TO BE HERE, AND THIS IS TRULY THE RESULTS

OF THE COMMITTEE, ESPECIALLY THIS PRESENTATION. ROB DID THE SLIDES, AND I'M PRESENTING THEM TO YOU. SO THIS IS TRULY A RESULT OF EVERYBODY'S INPUT.

WHAT I'D LIKE TO DO TODAY IS TELL YOU THE CHARGE TO THE COMMITTEE, TO TELL YOU A LITTLE BIT ABOUT IVF BECAUSE I KNOW THE GROUP IS VERY HETEROGENEOUS, AND PERHAPS YOU MIGHT NOT KNOW THE MEDICAL PROCEDURE THAT THESE DONORS ACTUALLY INCUR TO DONATE EGGS, AND THEN CONCLUDE TO TELL YOU WHAT WE CAME UP WITH.

THE COMMITTEE ITSELF WAS COMPOSED OF MYSELF AND ROB AND DR. DAVID ESCHENBACH, WHO WAS THE CHAIRMAN OF THE DEPARTMENT OF OB-GYN IN WASHINGTON AND AN EXPERT IN INFECTIOUS DISEASE. VALERIE MONTGOMERY RICE IS THE DEAN AT MEHARRY MEDICAL COLLEGE AND IS A REPRODUCTIVE ENDOCRINOLOGIST. MARK SAUER IS AT COLUMBIA AND IS A REPRODUCTIVE ENDOCRINOLOGIST AND HAS LARGE, EXTENSIVE EXPERIENCE IN OOCYTE DONATION; AND, OF COURSE, ROB YOU ALL KNOW.

AND GEOFF HAS BEEN WONDERFUL IN HELPING US COLLATE EVERYBODY'S ADVICE AND COME UP WITH OUR FINAL RECOMMENDATION.

THE COMMITTEE CAME ABOUT BECAUSE CIRM

HAD COMMISSIONED THE INSTITUTE OF MEDICINE OF THE NATIONAL ACADEMY OF SCIENCES TO CONVENE A WORKSHOP ENTITLED "ASSESSING RISKS OF OOCYTE DONATION FOR STEM CELL RESEARCH." AND THE IOM REPORT CAME UP WITH PREDOMINANTLY TWO PRINCIPLES. ONE IS THAT WE NEEDED TO MINIMIZE THE MEDICAL RISK IN OOCYTE DONORS BECAUSE THEY VIRTUALLY HAD NO DIRECT BENEFIT, BUT RATHER HAD A BENEFIT TO SOCIETY AND TO MEDICAL RESEARCH, BUT NOT ON A PERSONAL ONE-TO-ONE LEVEL, AND THAT THERE WERE NO GUIDELINES SUBMITTED BY THE IOM REPORT AS TO HOW TO DO THIS.

SO CIRM DECIDED THAT WHAT YOU REALLY NEEDED TO DO WAS COME UP WITH A COMMITTEE TO LOOK AT HOW TO MINIMIZE THE RISK IN OOCYTE DONORS FOR RESEARCH. AND THE CHARGE TO OUR COMMITTEE WAS TO DEVELOP THESE RECOMMENDATIONS, RECOMMENDATIONS WHICH WOULD PROTECT OOCYTE DONORS FROM OVARIAN HYPERSTIMULATION; THAT IS, WHEN THE OVARIES GET LARGE ENOUGH TO RESULT IN FLUID COLLECTION IN THE ABDOMEN AND THE PLEURAL SPACE, ASCITES AND PLEURAL EFFUSION, AND CAUSE HEMOCONCENTRATION AND ITS SIDE EFFECTS, AS WELL AS TO BRING UP WHAT OTHER ACUTE COMPLICATIONS MIGHT BE INCURRED WITH OOCYTE DONATIONS, AND THAT WE WERE ALSO CHARGED WITH

DEVELOPING GUIDELINES BASED UPON THE BEST EVIDENCE WE HAD, EVIDENCE FROM PEER REVIEW JOURNALS, FROM CLINICAL JUDGMENT, AND FROM THE BEST PRACTICES THAT WE'VE USED IN THE LAST 25 YEARS OF TAKING CARE OF WOMEN WHO DONATE THEIR OOCYTES.

NOW, THE GUIDING PRINCIPLES THAT WE USED WERE, FIRST, WE ASSUMED THAT SCNT WAS PRACTICAL FOR THE DEVELOPMENT OF NEW HUMAN EMBRYONIC STEM CELL LINES. ALTHOUGH THIS ASSUMPTION MAY OR MAY NOT BE TRUE AND NEEDS FURTHER CONSIDERATION BY YOUR COMMITTEE, IN ORDER TO DEVELOP THESE GUIDELINES, WE ASSUMED THAT, IN FACT, IT WOULD BE PRACTICAL AND THAT YOU WOULD NEED OOCYTE DONORS. AS I SAID EARLIER, OOCYTE DONORS FOR OTHER RESEARCH ARE AWFULLY IMPORTANT AND THAT YOU WILL REALLY LEAD THE NATION IN PROTECTING THESE WOMEN WHO WILL DONATE THEIR OOCYTES FOR REASONS OTHER THAN SCNT.

WE ALSO REALIZED, AGAIN, THAT THERE WAS LITTLE DIRECT ONE-TO-ONE BENEFIT TO THE OOCYTE DONORS, AND THAT WE HAD TO MINIMIZE THE ACUTE AND LONG-TERM RISKS THAT THESE WOMEN INCURRED. AND SO OUR CHARGE, ONCE AGAIN, WAS TO DEVELOP GUIDELINES, NOT STRICT RULES, BUT GUIDELINES THAT WOULD ALLOW SOCIETIES AND ORGANIZATIONS THAT ACTUALLY

DEVELOPED MEDICAL AND ETHICAL STANDARDS FOR THEIR MEMBERS TO LOOK BACK AND USE THESE GUIDELINES IN DEVELOPING THOSE CLINICAL STANDARDS.

THERE ARE A LOT OF ORGANIZATIONS, FOR EXAMPLE, THE AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE, THAT DO WRITE ETHICAL AND MEDICAL STANDARDS FOR CLINICAL PRACTICE, BUT OFTENTIMES HAVE LITTLE EXPERIENCE TO GO BACK ON EXCEPT WHAT THEY HEAR FROM THEIR OWN MEMBERS. AND SO WE FELT THAT THIS WAS, INDEED, AN OPPORTUNITY TO SET THE GUIDELINES FOR PROFESSIONAL ORGANIZATIONS AS WELL.

ALSO, THE GUIDELINES, THE PURPOSE OF THE GUIDELINES WERE TO ASSIST THE CIRM INVESTIGATORS IN STUDY DESIGN AND TO HELP INSTITUTIONAL REVIEW BOARDS EVALUATE THE PROTOCOLS THAT THEY WERE GOING TO INCUR FOR CARRYING ON THE RESEARCH THAT CIRM FUNDS.

NOW, WHEN WE TOOK ABOUT THE -- WHEN WE LOOKED AT DEVELOPING THE FRAMEWORK OF GUIDELINES FOR RISK REDUCTION, WE WANTED TO CONSIDER TWO PRINCIPLES. ONE WAS TO HELP THE INVESTIGATOR SELECT PATIENTS THAT HAD A HIGH CHANCE OF SUCCESSFULLY PROVIDING ENOUGH EGGS THAT WOULD GIVE THIS STUDY A REALISTIC NUMBER. ALSO, WE WANTED TO CHOOSE PATIENTS OR DONORS THAT HAD A LOW

PROBABILITY OF ADVERSE EVENTS.

SO IN DOING THIS, THE COMMITTEE RECOMMENDED A FOUR-POINT FRAMEWORK. ONE WAS TO BEGIN WITH SCREENING AND SELECTION OF DONORS WHO WOULD, ONE, PROVIDE A GOOD NUMBER OF EGGS AND, TWO, HAVE MEDICAL DISEASES, IF YOU WOULD, OR CONDITIONS THAT WOULD PUT THEM AT LEAST RISK.

THE SECOND WAS TO LOOK AT THE POINTS IN OVULATION INDUCTION WHERE WE WOULD MINIMIZE THE RISKS OF COMPLICATIONS BY TREATING THESE PATIENTS WITH THE LEAST AMOUNT OF DRUGS THAT WOULD SUCCESSFULLY ALLOW A PRACTICAL COHORT OF EGGS TO BE ASPIRATED. AND THEN, OF COURSE, WANTED TO LOOK CLOSELY AT ASPIRATION AND MINIMIZE THE MEDICAL RISKS OF ASPIRATION.

AND, FINALLY, LOOK AT WHAT ASPECTS OF IMMEDIATE FOLLOW-UP AFTER THE PROCEDURE WE NEEDED TO ADDRESS IN ORDER TO MAKE SURE THAT THE DONOR CONTINUED ON TO HER UNSTIMULATED HEALTHY FERTILE LIFE.

NOW, LET ME TELL YOU A LITTLE BIT, IN CASE YOU DON'T KNOW, JUST ABOUT HOW WE STIMULATE A DONOR, REALLY HOW WE DO IVF. THIS IS JUST AN ULTRASOUND THAT'S ACTUALLY DONE THROUGH THE ABDOMEN OF A PATIENT EARLY IN HER MENSTRUAL CYCLE.

THIS BIG BLACK AREA IS THE BLADDER AND HERE IS THE UTERUS, AND THIS AREA IS THE RIGHT OVARY AND THE LEFT OVARY. NOW, IF YOU WILL WATCH THIS RIGHT OVARY, THIS PATIENT WAS GIVEN OVULATION INDUCTION. AND AFTER ABOUT FIVE DAYS YOU CAN SEE FOLLICLES, FLUID-FILLED CYSTS THAT DEVELOP ON THAT RIGHT OVARY. AFTER ABOUT SEVEN OR EIGHT DAYS, THOSE FLUID-FILLED CYSTS GET LARGER. AND FINALLY, THEY'RE AT THEIR LARGEST JUST BEFORE OVARIAN ASPIRATION.

WHAT WE DO IS UNDER ULTRASOUND GUIDANCE, AND THIS IS A TRANSVAGINAL ULTRASOUND WITH A VAGINAL PROBE THAT HAS A NEEDLE ON IT AND IT HAS A NEEDLE GUIDE. THE NEEDLE IS PUT THROUGH THE VAGINA INTO THE OVARY, AND WE USE CONSCIOUS SEDATION. THE PATIENT DOES NOT HAVE TO GO TO SLEEP FOR THIS PROCEDURE. THE EGG IS ASPIRATED THROUGH THIS NEEDLE AND IT'S SUCTIONED INTO THIS TRAP. AND THEN THIS FLUID-FILLED TUBE IS PASSED OVER INTO THE LAB, ALL DONE UNDER STERILE TECHNIQUE, AND THE EGGS ARE IDENTIFIED AS WE DO THE PROCEDURE. SO THE PATIENT, THE DONOR, KNOWS HOW MANY EGGS SHE'S GETTING AS SHE'S GETTING THEM, IF SHE'S AWAKE ENOUGH TO HEAR THAT.

AND YOU CAN SEE THAT HERE'S THE DOTTED

LINE, AND THIS IS THE NEEDLE GOING INTO THAT OOCYTE, AND WE SIMPLY SUCTION VERY GENTLY. THE FLUID COMES OUT, AND THE EGG IS IDENTIFIED IN THE LAB.

THIS IS A HUMAN EGG. IT'S THE LARGEST CELL IN THE HUMAN BODY, ABOUT 90 MICRONS IN DIAMETER. THE CELLS AROUND IT ARE CALLED THE CORONA RADIATA. AND NOW, AT THIS POINT THIS IS AS FAR AS THE OOCYTE DONOR WOULD GO. LET ME JUST SHOW YOU, FOR THOSE OF YOU WHO DON'T KNOW, WHAT HAPPENS IN ACTUAL IN VITRO FERTILIZATION. WE MIX THE EGG WITH SPERM IN A PETRIE DISH. I DON'T KNOW WHY IT'S BEEN CALLED A TEST TUBE BABY. IT'S NEVER REALLY IN A TEST TUBE. AND THEN 18 HOURS LATER, IT TAKES 18 HOURS TO FERTILIZE THE HUMAN EGG, WE CAN SEE THE SPERM CONTRIBUTION OF THE CHROMOSOMES AND THE EGG'S CONTRIBUTION AND THE SPERM CONTRIBUTION. THE EGG'S NUCLEUS IS A LITTLE BIT BIGGER. AND THEN AT 24 HOURS THE FIRST CELLULAR DIVISION OCCURS.

THIS IS ACTUALLY -- THIS ACTUALLY, AS YOU CAN SEE, IS A LITTLE BOY, A MALE EMBRYO THAT WAS BORN AS A LITTLE BOY, AND IS NOW 25 YEARS OLD AND LIVING IN CHICAGO. BUT THIS IS A FOUR-CELL EMBRYO; BUT BECAUSE YOU CAN'T SEE THE

THREE-DIMENSIONAL NATURE OF THIS, IT'S HARD TO SEE THE OTHER CELLS. YOU CAN SEE THE TOP OF THE THIRD CELL DOWN HERE AND THEN THE OTHER FOURTH CELL IS ABOVE IT.

MS. CHARO: IT DID LOOK A LITTLE BIT LIKE A SNOWSTORM IN CHICAGO.

DR. CARSON: THIS IS AN EMBRYO AFTER FIVE DAYS. THIS EMBRYO WAS ACTUALLY LAVAGED FROM A HUMAN UTERUS 15 YEARS AGO, AND ALSO YOU CAN SEE THIS IS A MALE AS WELL. AND IT'S, I BELIEVE, A 15-YEAR-OLD BOY IN LOS ANGELES. NOW, THIS IS A FIVE-DAY EMBRYO. WE CULTURE THESE. THIS IS A BLASTOCYST. THIS IS THE INNER CELL MASS, WHICH WILL DEVELOP INTO THE EMBRYO AND -- I MEAN INTO THE FETUS AND THE BABY. AND ALL THESE CELLS AROUND HERE ARE THE TRIFECTODERM WHICH WILL DEVELOP INTO THE PLACENTA. THESE CELLS, THE INNER CELL MASS ARE THE CELLS THAT EVERYBODY TALKS ABOUT. THEY ARE HUMAN EMBRYONIC STEM CELLS WHEN THEY'RE REMOVED AND CULTURED.

SO COMING BACK NOW TO THE EGG DONOR, SHE WILL UNDERGO, OF COURSE, A MEDICAL HISTORY/PHYSICAL, THE OVULATION INDUCTION, THE STIMULATION THAT I TOLD YOU ABOUT, THE ASPIRATION, AND THEN IT STOPS FOR HER.

SO WE LOOKED AT THESE FOUR POINTS. FIRST, THE EXCLUSION FROM MEDICAL HISTORY, AND WE SUGGESTED THAT THESE WOMEN CHOSEN TO DONATE THEIR OOCYTES NOT BE CHOSEN IF THEY HAD HISTORIES OF DISEASES THAT WOULD PUT THEM AT RISK FOR CLOTTING AND FOR HYPERSTIMULATION, SUCH AS POLYCYSTIC OVARIAN DISEASE, SUCH AS A HISTORY OF PELVIC INFECTION. WE ALSO SUGGESTED SOME EXCLUSION DIAGNOSTIC CRITERIA THAT WOULD, ONE, MINIMIZE THEIR RISK OF INFECTION, SUCH AS HAVING HYDROSALPINX, WHICH IS A FLUID-FILLED TUBE THAT MIGHT LEAD TO PELVIC INFECTION, AND ALSO WOULD INCREASE THEIR CHANCES OF DEVELOPING A LOT OF EGGS. AND THAT IS, IF A PATIENT HAD AN ELEVATED AMH OR HAD AN ELEVATED FSH, SUGGESTING THAT PERHAPS THEY WOULD NOT BE GOOD EGG DONORS.

IN ADDITION, IF THEY WERE OLDER, HAD ADVANCED AGE, OR HAD AN ELEVATED BODY MASS INDEX, THEY MIGHT NOT BE GOOD EGG DONORS AND ALSO WITH AN ELEVATED BODY MASS INDEX MIGHT INCUR SOME RISKS AT ASPIRATION. SO OUR FIRST POINT WAS, BY USING SELECTION CRITERIA AND EXCLUSION CRITERIA, PICK THE POPULATION OF DONORS THAT WOULD BE AT LEAST RISK.

AND THEN WE DEVELOPED RECOMMENDATIONS TO

DOSE GENTLY THE OVULATION INDUCTION DRUGS THAT WE GAVE TO SUGGEST WE GET SOME EGGS, SOME FOLLICULAR DEVELOPMENT THAT I SHOWED YOU, BUT YET HAVE BUILT-IN CRITERIA TO STOP A HYPER RESPONSE. SO AS WE'RE MONITORING THE PATIENTS WITH ULTRASOUNDS AND BLOOD TESTS FOR ESTROGEN, WE WOULD STOP IF WE FELT THE PATIENT WAS BECOMING AT RISK, HIGHER RISK FOR HYPERSTIMULATION. AND ALSO WE WOULD STOP IF SHE DIDN'T DEVELOP A LOT OF EGGS.

NOW, LET ME TELL YOU THAT 25,000 BABIES ARE BORN EACH YEAR IN THE UNITED STATES, AND THIS IS NOT SOMETHING THAT MOST PRACTITIONERS DON'T DO EVERY SINGLE DAY MANY, MANY TIMES. AND SO MANY OF THESE CRITERIA ARE ALREADY BEING DONE, AND IT'S BEING DONE WITH EGG DONORS, SO THIS IS NOT ANYTHING NEW. WE JUST PERHAPS LIFTED IT A LITTLE BIT MORE TO MAKE SURE THAT THESE EGG DONORS WERE PROTECTED AGAINST THE RISKS TO REALLY MINIMIZE THE RISK OF HYPERSTIMULATION.

NOW, WHEN YOU PUT A NEEDLE THROUGH THE VAGINA, WHICH HAS A LOT OF BACTERIA, AND INTO THE OVARY, YOU ARE AT RISK OF INFECTION AND ARE AT RISK FOR BLEEDING. AND SO WE BUILT IN SOME CRITERIA THAT WOULD MINIMIZE THAT RISK. AND, AGAIN, THE CHANCES OF THAT ARE VERY, VERY LOW.

THIS IS HAPPENING RIGHT NOW AS WE SPEAK, I'M SURE, IN A THOUSAND WOMEN EASILY RIGHT AT THIS MOMENT. AND THERE ARE VERY FEW CHANCES OF INFECTION AND BLEEDING. AND WHEN YOU SELECT WOMEN WHO, ONE, DON'T HAVE A HISTORY OF PELVIC INFECTION, WHO DON'T HAVE ENDOMETRIOMAS ON THEIR OVARY, AND WHO DON'T HAVE FLUID IN THEIR TUBE, THAT RISK FURTHER DECREASES.

AND THEN THE FOURTH POINT WAS TO FOLLOW THE PATIENT OR THE DONOR IMMEDIATELY AFTER FOLLOW-UP. TWO WEEKS AFTER SHE HAS HER EGGS REMOVED, SHE WILL GET HER MENSTRUAL PERIOD. AND SO AT THAT TIME WE WOULD ASK HER TO CALL IF SHE BLEEDS BEFORE THOSE TWO WEEKS OR WE RECOMMEND THAT A CALL BE MADE TO HER IN THESE PROTOCOLS SO THAT WE KNOW THAT SHE'S OKAY AND IS ON HER WAY TO ONCE AGAIN HER REGULAR MENSTRUAL PERIODS.

THE IOM REPORT ALSO BROUGHT UP THE FACT THAT RIGHT NOW THERE WAS REALLY AN ABSENCE OF REGISTRIES TO FOLLOW UP FOR OOCYTE DONORS, AND IT WAS LARGELY BECAUSE, IN GENERAL, THERE AREN'T VERY MANY, ESPECIALLY COMPARED TO OTHER POPULATIONS OF INFERTILE WOMEN, SUCH AS WOMEN UNDERGOING IVF ITSELF. AND BECAUSE OF THAT VERY SMALL COHORT, ESPECIALLY OF FERTILE WOMEN, WE REALLY CANNOT

TRACK IN ANY MEANINGFUL WAY THE LONG-TERM RISKS THAT WOMEN MAY INCUR WHO UNDERGO THESE DRUGS.

WE KNOW THAT INFERTILE WOMEN, WHEN THEY TAKE THESE DRUGS OVER A LONG PERIOD OF TIME, ARE NOT AT RISK FOR CANCER, NOT THESE. AND WE KNOW AND WE FEEL QUITE SAFE IN OUR KNOWLEDGE THAT WE CAN TELL INFERTILE WOMEN THAT THEY DON'T HAVE ANYTHING TO WORRY ABOUT LONG TERM. HOWEVER, WE DON'T HAVE THE SAME CONFIDENCE SIMPLY BECAUSE WE DON'T HAVE THE SAME NUMBERS IN FERTILE WOMEN. THE STEM CELL RESEARCH AND EGG DONOR RESEARCH AS IT ADVANCES MAY ALLOW US TO HAVE A LARGER COHORT OF WOMEN AND MAY ALLOW A REGISTRY THAT PROVIDES REAL NUMBERS AND THAT CAN LEAD TO VERY VIABLE CONCLUSIONS.

SO, IN SUMMARY, WE FELT THAT THESE GUIDELINES WERE PRECAUTIONARY. THEY SHOULD NOT BE STRINGENT. THE INVESTIGATORS THAT ARE GOING TO BE FUNDED BY YOU ARE WELL-EXPERIENCED REPRODUCTIVE ENDOCRINOLOGISTS WHO DO THIS EVERY DAY, BUT SHOULD BE REMINDED ALSO EVERY DAY THAT THE RISK TO OOCYTE DONATION MUST BE VIRTUALLY ZERO. AND THE RECOMMENDATIONS THAT WE MADE WERE BASED ON THE BEST EVIDENCE AND PRACTICE THAT WE HAVE IN 2008, BUT THAT DOESN'T MEAN WE SHOULD STOP HERE OR BE

SATISFIED YEAR AFTER YEAR WITH THESE, AND THAT WE SHOULD MONITOR ONGOING DEVELOPMENTS AS THEY WILL LIKELY GENERATE NEW EVIDENCE AND WARRANT REEVALUATION AS WE DO THIS.

AND I WANT TO SHOW YOU A PICTURE OF THAT FOUR-CELL EMBRYO. I'D BE HAPPY TO ANSWER ANY QUESTIONS. ROB, DO YOU HAVE ANY ADDITIONS?

DR. TAYLOR: NO. THAT'S GREAT.

(APPLAUSE.)

DR. PRIETO: JUST WONDERED IF WE HAVE A ROUGH IDEA HOW MANY WOMEN HAVE UNDERGONE OOCYTE DONATION.

DR. CARSON: THAT IS KNOWN. I DON'T KNOW THAT NUMBER. IT CAN BE GOTTEN AT WWW.CDC.GOV AT THE /CDCSART WEBSITE. I DON'T KNOW WHAT IT IS. I JUST CAN'T REMEMBER.

I WOULD SAY IT WOULD BE -- MY BALLPARK FIGURE WOULD BE PROBABLY ABOUT A THOUSAND PER YEAR, AND IT HAS BEEN DONE SINCE 1988.

DR. CIBELLI: I HAVE TWO QUESTIONS. FIRST ONE, IF CAN YOU GO BACK TO THIS SLIDE WHERE YOU SHOW THE PROCEDURE. CAN YOU POINT ME TO THE PLACES WHERE THESE GUIDELINES DIFFER FROM WHAT YOU DO TODAY FOR A NORMAL? I'D LIKE TO KNOW THE SPECIFICS.

DR. CARSON: LET'S GO TO THE VERY TOP. A SINGLE OVARY IS NOT A LIMITATION TO IN VITRO FERTILIZATION OR TO DONATING FOR ANOTHER FERTILE WOMAN.

DR. CIBELLI: I'M JUST REFERRING TO A DONATION.

DR. CARSON: A SINGLE OVARY DOES NOT LIMIT AN OOCYTE DONOR FROM DONATING TO ANOTHER WOMAN. A PREVIOUS HISTORY OF OVARIAN HYPERSTIMULATION IS A RELATIVE CONTRAINDICATION TO OOCYTE DONATION.

DR. TAYLOR: THROMBOPHILIA HISTORY DOESN'T NECESSARILY RULE OUT --

DR. CARSON: THAT'S CORRECT.

MR. KLEIN: WHAT WAS THAT LAST COMMENT?

DR. CARSON: LET'S GO THROUGH ALL OF THEM. THROMBOSIS, BLEEDING DIATHESIS, FAMILIAL THROMBOPHILIA DOES NOT NECESSARILY RULE OUT A CLINICAL DONOR. LET'S CALL THOSE CLINICAL DONORS. UNCONTROLLED HYPERTENSION, DIABETES, AND ASA 3 ANESTHETIC RISK IS NOT A STATED CONTRAINDICATION FOR CLINICAL DONATION, BUT IT WOULD BE -- I DON'T THINK ANYBODY WOULD ACTUALLY DO THAT. AND IT WOULD BE UNDER THE REALM OF CHRONIC MEDICAL DISEASES, WHICH IS STATED, BUT WE'RE MORE EXPLICIT

IN THIS. ESTROGEN SENSITIVE CANCERS WOULD PROHIBIT A CLINICAL DONOR. HISTORY OF PELVIC INFLAMMATORY DISEASE REQUIRING HOSPITALIZATION DOES NOT LIMIT A CLINICAL DONOR.

FOR THE EXCLUSION DIAGNOSIS --

MR. KLEIN: BEFORE YOU GO TO THE SECOND CATEGORY, COULD WE ASK A QUESTION ON THE FIRST CATEGORY? IF WE WANT -- IF AT SOME POINT DOWNSTREAM WE WERE GOING TO TRY, I MEAN WITH MORE PROOF THAT SCNT WERE ABLE TO BE ACCOMPLISHED EFFECTIVELY, WOULDN'T WE WANT PEOPLE WITH DIABETES TO BE OOCYTE DONORS SO WE COULD CREATE DISEASE-SPECIFIC CELL LINES? AND SO MY QUESTION IS IF WE'RE GOING TO ELIMINATE PEOPLE WITH CHRONIC DISEASE AS OOCYTE DONORS, AREN'T WE THEN DEFEATING ONE OF OUR FUTURE GOALS, ASSUMING THAT WE CAN GET ADEQUATE PROOF THAT WE CAN EFFICIENTLY DO SCNT?

DR. CARSON: REMEMBER THAT THE DISEASE IS GOING TO BE COMING FROM THE NUCLEUS THAT YOU PUT INTO THIS EGG. THIS EGG IS GOING TO HAVE ITS NUCLEUS REMOVED.

MR. KLEIN: BUT IN THE CYTOPLASM THERE'S NO CONTRIBUTIONS? I THINK THERE'S A DEBATE ABOUT THIS ISSUE, ISN'T THERE?

DR. CARSON: NOT THAT I KNOW OF. GEOFF,

DO YOU WANT TO ANSWER THAT OR ROB?

DR. LOMAX: I WAS JUST GOING TO REFRESH. I THINK THIS WAS TOUCHED ON IN THE COMMITTEE DELIBERATIONS, AND IT'S IN THE INITIAL SORT OF FRAMING OF THE GUIDELINES WHERE I THINK THERE IS REFERENCE TO THE IDEA THAT ONE HAS TO CONTINUE TO EVALUATE THE RISK-BENEFIT ANALYSIS, AND THAT THAT WOULD, PRESUMING, BOB, THAT THAT WOULD BE A CASE WHERE THE BENEFIT THEN SHIFTS BECAUSE YOU HAVE AN EFFICACIOUS --

MR. KLEIN: I WANT TO ASK THE SCIENTIFIC QUESTION. DOWN AT THE OTHER END SOMEONE MIGHT ANSWER.

DR. EGGAN: BUT I CAN ALSO. JUST TO SAY ONE COULD IMAGINE A NUMBER OF STEM CELL PROTOCOLS THAT DON'T NECESSARILY INVOLVE SOMATIC CELL NUCLEAR TRANSFER WHICH MIGHT INVOLVE EGG DONATION TO MAKE A STEM CELL LINE WHICH HAS A PARTICULAR GENOTYPE. IT MIGHT BE DESIRABLE UNDER THOSE CIRCUMSTANCES TO HAVE THE EGG DONOR BE THE PERSON WHO HAS THE DISEASE GENOTYPE. JUST, FOR INSTANCE, DO IVF TO CREATE AN EMBRYO WITH A PARTICULAR GENOTYPE AND THEN DERIVE A STEM CELL FROM IT. THIS GOES AGAINST ASRM GUIDELINES, BUT IT IS NOT STRICTLY PROHIBITED BY NAS GUIDELINES FOR STEM

CELL RESEARCH AND IS SOMETHING YOU COULD IMAGINE DOING.

BUT FOR THE DISEASES I WOULD IMAGINE, NONE OF THESE THINGS SEEM TO STAND IN THE WAY OF THAT PARTICULARLY.

DR. CARSON: THAT'S A GOOD POINT. THE POINT IS, LET ME JUST SUMMARIZE, SO IF A WOMAN HAS DIABETES AND HER EGGS ARE GOING TO BE FERTILIZED WITH HER NUCLEUS AND THEN STEM CELLS FROM THAT DIABETIC'S NUCLEUS, THEN, YES. BUT I THINK THAT RIGHT NOW THAT'S PROBABLY NOT THE MODEL THAT IS BEING USED. RATHER, THAT THE WOMAN WHO'S THE DIABETIC GIVES UP A SOMATIC CELL NUCLEUS TO AN EGG DONOR'S EGG WHOSE NUCLEUS HAS BEEN REMOVED AND EMBRYOS MADE FROM THAT, OR THAT THAT DIABETIC HOPEFULLY GIVES UP HER SOMATIC CELL; AND THEN WHEN THAT NUCLEUS IS REPLACED AND ONE GETS THE STEM CELLS, THEN A GENE FOR INSULIN CAN BE INSERTED AND SHE MAKES HER OWN INSULIN IN VITRO.

MR. KLEIN: I'M WITH YOU ON THE FUNDAMENTAL MODEL. I'M CONCERNED ABOUT THIS OTHER REFINEMENT OF THE ARGUMENT. I THINK THERE'S INDIVIDUALS AT THE OTHER END.

DR. TAYLOR: I WAS JUST GOING TO SAY THAT WE REALLY SORT OF SAW THIS AS A FIRST PASS,

AND WE WANTED TO HAVE WHAT WE THOUGHT WERE THE KIND OF SAFEST GENERALIZABLE GUIDELINES FOR JUST ESTABLISHING REALLY WHETHER SCNT WAS GOING TO BE A PRACTICABLE APPROACH. I AGREE THAT IF SOMEBODY WANTS TO UNDERSTAND THE SORT OF MITOCHONDRIAL CONTRIBUTION TO DIABETES, THAT YOU'D REALLY WANT TO HAVE THE EGG DERIVED FROM THAT INDIVIDUAL. WE REALLY DID TRY TO BUILD INTO THE END OF OUR RECOMMENDATIONS HERE A LOT OF FLEXIBILITY THAT -- FRANKLY, WHEN WE STARTED THIS, EVEN THE IPS STORY WAS JUST STARTING TO BREAK OUT IN THE MOUSE MODEL. WE DIDN'T REALLY KNOW IT WAS GOING TO BE APPLICABLE IN THE HUMAN. SO THIS IS REALLY A MOVING TARGET, AND I THINK WE WANTED TO BE AS FLEXIBLE AS POSSIBLE.

THESE GUIDELINES ARE REALLY TO TRY TO BE AS SAFE AS POSSIBLE UP FRONT TO TRY TO REDUCE THE RISKS OF WOMEN SO A DIABETIC, A HYPERTENSIVE, THINGS THAT WE'RE ULTIMATELY GOING TO BE INTERESTED IN KNOWING MORE ABOUT WOULDN'T BE THE FIRST ONES TO SORT OF GET STUDIED IN THE SETTING.

DR. CIBELLI: I'M GOING TO ADD TO THAT, THAT WE ALL KNOW AND ARE AWARE THAT MANY OF THE DISEASES, ACTUALLY THEIR ORIGIN IS NOT EXCLUSIVELY GENETIC DUE TO A GENE, BUT EPIGENETICS. SO I

WOULD ARGUE THAT WHAT MR. KLEIN WAS SAYING ACTUALLY MAKES SENSE, AT LEAST JUST TO SEE -- TO ANSWER THE QUESTION WHETHER THE ENVIRONMENT OF THE OOCYTE WILL HAVE AN EFFECT. SO YOU COULD THINK OF AN EXPERIMENT OF TAKING A NORMAL PERSON THAT NEVER DEVELOPED DIABETES AND USE OOCYTES FROM A PERSON THAT IS KNOWN TO HAVE DIABETES AND SEE IF THAT CAN BE ONE OF THE CAUSES.

DR. CARSON: THANK YOU.

LET'S GO ON TO OUR EXCLUSION DIAGNOSTICS. ADVANCED AGE IS A LIMITATION TO CLINICAL DONORS. BODY MASS INDEX DEPENDS ON THE PROGRAM. IT IS NOT -- I THINK THAT MOST PROGRAMS PROBABLY HAVE THEIR OWN BODY MASS INDEX LIMITATION, BUT WE DECIDED THIS WOULD BE THE MOST CONSERVATIVE FOR THIS GROUP. ELEVATED OR DIMINISHED ANTIMALARIAN HORMONE, AGAIN, THAT IS NOT WIDELY USED, BUT WE FELT THAT IT WOULD -- RIGHT NOW IT WAS THE BEST CLINICAL PROTECTOR AGAINST HYPERSTIMULATION.

DR. CIBELLI: IS THERE A NUMBER?

DR. CARSON: WELL, THAT IS IN -- ALL OF THESE GUIDELINES, WE WERE VERY CAREFUL NOT TO GIVE A NUMBER BECAUSE WE WANTED EACH INVESTIGATOR WHO -- THIS PARTICULAR ASSAY IS BASED ON THE KIT,

THE ELISA KIT THAT IS USED. THERE IS ONE NUMBER IN EUROPE THAT IS USED WHICH IS A LITTLE DIFFERENT FROM THE NUMBER IN THE ASSAY USED IN NEW YORK, AND THAT EACH INVESTIGATOR WHO USES THIS WILL KNOW IN THEIR OWN GROUP WHAT THEY CAN USE TO JUDGE PATIENTS.

SO WE WERE -- THE SAME THING WITH ADVANCED AGE. WE REALLY DIDN'T WANT TO SET A NUMBER BECAUSE, AGAIN, THESE ARE VERY EXPERIENCED REPRODUCTIVE ENDOCRINOLOGISTS, AND THEY WILL KNOW WHAT THEIR IDEA OF ADVANCED AGE AND BODY MASS INDEX IN THEIR PROGRAM IS.

DR. CIBELLI: I WOULD ARGUE THAT AT SOME POINT WE WILL HAVE TO HAVE NUMBERS, AT LEAST RELATIVE NUMBERS, TO SAY, OKAY, FOR AMH WE'D LIKE TO HAVE WHATEVER IS ABOVE 30 PERCENT OR 40 PERCENT OF WHAT AVERAGE YOU HAVE. REMEMBER, WE'RE NOT -- I'M NOT A DOCTOR, SO I HAVE NO IDEA WHAT IS A GOOD NUMBER OR A BAD NUMBER.

DR. CARSON: GOOD POINT.

DR. TAYLOR: I WAS JUST GOING TO SAY I THINK FOR AMH AT THIS POINT WE DON'T EVEN REALLY KNOW OURSELVES WHAT THE RIGHT NUMBERS ARE. AGAIN, WE WANTED TO PROVIDE SOME GENERAL GUIDELINES WITHOUT NECESSARILY MANDATING STRICT

RECOMMENDATIONS, ALTHOUGH IT MIGHT BE THAT, YOU KNOW, OUR CHARGE GETS ALTERED A LITTLE BIT, AND WE COULD BE MORE STRINGENT AND MORE PRECISE ABOUT THIS. WHEN WE GOT SORT OF FIVE PEOPLE TOGETHER IN THE SAME ROOM WHO HAD A REASONABLE AMOUNT OF KNOWLEDGE, IT WAS AWFULLY HARD TO COME UP WITH A CONSENSUS THAT EVERYBODY WAS HAPPY ABOUT.

MR. KLEIN: I'D JUST LIKE TO SAY I THINK THE IDEA OF NOT ASSIGNING THE NUMBERS AND LETTING THE JUDGMENT OF THE EXPERIENCED INVESTIGATOR OR THE EXPERIENCED DOCTOR, I'D ARGUE FOR THAT POINT OF VIEW BECAUSE WITH AGE, THE HEALTH OF THE WOMAN AND OTHER ISSUES MIGHT INTERPLAY WITH THEIR NOMINAL AGE. THEIR PHYSIOLOGICAL AGE MIGHT BE DIFFERENT THAN THEIR NOMINAL AGE. AND SO ASSIGNING -- CREATING A CODIFICATION OF THIS, I THINK, TAKES AWAY THE TRAINING AND EXPERIENCE OF THE PHYSICIAN ATTENDING THE PATIENT.

DR. CARSON: THANK YOU. ADVANCED ENDOMETRIOSIS IS ACTUALLY NOT A PROHIBITION FROM CLINICAL EGG DONATION AND IS LEFT TO CLINICAL JUDGMENT. AGAIN, I THINK THERE WOULD BE FEW REPRODUCTIVE ENDOCRINOLOGISTS THAT WOULD ACTUALLY ACCEPT THAT FOR CLINICAL DONATION.

ABNORMAL TUBO-OVARIAN MORPHOLOGY,

ESPECIALLY WITH A HYDROSALPINX, IS NOT A PROHIBITION FOR A CLINICAL DONATION, NOR IS FIBROIDS ON ULTRASOUND THAT MIGHT IMPACT RETRIEVAL SUCCESS. AND THE REASON FOR THAT IS THAT FOR CLINICAL DONATION OFTENTIMES THE DONOR WOULD AGREE TO UNDERGO LAPAROSCOPIC OR TRANSABDOMINAL ASPIRATION, AND WE DID NOT FEEL THAT THIS LITTLE BIT OF ADDED RISK SHOULD BE INCURRED BY AN EGG DONOR FOR RESEARCH.

A HIGH VAGINAL PH GREATER THAN 4.5, TO DECREASE IS NOT A LIMITATION FOR CLINICAL DONATION. PROBABLY SHOULD BE, BUT IS NOT. AND IT'S TO DECREASE THE RISK OF BACTERIAL VAGINOSIS AND WHAT EFFECT IT MIGHT HAVE ON ASCENDING CLINICAL INFECTION. VIRGINAL INTROITUS IS A LIMITATION ALSO FOR CLINICAL DONATION SIMPLY BECAUSE YOU CAN'T MONITOR SAFELY WITH ULTRASOUNDS.

MS. CHARO: I'M NOT SURE WHAT VIRGINAL INTROITUS IS.

DR. CARSON: IT MEANS AN INTROITUS NOT NECESSARILY RELATED TO INTERCOURSE, BUT RATHER INTROITUS THAT CANNOT COMFORTABLY ADMIT THE VAGINAL PROBE OR THE SPECULUM. ANYTHING ELSE?

DOSING, THE GENERAL RECOMMENDATION WAS STARTING AT 2 AMPS IF AGE LESS THAN 30, 3 IF AGE

30 TO 40. THIS IS PROBABLY JUST SLIGHTLY DECREASED FROM CLINICAL DONORS, BUT NOT THAT MUCH. THIS PROBABLY IS THE MOST VARIABLE IN TERMS OF RECOMMENDATIONS, AND THAT WOULD BE REALLY LEFT UP TO THE CLINICIAN. BUT I THINK THAT THIS IS A CONSERVATIVE APPROACH, BUT A GOOD ONE NONETHELESS.

AND MAINTAIN STARTING DOSE FOR AT LEAST THE FIRST FIVE DAYS OF STIMULATION, AND THAT IS ALSO THE CLINICAL DONOR REGIMEN. STOPPING DUE TO HYPER RESPONSE GREATER THAN A THOUSAND PICOGRAMS OF ESTRADIOL AND/OR MORE THAN TWENTY 12-MILLIMETER FOLLICLES ON DAY SIX, AS WELL AS AN ESTROGEN GREATER THAN 3,000 ON THE DAY OF HCG IS PROBABLY WITHIN KEEPING FOR CLINICAL DONATION, ALTHOUGH MIGHT BE A BIT CONSERVATIVE, ESPECIALLY THE ESTROGEN GREATER THAN 3,000, BUT IT'S CLOSE, IF NOT EXACT.

STOPPING BECAUSE OF HYPO RESPONSE, AN ELEVATED FSH, OR ESTRADIOL MAY PREDICT A POOR RESPONSE, AS WELL AS CONSIDERING CANCELLATION IF LESS THAN THREE ACTIVE FOLLICLES ARE GROWING. IT'S ALSO WITHIN KEEPING OF CLINICAL OOCYTE DONATION.

NOW, AT THE ASPIRATION, WE RECOMMENDED CONSCIOUS SEDATION UNDER THE CARE OF A BOARD

CERTIFIED ANESTHESIOLOGIST. THIS IS MUCH MORE CONSERVATIVE THAN CLINICAL OOCYTE DONATION. ASPIRIN-CONTAINING MEDICATIONS AND OTHER ANTI-PLATELET DRUGS, AVOIDING FOR UP TO TWO WEEKS PRIOR TO RETRIEVAL IS ALSO MUCH MORE CONSERVATIVE THAN IN CLINICAL OOCYTE DONATIONS. WE DID RECOMMEND NSAID'S BE USED FOR PAIN, AND THAT WAS IN KEEPING WITH CLINICAL OOCYTE DONATION.

DR. TAYLOR: JUST TO CLARIFY FOR THE PEOPLE THAT DON'T KNOW, TO REDUCE THE RISK OF BLEEDING, EXCESSIVE BLEEDING DUE TO ASPIRIN THERAPY. I GUESS THAT'S MAYBE CLEAR TO SOME.

DR. CARSON: IN TERMS OF SHORT-TERM SURVEILLANCE, IF THE DONOR CALLS WITH SYMPTOMS, SHE MUST BE SEEN, AND SHE SHOULD CALL WITH MENSES. IF SHE DOESN'T CALL, THEN WE WOULD CALL TWO WEEKS AFTER RETRIEVAL. AND, YES, THAT'S ALSO IN KEEPING WITH STANDARD CLINICAL CARE.

DR. CIBELLI: MY OTHER QUESTION WAS REGARDING HOW MANY TIMES A DONOR COULD BE CALLED TO DONATE OOCYTES.

DR. CARSON: I THINK ACTUALLY THIS IS SOMETHING THAT'S TALKED ABOUT ALL THE TIME. WE DIDN'T ADDRESS THAT IN OUR COMMITTEE. IN TERMS OF WHAT IS DONE CLINICALLY, ACTUALLY THE

RECOMMENDATION WAS ACTUALLY BASED ON POPULATION GENETICS. AND THE IDEA WAS THAT YOU DID NOT WANT TO HAVE A DONOR BE THE BIOLOGIC PARENTS OF SOMEONE WHO MARRIES -- OF TWO PEOPLE WHO MARRY EACH OTHER. SO BASED ON POPULATION GENETICS, THAT DEPENDS ON THE RISK -- THE SIZE OF THE REFERRAL POPULATION. SO IT DEPENDS ON THE SIZE OF THE CITY.

MS. CHARO: TRY THAT ONE AGAIN.

DR. CARSON: IF THE DONOR DONATES AN EGG AND THAT RESULTS IN A MALE, AND ALSO ANOTHER COUPLE DONATES AN EGG AND THAT RESULTS IN A FEMALE, 20 YEARS LATER YOU DON'T WANT THAT MALE AND FEMALE MARRYING EACH OTHER. SO BASED ON POPULATION GENETICS, THERE'S A MATHEMATICAL MODEL THAT WILL LIMIT THE AMOUNT OF PREGNANCIES THAT THAT DONOR HAS. AND SO IN THE CITY THE SIZE OF CHICAGO, THAT WOULD BE SOMEWHERE AROUND 15.

DR. CIBELLI: HOW ABOUT SAFETY REASONS, HEALTH OF THE DONOR?

DR. CARSON: THAT'S HOW THE CLINICAL NUMBER CAME UP. IN TERMS OF THE DONOR, WE DIDN'T ADDRESS THAT. THE MEDICAL RISK OF IN VITRO FERTILIZATION IS NOT ADDITIVE. SO EACH TIME A CYCLE IS INCURRED, THE MEDICAL RISK IS INDEPENDENT OF THE PRIOR CYCLE. THE ONLY THING THAT YOU MIGHT

CONSIDER MAY BE ADDITIVE IS, OF COURSE, THE OVULATION INDUCTION. BUT NOW USING GONADOTROPINS, NOT ANYTHING ELSE, JUST GONADOTROPINS THAT WE USE, IT'S BEEN SHOWN NOW FROM LARGE STUDIES FROM ISRAEL THAT THERE IS NO INCREASED RISK LATER IN LIFE TO WOMEN WHO RECEIVE GONADOTROPINS. HOWEVER, THESE ARE INFERTILE WOMEN. DON'T REALLY KNOW IN FERTILE WOMEN. WE ASSUME THAT IT'S THE SAME, BUT THAT MAY NOT BE.

DR. CIBELLI: TO GET TO THAT POINT THAT WE HAVE TO ASK YOU TO MAKE A RECOMMENDATION, WOULD YOU BE ABLE TO DO IT?

DR. CARSON: A RECOMMENDATION REGARDING?

DR. CIBELLI: REGARDING HOW MANY TIMES A DONOR CAN COME AND DONATE OOCYTES.

DR. CARSON: WELL, I THINK FOR RESEARCH PURPOSES, I WOULD SAY THAT, BECAUSE THE MEDICAL RISK IS NONADDITIVE, THAT WOULD BE UP TO HER.

DR. KIESSLING: I JUST LOOKED UP THE CDC NUMBERS. FOR 2004, EGG DONORS WERE 10 PERCENT OF THE TOTAL EGG COLLECTIONS.

DR. CARSON: SO THAT'S 2,000 THEN.

DR. KIESSLING: NO. IT'S TEN. SO THERE WERE 100,000 EGG COLLECTIONS OR 100,000 ART PROCEDURES, AND 10,000 WERE DONOR EGGS FOR 2004.

DR. CARSON: THAT PROBABLY INCLUDES FROZEN EMBRYO TRANSFER AS WELL.

DR. KIESSLING: FRESHLY FERTILIZED EMBRYOS. DONOR EGGS USED, FRESHLY FERTILIZED EMBRYOS, 10,000.

SO THAT MEANS THAT THERE ARE, IF NOBODY IS TRACKING THESE PEOPLE NOW, IT WOULD CERTAINLY NOT TAKE VERY LONG TO GET SOME PRETTY GOOD FOLLOW-UP. WHEN I CAME TO THE NATIONAL ACADEMY OF SCIENCES WORKSHOP ON THE RISK FOR EGG DONATION, ONE OF THE THINGS THAT THEY BROUGHT OUT WAS THAT IT'S PRETTY CLEAR THAT THE STATISTICS FOR AN INCREASE IN OVARIAN CANCER ARE PROBABLY NOT REAL, AND THAT'S NOT AN ISSUE. BUT WHOEVER GAVE THAT REPORT TALKED ABOUT THAT THEY WEREN'T POSITIVE THAT THERE WAS ENOUGH DATA TO TALK ABOUT ENDOMETRIAL CANCER AND BREAST CANCER INCREASE AS A RISK OF REPEATED GONADOTROPIN STIMULATION.

DR. CARSON: THAT HASN'T REALLY BEEN --

DR. KIESSLING: IS THAT ADDRESSED IN THE ISRAEL STUDY?

DR. CARSON: IT WAS NOT. ONLY OVARIAN CANCER WAS LOOKED AT.

DR. TAYLOR: JUST TO COMMENT, IT'S KIND OF SURPRISING BECAUSE THE PREVALENCE OF THOSE

OTHER TWO CANCERS ARE ACTUALLY QUITE A BIT HIGHER THAN OVARIAN CANCER. SO ONE WOULD THINK IF THE DATA WERE THERE, THEY WOULD HAVE BEEN RECOGNIZED. NOW, THERE ARE A LOT OF ENDOMETRIAL CANCERS THAT WE NEVER SEE, BUT I DON'T KNOW THAT THERE ARE A LOT OF BREAST CANCERS THAT WE NEVER SEE.

CHAIRMAN LO: OTHER QUESTIONS?

DR. CARSON: THANK YOU VERY MUCH.

MR. JANUS: I'M SORRY THEY MAKE YOU DO THIS. ARE THERE ANY LIFESTYLE QUESTIONNAIRES FOR THESE DONORS THAT ARE REQUIRED FOR TISSUE DONORS AND SOME FEDERAL GUIDELINES THAT ARE DIFFERENT?

DR. CARSON: THERE ARE NOT FEDERAL GUIDELINES IN TERMS OF LIFESTYLE. AND OUR COMMITTEE DID NOT REALLY ADDRESS THAT.

DR. TAYLOR: WE DID ADDRESS SOME OF THE INFECTIOUS -- I'M SORRY I DIDN'T PUT A SLIDE, BUT WE DID ADDRESS SOME OF THE INFECTIOUS DISEASES THAT ARE TYPICALLY SCREENED FOR TISSUE DONATION AND PART OF A TYPICAL IVF EVALUATION. SO THOSE AREN'T LISTED HERE, BUT THEY WERE A LITTLE BIT, AGAIN, MORE CONSERVATIVE WITH THE INTENT THAT IF WE DO DERIVE CELLS THAT COULD BE THERAPEUTICALLY BENEFICIAL IN THE FUTURE, WE WOULDN'T WANT THOSE CELLS TO HAVE SORT OF ANY EVIDENCE OF SORT OF

VIRAL CHRONIC INFECTION.

DR. CARSON: AND THANK YOU. THAT'S A GOOD POINT. WE ALSO FELT THAT THESE DONORS SHOULD UNDERGO THE REGULAR OOCYTE SCREENING AND A CLINICAL DONOR WOULD AS WELL. SO THAT WOULD BE CHLAMYDIA AND GONORRHEA SCREENING OF THE CERVIX, BLOOD SCREENING FOR HIV, SYPHILIS, HEPATITIS B AND C. I THINK THAT'S IT.

DR. TAYLOR: I THINK WE SUGGESTED JAKOB CREUTZFELDT AND SOME OTHER THINGS THAT WERE A LITTLE BIT MORE EXOTIC, BUT, AGAIN, BEING MORE ON THE CONSERVATIVE SIDE.

CHAIRMAN LO: ANY OTHER AUDIENCE COMMENTS, QUESTIONS?

MS. FOGEL: ASRM, I THINK, RECENTLY ANNOUNCED THEY WERE PLANNING AN EGG REGISTRY BECAUSE OF WHAT HAPPENED WITH THIS WOMAN WHO WAS A TAY-SACHS CARRIER THAT WAS NOT SCREENED FOR, AND THERE WERE SOME ISSUES AROUND THAT. SO I'M SORT OF WONDERING HOW YOU SEE RESEARCH DONATION, IF THERE IS ANY, FITTING IN WITH THIS IDEA OF A NATIONAL REGISTRY.

THE CDC DATA IS INCREDIBLY LACKING BECAUSE IT ONLY REALLY LOOKS AT BIRTH OUTCOMES. IT DOESN'T LOOK AT DONORS PER SE. AND WE ALSO

KNOW THAT WE'RE SEEING MORE WOMEN GOING THROUGH IVF EITHER BECAUSE THEY ARE IN SAME SEX RELATIONSHIPS OR SINGLE WOMEN WHO ARE NOT INFERTILE. AND THIS WAS BROUGHT UP AT THE IOM MEETING, AND WE REALLY HAVE NO INFORMATION AT ALL ABOUT THOSE LONG-TERM EFFECTS.

AND I GUESS THE OTHER THING THAT CAME UP AT IOM, FOLLOWING ON DR. KIESSLING'S COMMENT, WAS THERE IS RESEARCH SUGGESTING POSSIBLE UTERINE CANCER. AND THEY WERE CORRELATING SOME OF THAT DATA WITH THE HRT STUDIES THAT ACTUALLY WERE STOPPED. AND THIS WAS, ALTHOUGH A SMALL STUDY, AND I THINK IT WAS AN NCI-SPONSORED STUDY, AND THERE WAS THE RECOMMENDATION THAT THERE BE MORE RESEARCH ABOUT THOSE LONG-TERM RISKS. I THINK WE SHOULD BE LESS CONFIDENT ABOUT WHAT WE DO OR DON'T KNOW ABOUT LONG-TERM RISKS. I WOULD BE INTERESTED IN THE DONOR REGISTRY.

DR. CARSON: AGAIN, I DON'T KNOW SPECIFICS AND PROBABLY HEARD JUST AS MUCH AS YOU. MY UNDERSTANDING IS THAT ASRM IS STARTING ONE. I DON'T KNOW ANYTHING MORE ABOUT IT THAN THAT. THE CDC HAS NOT BEEN BUDGETED TO DO THAT. AND FOR A LONG TIME WE HAVE ASKED FOR IVF FOLLOW-UP, HAVE TRIED TO GET IT IN THE NATIONAL CHILDREN'S STUDY,

HAVE TRIED TO GET DONOR EGG FOLLOW-UP. AND ONE OF THE THINGS, AS I SAID, THAT THE COMMITTEE, THIS COMMITTEE, ABSOLUTELY FELT WOULD BE A GREAT ADVANTAGE TO THIS WOULD BE TO HAVE AN ABILITY TO LOOK LONG TERM AT THIS. AND ABSOLUTELY, WE'RE RIGHT ON TRACK WITH YOU.

DR. PRIETO: JUST A QUESTION, WHETHER ANY OTHER COUNTRY USING THIS TECHNOLOGY DOESN'T HAVE A REGISTRY. IT JUST WOULD SEEM REMARKABLE TO ME THAT NO ONE WOULD HAVE PICKED THAT UP.

DR. CARSON: WELL, IT'S -- YOU KNOW, THERE ARE, AND I'M FORGETTING RIGHT NOW THE SPECIFIC COUNTRIES, BUT THERE ARE COUNTRIES THAT TAKE THEIR IVF REGISTRY FOR BOTH DONORS AND IVF AND THEY LINK IT TO THEIR BIRTH RATES AND THEIR CANCER DATABASES. SO ALTHOUGH THEY DON'T HAVE -- YES, WOULD LOVE TO DO THIS FOR LOTS OF REASONS, RIGHT. AND THEY HAVE LIKE -- I'M THINKING THAT FRANCE MAY BE ONE OF THOSE COUNTRIES, BUT I'M NOT SURE IF SWEDEN IS. AND THERE'S A LOT OF DATA THAT COMES OUT OF THOSE COUNTRIES THAT LOOK AT LINKING THESE REGISTRIES. BUT WE HAVEN'T BEEN ABLE TO DO THAT, BUT ABSOLUTELY THAT'S WHAT WE NEED. AND THERE ARE OTHER COUNTRIES WHO DO IT, NOT AS EGG DONORS, BUT WHO DO IT AS IVF AND AS EGG DONORS SO

THEY CAN BE LINKED.

DR. PRIETO: I KNOW WE WANT TO MOVE OFF THIS TOPIC OR FINISH IT UP, BUT COULDN'T THAT DATA BE ABSTRACTED THAT WOULD BE VERY USEFUL FOR US?

DR. CARSON: I DON'T KNOW WHETHER THOSE COUNTRIES WITH THE LINKED DATABASES ALLOW EGG DONATION THOUGH. I JUST DON'T KNOW THAT.

CHAIRMAN LO: SANDRA AND ROB, I WANT TO THANK YOU ON BEHALF OF THE WORKING GROUP. I THANK YOUR COMMITTEE MEMBERS AS WELL.

DR. CARSON: THIS HAS BEEN A WONDERFUL OPPORTUNITY. THOSE OF YOU, OF COURSE, WHO KNOW ROB AND GEOFF KNOW THAT THEY ARE FANTASTIC TO WORK WITH, AND I APPRECIATE THE OPPORTUNITY OF DOING THAT WITH BOTH OF YOU.

CHAIRMAN LO: IN TERMS OF NEXT STEPS, I THINK THE PRESENTATION WAS WONDERFUL. WE NEED TO SORT OF READ THE FULL REPORT, THINK ABOUT IT. I THINK WE NEED TO POST THIS ON OUR WEBSITE TO GET GENERAL COMMENTS AS WELL FROM THE PUBLIC, FROM STAKEHOLDERS IN THE COMMUNITY. I UNDERSTAND YOUR GROUP, I HOPE, IS PLANNING TO PUBLISH THIS IN A MEDICAL JOURNAL, SO THERE'S SORT OF TWO TRACKS WHERE YOU WILL GET PEER REVIEW FROM YOUR REPRODUCTIVE SCIENCE COLLEAGUES. THANKS VERY

MUCH.

I WANT TO SORT OF NOW SORT OF ASK US TO TURN OUR SIGHTS TO THE SORT OF PRIORITY SETTING THAT I THINK WE NEED TO DO.

WE SPENT A LOT OF TIME THIS MORNING TALKING ABOUT OOCYTE DONATION COMPENSATION. THESE ARE COMPLICATED, DIFFICULT ISSUES. I ALSO WANT TO MAKE SURE THAT WE SORT OF THINK ABOUT OTHER POSSIBLE THINGS WE MIGHT WORK ON EITHER IN ADDITION TO OR AS A HIGHER PRIORITY.

I'D LIKE TO -- UNFORTUNATELY JOHN HAD TO LEAVE, BUT I WANT TO SORT OF GO BACK AND SORT OF ASK YOU TO THINK ABOUT A LITTLE BIT THE IMPLICATIONS OF WHAT HE SAID IN HIS PRESENTATION. JUST TO SET THE BACKGROUND, I THINK THERE WILL BE A NUMBER OF PROPOSALS MADE TO CIRM FOR FUNDING OR PARTIAL FUNDING OF STEM CELL CLINICAL TRIALS. AND I THINK JOHN'S PRESENTATION RAISED A LOT OF ISSUES. FIRST, SORT OF THE REAL PROMISE OBVIOUSLY AND SORT OF WHAT WITH HIS ONE SUBJECT HE WAS ABLE TO SHOW IN SHORT-TERM FOLLOW-UP. I THINK ALSO SOME OF THE THINGS HE SAID ABOUT THE REAL PRESSURE FROM IN THIS CASE PARENTS OF VERY SICK CHILDREN WHO HAD NO OTHER THERAPEUTIC OPTIONS. I THINK HE SAID THEY WOULD RATHER GO DOWN FIGHTING THAN TO

SORT OF NOT DO ANYTHING.

SO THE REAL SORT OF HOPE BEING PUT IN THESE TRIALS, AND YET, AS JOHN POINTED OUT, THESE ARE REAL UNKNOWNS, PHASE I STUDIES. WHAT ARE THE IMPLICATIONS OF THAT FOR INFORMED CONSENT, SELECTION OF PARTICIPANTS? JOHN MENTIONED THAT HE GOT MANY, MANY MORE PHONE CALLS THAN HE HAD SLOTS IN HIS TRIAL. HOW ARE THOSE PEOPLE SELECTED? IS CALIFORNIA GEOGRAPHY A FACTOR THERE?

HE MENTIONED THAT IN THIS CASE INSURANCE COVERED THE COSTS OF THE FIRST TRANSPLANT. AND I THINK CERTAINLY IN TERMS OF COST SHARING, THERE'S PRECEDENT NOW FOR MEDICARE, CMS, AND OTHERS COVERING THE COSTS OF CARE GIVEN IN CONJUNCTION WITH THE CLINICAL TRIAL, BUT NOT PAYING FOR THE ACTUAL RESEARCH ACTIVITIES.

I THINK THERE ARE JUST A LOT OF OTHER ISSUES WE MIGHT WANT TO THINK ABOUT IN THE CONTEXT OF WHAT ELSE IS GOING ON WITH CLINICAL TRIALS. AS YOU KNOW, THERE'S JUST BEEN A NUMBER OF REPORTS OVER THE LAST COUPLE OF YEARS OF PRIMARILY PHASE III TRIALS NOT REPORTING NEGATIVE RESULTS. SO IF YOU THINK ABOUT -- OR REPORTING THEM IN A SORT OF INCOMPLETE, DISTORTED FASHION. SO CERTAINLY THE VIOXX EPISODE, OTHER COX-2 INHIBITORS, THE SSR,

SEROTONIN REUPTAKE INHIBITORS FOR DEPRESSION. LOTS OF BIG CLINICAL TRIALS TURNED OUT ON THE BASIS OF INTERNAL MEMOS AND FDA FILINGS DID NOT PUBLISH IN THE SCIENTIFIC LITERATURE NEGATIVE FINDINGS.

I THINK OBVIOUSLY THERE ARE CONCERNS IN PHASE I TRIALS ABOUT INTELLECTUAL PROPERTY AND NOT GIVING COMPETITORS AN ADVANTAGE. I THINK AS PUBLIC FUNDING COMES IN, THERE MAY BE REAL CONCERNS ABOUT NOT MAKING ALL THE RESULTS KNOWN, BOTH POSITIVE AND NEGATIVE. THERE MAY BE SOME ISSUES THERE THAT MAY COME UP AS CIRM CONTEMPLATES CONTRIBUTING TO THE FUNDING OF STAGE I TRIALS. I GUESS THE QUESTION FOR US IS IS THIS SOMETHING THAT WE VIEW AS AN IMPORTANT AREA FOR US TO ADDRESS.

COMMENTS ON THAT? ALSO, ANY OTHER SUGGESTIONS OTHERS OF YOU HAD FOR OTHER TOPICS WE HAVEN'T YET MENTIONED THAT DESERVE OUR ATTENTION?

MR. KLEIN: WELL, GIVEN THAT GERON IS APPLYING FOR FDA TRIALS HERE IN THE IMMEDIATE FUTURE, AND GIVEN THAT THERE ARE FDA COMMENT PERIOD, AS WELL AS PUBLIC HEARING IN APRIL, I WOULD THINK IT'S VERY IMPORTANT THAT THE LEADING EDGE OF THIS MOVEMENT INTO CLINICAL TRIALS IN THIS

AREA, FOR US TO FOCUS SOME ATTENTION TO IT.

CHAIRMAN LO: OKAY. OTHER THOUGHTS AND COMMENTS?

DR. OLDEN: WHEN WE HEARD THE PRESENTATION THIS MORNING ABOUT THIS ONE TRIAL COSTING ANYWHERE FROM 250 TO $500,000, AND WE HAD SOME DISCUSSIONS EARLY ON ABOUT AFFORDABILITY AND EQUITY AND JUSTICE AS WE SET OUR RESEARCH PRIORITIES. SO I DON'T WANT TO SAY THAT SOMEONE WHO COULD AFFORD $500,000 SHOULDN'T HAVE ACCESS TO IT; BUT IF WE'RE SPENDING TAXPAYERS' MONEY, SHOULD NOT AFFORDABILITY BE FACTORED INTO THE PRIORITY SETTING PROCESS? IN OTHER WORDS, IF IT'S NOT AVAILABLE OR ACCESSIBLE TO MANY MILLIONS OF CALIFORNIANS, WOULD WE WANT TO MAKE THAT A TOP PRIORITY? AND SO I JUST WONDER IF WE SHOULD REVISIT THAT DISCUSSION.

MR. KLEIN: I THINK IT'S IMPORTANT TO SEGREGATE THE ISSUE OF A SCIENTIFIC AND MEDICAL TRIAL TO TRY AND DEVELOP TECHNIQUES FROM THE REPEATABLE COSTS, AND AS WELL THE NEED TO LOOK AT RECURRING COST OF SOMEONE MAINTAINING WITH THE DISEASE, SPLITTING THAT INTO TWO PARTS. THE INITIAL COST OF CREATING ARTIFICIAL HUMAN INSULIN WAS ABOUT $10 MILLION. THE COST NOW TO PRODUCE IT

IS ABOUT TEN CENTS A DOSE.

SO THE THRESHOLD CLINICAL TRIAL COST, I DON'T THINK, SHOULD BE OUR BARRIER BECAUSE WE HAVE TO LOOK DOWNSTREAM AND SAY, ONCE WE CAN MASTER THIS, WHAT'S THE ABILITY, THEN, TO MAKE THAT INTO AN AFFORDABLE THERAPEUTIC.

THE SECOND ISSUE IS THAT IF WE'RE GOING TO LOOK AT THE VALUE TO PATIENTS IN CALIFORNIA AND THE SOCIETY, IT MAY BE THAT THERE IS A BREAKTHROUGH IN ALS, WHICH HAS A SMALL POPULATION, BUT THAT BREAKTHROUGH IS GOING TO TEACH US SO MUCH ABOUT IMMUNE-BASED DISEASES, THAT IT BREAKS HOPE IN THE WHOLE FIELD. WE NEED TO BE CAREFUL BECAUSE IT IS IN THESE EXTREME DISEASES THAT YOU GET YOUR APPROVALS FOR CLINICAL TRIALS, AND WE DON'T WANT TO SET UP A SYSTEM THAT SAYS BECAUSE TREATING THESE EXTREME DISEASES IS SO EXPENSIVE, WE SHOULDN'T GO THROUGH A CLINICAL TRIAL BECAUSE IT MAY OPEN UP VERY FINANCIALLY EFFECTIVE ROUTES TO SAVING PATIENTS AND REDUCING SUFFERING IN A BROAD SPECTRUM OF RELATED DISEASES. SO IT'S AN IMPORTANT, BUT COMPLICATED AREA, AND WE NEED TO BE, I THINK, VERY CAREFUL IN HOW WE LOOK AT THESE ISSUES.

DR. EGGAN: JUST TO SECOND THAT. YOU

KNOW, EPIGEN WAS ORIGINALLY APPROVED FOR NOT THE INDICATION FOR WHICH IT IS MOST WIDELY USED, BUT THAT WAS CRITICAL TO RAPID APPROVAL PROCESS FOR THAT DRUG. SO ARE THINGS TO BALANCE OUT IN THE LONG TERM.

DR. TAYLOR: YOU'RE TALKING ABOUT CYCLING?

DR. EGGAN: THAT'S MAYBE IT'S MOST COMMON USE NOW.

CHAIRMAN LO: OTHER COMMENTS, QUESTIONS? ALTA, YOU REMINDED ME AT THE BREAK THAT THERE ARE IRB ISSUES, AND THAT THERE'S ALREADY AN EXISTING SET OF FDA AND FEDERAL REGULATIONS ABOUT CLINICAL TRIALS, AND THERE'S A SYSTEM IN PLACE WITH IRB'S AND ESCRO'S TO OVERSEE THEM.

MS. CHARO: THE COMMENT WAS MOSTLY JUST A CAUTIONARY ONE BECAUSE, FROM THE VERY BEGINNING WHEN THE NATIONAL ACADEMIES HAD RECOMMENDED THE CREATION OF ESCRO'S, THERE HAD BEEN AN OUTCRY THAT THERE WAS GOING TO BE AN OVERLAP WITH THE ROLE OF THE IRB'S AND THAT THERE WOULD BE SOME DUPLICATION OF EFFORT, AND THAT CAN ACTUALLY RESULT IN AN EXPONENTIAL INCREASE IN BUREAUCRACY.

SO OBVIOUSLY THE FDA, IF WE'RE WORKING WITH MANIPULATED BONE MARROW, FOR EXAMPLE, AS

OPPOSED TO THE KIND OF BONE MARROW THAT JOHN TALKING WAS ABOUT, AND THE NIH, IF YOU GET FUNDING FROM THEM, WILL HAVE THEIR OWN FIRST VETTING IN TERMS OF RISK-BENEFIT ANALYSIS WITH REGARD TO THE PARTICULAR DISEASE AND PATIENT POPULATION. AND THE IRB'S WILL GET A SECOND LOOK AT THAT VERY SET OF CHOICES.

ON THIS POINT, INTERESTINGLY, LARRY GOLDSTEIN FROM UCSD HAD ACTUALLY DONE A PRESENTATION ON SEVERAL OCCASIONS WHICH STRONGLY SUGGESTED, FOR EXAMPLE, THAT GERON'S TRIAL OUGHT NOT BE THE FIRST TRIAL BECAUSE OF THE NATURE OF THE INJURY BEING ONE THAT'S NOT LIFE-THREATENING. AND SO THE RISKS MAY NOT BE APPROPRIATELY BALANCED IN A CASE OF SOMETHING LIKE A TRAUMATIC SPINAL CORD INJURY AS OPPOSED TO THE RISKS FROM A TERMINAL DEGENERATIVE DISEASE. NONETHELESS, WE KNOW THE SCIENCE AND CLINICAL MEDICINE IS DRIVEN BY WHERE THE ADVANCES ARE.

IT DOES SEEM TO ME THAT IRB'S MAY WELCOME ESCRO EXPERTISE ON THE SPECIFIC ADDED RISKS ASSOCIATED WITH THE USE OF TISSUES DERIVED FROM STEM CELLS. BEYOND THAT, I THINK THERE MAY BE SOME DEGREE OF RESISTANCE TO HAVING THE ESCRO IN ANY WAY TAKE OVER THE FUNCTION OF THE OVERT

RISK-BENEFIT BALANCING. I KNOW IRB'S WILL SOMETIMES CALL FOR A CONSULT, AND THAT MIGHT BE A USEFUL MODEL FOR THE KIND OF INTERACTION YOU WOULD HAVE HERE.

CHAIRMAN LO: OTHER COMMENTS? I ACTUALLY ALSO SHOULD MENTION THE ISSCR, INTERNATIONAL SOCIETY FOR STEM CELL RESEARCH, HAS A WORKING GROUP, A BIG WORKING GROUP WORKING, ON THE ISSUE OF PROFESSIONAL GUIDELINES FOR STEM CELL CLINICAL TRIALS, AND THE PLAN FOR THEM TO ISSUE A REPORT EARLY THIS SUMMER. SO THERE IS OTHER INTEREST IN THIS TOPIC BY OTHER GROUPS.

ANY OTHER TOPICS WE WANT TO SORT OF AT LEAST CONSIDER? ALTA, FROM WHERE YOU SIT AT NAS, SORT OF SUGGEST ARE THERE THINGS THAT YOU THINK IT WOULD BE USEFUL FOR THIS GROUP TO WORK ON?

MS. CHARO: I'LL JUST SHARE WITH YOU WHAT'S BEEN HAPPENING. NAS HAS BEEN RUNNING LISTENING SESSIONS AROUND THE COUNTRY AND HEARING FROM ESCRO'S THAT HAVE BEEN ATTEMPTING TO IMPLEMENT THE GUIDELINES, WHICH ARE SO SIMILAR IN SOME RESPECTS TO THE CIRM REGULATIONS, THAT IT MAY BE INSTRUCTIVE HERE. AND YOU'RE PROBABLY FAMILIAR WITH ONE OF MOST FREQUENT ASSISTANTS IN THAT. THAT'S PEARL O'ROURKE FROM HARVARD. EVERYBODY

MUST KNOW OF HER. SHE SEEMS TO BE EVERYWHERE AND RUNNING EVERYTHING.

ONE OF THE THINGS THAT WE'RE HEARING IS THAT AS THE ESCRO'S BEGIN TO ANTICIPATE THE PHASE OF PRECLINICAL RESEARCH THAT INVOLVES TESTING HUMAN TISSUES DERIVED FROM STEM CELLS IN ANIMAL MODELS, THAT THEY FIND THAT OFTEN THE GUIDELINES, AND I SUSPECT THE CIRM REGS, WHICH ARE VERY SIMILAR, ARE FAIRLY VAGUE. AND THAT THEY DON'T NECESSARILY HAVE A LEVEL OF DETAIL THAT GIVES THE ESCRO'S CONFIDENCE THAT THEY'LL KNOW HOW TO REVIEW THESE.

ON THE OTHER HAND, SINCE THERE REALLY IS NO ACTUAL BASIS FOR MORE DETAIL IN THOSE RULES, FOR EXAMPLE, THERE'S NO BASIS FOR SAYING THAT A CERTAIN PERCENTAGE OF CELLS AND NO MORE OR CERTAIN KIND OF ARCHITECTURE AND NO MORE SHOULD BE A STOPPING POINT IN YOUR RESEARCH, ONE THING THAT IS WORTH TRYING TO FOCUS ON, PERHAPS AT LEAST WITHIN THE CALIFORNIA SETTING WHERE PEOPLE CAN MAYBE COMMUNICATE MORE EFFECTIVELY BECAUSE THEY'RE ALL GRANTEES, IS A SHARING OF THE DISCUSSIONS THAT ARE GOING ON WITHIN THE ESCRO'S TO AT LEAST LET ONE ESCRO IN NORTHERN CALIFORNIA KNOW WHAT'S GOING ON IN AN ESCRO IN SOUTHERN CALIFORNIA IF IT TURNS OUT

THAT THEY'RE LOOKING AT SIMILAR PROTOCOLS INSTEAD OF REINVENTING THE WHEEL WHEN IT COMES TO THE DISCUSSION OF WHETHER THEY THINK THIS IS A PARTICULARLY PROBLEMATIC EXPERIMENT THAT SHOULD PROCEED MORE SLOWLY WITH A DIFFERENT ANIMAL MODEL, FOR EXAMPLE, OR WHETHER IT'S FINE TO GO FORWARD WITH THE PARTICULAR ANIMAL AND THE PARTICULAR STAGE OF DEVELOPMENT THAT YOU ARE PROPOSING TO USE.

CHAIRMAN LO: OTHER ISSUES? DO YOU WANT TO SAY ANYTHING ABOUT WHAT NAS IS DOING?

MS. CHARO: ON IPS?

CHAIRMAN LO: THE TOPICS YOU'RE LOOKING AT. I KNOW YOU CAN'T TALK ABOUT THE --

MS. CHARO: THE IPS CELLS, OBVIOUSLY CIRM REGULATIONS ALREADY CAPTURE A WIDE VARIETY OF PLURIPOTENT STEM CELLS. I'M GOING TO USE THE WORD "PLURIPOTENT" WITH SOME CAUTION BECAUSE I KNOW THAT THERE ARE SOME REALLY GOOD SCIENTISTS WHO FIND THE TERMINOLOGY HERE PROBLEMATIC, BUT IT IS WHAT THE NIH IS USING AND WHAT WE'RE USING HERE. SO WE ALREADY COVER PLURIPOTENT STEM CELLS THAT COME FROM NONEMBRYONIC SOURCES IN THE REGULATIONS, BUT THE NAS GUIDELINES DO NOT. AND SO THE QUESTION AROSE IMMEDIATELY AFTER THE PUBLICATION

OF THE YAMANAKA AND THOMPSON PAPERS WHETHER THE NAS GUIDELINES SHOULD BE EXTENDED.

OBVIOUSLY THERE ARE -- OBVIOUSLY THE POLITICS IS VERY DIFFERENT. THE POLITICAL IMPETUS FOR GUIDELINES SELF-REGULATION ORIGINALLY CAME LARGELY OUT OF THE POLITICS AROUND EMBRYO RESEARCH, AND NOT THE POLITICS SUCH AS THERE WAS AROUND THE USES OF STEM CELL LINES IN RESEARCH. SO TO THAT EXTENT, IT WOULD SEEM TO MAKE NO SENSE AT ALL.

ON THE OTHER HAND, IT WAS QUITE CLEAR THAT ONCE YOU HAVE THE STEM CELL LINES AND YOU'RE BEGINNING TO DO THE CHIMERIC RESEARCH, THE QUESTIONS REMAIN FUNDAMENTALLY THE SAME REGARDLESS OF THE UNDERLYING SOURCE OF THE DERIVATIONS. SO THE NAS HAD A MEETING ON FEBRUARY 15TH. GEORGE DALEY PRESENTED THE ISSCR'S VERY EARLY DRAFT SET OF GUIDELINES, WHICH THEY DO PROPOSE TO EXTEND TO OVERSIGHT OF RESEARCH USING IPS CELLS. PEARL O'ROURKE, THE INFAMOUS PEARL O'ROURKE FROM HARVARD, PRESENTED THE HARVARD ESCRO'S OR AT LEAST HER END OF THE HARVARD CAMPUS, SHE'S AT THE GENERAL, THEIR APPROACH ON THIS, WHICH ALSO WAS FAIRLY COMPREHENSIVE. STORY LANDIS, WHO IS THE NEW JIM BATTY AT NIH, PRESENTED HER PERSPECTIVES

SPECIFICALLY IN RESPONSE TO THE QUESTION OF WHETHER NIH WOULD FIND IT USEFUL TO EXTEND THE GUIDELINES, AND SHE ACTUALLY SAID IT WOULD. THEY'RE OBVIOUSLY ANTICIPATING A CHANGE OF POLICY IN 2009 REGARDLESS OF WHICH PARTY TAKES THE WHITE HOUSE BECAUSE THE MAIN NOMINEES STILL IN CONTENTION ALL SEEM TO AGREE ON EXPANDED FUNDING, AT LEAST FOR NONCLONING-RELATED LINES.

SO THE COMMITTEE TOOK ALL OF THAT IN. IT THEN WENT INTO CLOSED SESSION FOR CONFIDENTIAL DISCUSSIONS ABOUT WHAT IT WAS GOING TO DO WITH THIS. THERE ARE NO DECISIONS THAT HAVE BEEN MADE. I CAN TELL YOU THAT THE COMMITTEE IS ACTIVELY TRYING TO FIGURE OUT WHAT THE IMPLICATIONS WOULD BE. AND ONE WAY YOU DO THAT IS YOU ACTUALLY SIT DOWN AND YOU ASK WHAT WOULD EXTENDED GUIDELINES LOOK LIKE, AND ARE THERE THINGS YOU WOULD ACTUALLY WANT TO ASK PEOPLE TO IMPOSE UPON THEM THEMSELVES? I DON'T EXPECT THAT THERE WILL BE ANY CLEAR RESPONSE FROM THE COMMITTEE FOR AT LEAST A FEW MONTHS, BUT IT'S QUITE CLEAR THAT THE COMMITTEE UNDERSTANDS THAT THIS IS ON EVERYBODY'S MINDS.

CHAIRMAN LO: DO YOU HAVE A PROJECTED TARGET DATE FOR ANOTHER REPORT, OR IS THAT STILL --

MS. CHARO: WE ACTUALLY DID HAVE A PROJECTED TARGET DATE TO CLEAR UP SOME REALLY MINOR LITTLE THINGS THAT HAVE BEEN BUGGING PEOPLE THAT WE FIXED ALONG THE WAY HAVING TO DO WITH DOCUMENTATION OF PROVENANCE AND LITTLE MINOR CLARIFICATION THINGS. AND THEN WE JUST PUT EVERYTHING ON HOLD, RECOGNIZING THAT PUTTING OUT ANOTHER REPORT THAT TOUCHED ON TRIVIAL DETAILS, WITHOUT TOUCHING ON THE BIG TOPIC ON EVERYBODY'S MIND, WOULD BE A LITTLE PERVERSE.

I KNOW, BERNIE, THAT ONE OF THE QUESTIONS IS WHETHER TO TRY TO GET THIS OUT BEFORE OR AFTER NOVEMBER. THERE WAS A DISCUSSION ABOUT WHETHER THAT MATTERS. THE FIRST QUESTION YOU HAVE TO ASK ON ANY COMMITTEE IS WHETHER ANYTHING YOU'RE DOING ACTUALLY MATTERS. AND IF IT DOES, MATTERS IN WHAT WAY AND ARE YOU HAPPY ABOUT THAT? I CAN SAY THAT NOBODY WANTS TO SEE THIS DRAG ON TOO LONG.

THE OTHER THING THAT WE UNDERSTAND, AND I'M A LITTLE SORRY THAT ALAN ISN'T HERE BECAUSE I'M SURE IT WAS EASY TO MISUNDERSTAND ME EARLIER. THE OTHER THING THAT THE COMMITTEE UNDERSTANDS IS THAT IT'S VERY IMPORTANT THAT THE PRESS AND THAT MEMBERS OF CONGRESS, BOTH OF WHOM TEND TO BE

OPINION LEADERS, PRESS AND CONGRESS, UNDERSTAND THE CONTINUING NEED FOR NON-IPS STEM CELL RESEARCH, AND THAT THESE RECENT ADVANCES DO NOT IN SOME WAY SUPPLANT THE REST OF THE FIELD. AND DEFINITELY ATTENTION IS BEING PAID TO FINDING APPROPRIATE VENUES IN WHICH TO MAKE THAT CLEAR TO OPINION LEADERS SO THAT HAVE THEY THAT INFORMATION AT HAND AS THE POLITICAL DEBATES GO FORWARD.

ANYTHING YOU DO ON IPS CELLS IS GOING TO RAISE, AGAIN, THE QUESTION OF WHY WE'RE WORKING ON ANYTHING ELSE. SO THERE IS A SENSITIVITY TO HOW ONE HANDLES THIS TOPIC; AND THE TIMING, THEREFORE, IS SOMEWHAT IMPORTANT TO WATCH OUT FOR.

MR. KLEIN: I THINK, PICKING UP ON ALTA'S POINT, I WAS JUST IN AN ISCF INTERNATIONAL FORUM FOR THE PRIOR TWO DAYS. AND ONE OF THE PRINCIPAL TOPICS OF DISCUSSION WAS THAT AROUND THE WORLD IN AT LEAST EIGHT NATIONS THERE'S AN ATTEMPT TO SHUT DOWN ON EMBRYONIC STEM CELL RESEARCH BECAUSE OF A CLAIM THAT IPS IS SUFFICIENT IN AND OF ITSELF.

ADDITIONALLY, AT THE NIH, AFTER THE ANNOUNCEMENT OF IPS CELLS IN THE SCIENTIFIC JOURNALS, THE WHITE HOUSE DIRECTED THE NIH TO LOOK AT EXPANDING ITS REGISTRY OF EMBRYONIC STEM CELLS

AND TO RENAME IT AS PLURIPOTENT. AND ONE OF THE MAJOR ISSUES IS THAT THE NATIONS AT THE TABLE CLEARLY DIDN'T BELIEVE THAT THERE WAS ENOUGH INFORMATION TO KNOW WHETHER IPS CELLS REALLY MET THE LONG-TERM STABLE DEFINITION OF PLURIPOTENCY, WHETHER THERE WOULD BE STABLE DIFFERENTIATION, FOR EXAMPLE, OVER TIME OR NOT. AND THEY DID NOT WANT TO BE IN A POSITION AND DID NOT THINK IT WAS ADVISABLE TO BE CALLING IPS CELLS PLURIPOTENT UNTIL WE HAD A SIGNIFICANT TERM OF EXPERIMENTATION AND CONFIRMATION, INCLUDING THE IDENTIFICATIONS OF POTENTIAL DEFICIENCIES BESIDES THE OBVIOUS ONES OF ONCOGENES BEING INVOLVED. EVEN IF YOU CAN GET RID OF THE MYC-C GENE, YOU STILL HAVE THE OCT 4 GENE THAT'S THERE.

THERE ARE A NUMBER OF ISSUES THERE. AND ONE OF THE STANDARDS ISSUES IS DEFINING PLURIPOTENCY BECAUSE THE NIH IS GOING TO BE UNDER HUGE PRESSURE TO MAKE A DEFINITION THAT WOULD RESULT IN HUNDREDS AND HUNDREDS OF CELL LINES BEING ADDED TO THE DEFINITION THROUGH IPS AND OTHER APPROACHES. AND, THEREFORE, THE CLAIM WOULD THEN BE MADE THAT SO WHAT IF YOU HAVE 21 ANTIQUATED EMBRYONIC STEM CELL LINES? ALL THESE ARE EQUIVALENT.

SO I WOULD THINK AN IMPORTANT POINT FOR US IN CALIFORNIA, FOR US IN THE NATION, AND FOR US IN PART OF A WORLD SYSTEM, BECAUSE WE ARE MEMBERS OF THE ISCF, THE INTERNATIONAL STEERING COMMITTEE, BE IMPORTANT TO COME UP WITH A DEFINITION OF PLURIPOTENCY. AND IT WOULD BE IMPORTANT FOR US TO REALLY TRY AND SET OUT WHY EMBRYONIC STEM CELLS ARE STILL NECESSARY EVEN TO LEARN ABOUT THE IPS CELLS IN ADDITION TO NECESSARY UNTIL WE CAN GET ENOUGH INFORMATION TO REALLY UNDERSTAND WHETHER THESE ARE STABLE DIFFERENTIATIONS OR WHETHER THEY HAVE REALLY FULL PLURIPOTENCY AS DEFINED BY THE GOLD STANDARD IN EMBRYONIC STEM CELLS.

DR. TAYLOR: ACTUALLY I THINK THAT'S REALLY AN IMPORTANT POINT. IN SOME WAYS, ALAN, WHEN HE WAS HERE, RAISED A COUPLE OF ISSUES, AND THEY'RE WRITTEN IN OUR GUIDELINES. BUT I THINK WE SHOULD NOT LOSE SIGHT OF THE FACT THAT IT'S NOT JUST SCNT, BUT PARTHENOGENESIS AND ANDROGENESIS ACTUALLY, AND TO TRY TO BROADEN MAYBE THE POLEMIC AROUND THE USE OF OOCYTE-DERIVED PRODUCTS IN A WAY OF TRYING TO MITIGATE A BIT OF AN END RUN BY THE IPS MOVEMENT, I'D SAY.

SO I DO THINK IT'S GOING TO BE IMPORTANT TO KIND OF KEEP THAT BROADER CONSTRUCT. MAYBE WE

CAN JUST DO IT KIND OF ON SCIENTIFIC GROUNDS RATHER THAN THE ETHICAL ONES.

CHAIRMAN LO: THIS MORNING WE GOT INTO A VERY INVOLVED CONVERSATION. BEFORE WE SORT OF RETURN TO THAT, WHICH I THINK WE HAVE TO BEFORE WE LEAVE TODAY, I WANTED TO ASK GEOFF LOMAX TO SORT OF PUT OUT FOR US A COUPLE OTHER OPTIONS OF THINGS FOR THIS GROUP TO WORK ON WHICH ARE RELATED TO THE ISSUE OF PAYMENT FOR EMBRYONIC STEM CELL LINES, BUT THEY REALLY ARE SORT OF ONE STEP REMOVED IN THAT CIRM WOULD NOT BE FUNDING THE DERIVATION OF LINES, BUT WOULD BE FUNDING RESEARCHERS TO USE LINES DERIVED FROM OOCYTES THAT HAD SOME COMPENSATION BEYOND EXPENSES DERIVED IN OTHER JURISDICTIONS.

GEOFF, DO YOU WANT TO JUST WALK US THROUGH THAT, PLEASE.

DR. LOMAX: THANK YOU, BERNIE. I'VE TRIED TO ABSTRACT THESE ISSUES IN A DOCUMENT CALLED "SUMMARY OF REGULATORY ITEMS," WHICH IS IN THE BINDER AND ON THE TABLE OUTSIDE.

I'M GOING TO JUST POINT OUT THAT WE'VE KIND OF PICKED UP ON THIS INFORMATION THROUGH PARTICIPATION IN A NUMBER OF FORUMS, ALSO QUESTIONS FROM OUR GRANTEES. I'M GOING TO SKIP

THE ONE ON NOVEL APPLICATION OF REPROGRAMMED CELLS. I THINK ALTA TOUCHED ON THEM, AND THAT CONVERSATION IS VERY YOUNG AND DOESN'T HAVE THE SUBSTANTIVE QUALITY OF THE OTHER ONES, WHICH I'LL DESCRIBE.

EXCLUSION OF CELL LINES FOR PAYMENT, I PUT THE TERM IN HERE PAID IVF EMBRYOS. AND TO REMIND YOU ABOUT THE REGULATIONS, WE CREATED A VERY SORT OF CLEAR LINE OF DEMARCATION IN OUR CHARACTERIZATION OF AN ACCEPTABLY DERIVED CELL LINE. AND PART OF THAT WAS THAT NO PAYMENT WAS PROVIDED FOR GAMETES.

AND, AGAIN, TO REFRESH YOU, AT THE APRIL MEETING LAST YEAR I POINTED OUT SOME INTERACTIONS I'VE HAD WITH SOME COMMENTATORS THAT WERE QUERYING US ON THERE ARE IVF EMBRYOS THAT ARE IN CALIFORNIA THAT WERE CREATED FOR REPRODUCTIVE PURPOSES AND ARE NO LONGER NEEDED FOR THAT PURPOSE, BUT THEY'RE INELIGIBLE FOR DERIVATION BY CIRM GRANTEES BECAUSE THE ORIGINAL OOCYTE DONOR HAD BEEN PAID. AT THAT TIME THE COMMITTEE, THE SENSE OF THE COMMITTEE WAS THAT WE DON'T WANT TO CONCERN OURSELVES WITH THAT ISSUE. SO WE'VE HAD THAT DISCUSSION IN TERMS OF A CIRM GRANTEE WANTING TO USE A BLASTOCYST FOR WHICH THERE WAS A PAID GAMETE.

IN THIS CASE WE'RE TALKING NOW ABOUT THE ISSUE'S COME UP AGAIN. WHAT IF THAT CELL LINE IS DERIVED IN AN OUTSIDE JURISDICTION? AND LET ME JUST PUT UP AN EXAMPLE HERE. I THINK THE NEXT SLIDE. I'VE TRIED TO SORT OF GIVE YOU A MATRIX HERE TO EXPLAIN, TO SORT OF HOPEFULLY MAKE THIS CLEAR AND BE SPECIFIC ABOUT SOME OF THE JURISDICTIONS WE'RE TALKING ABOUT.

I'VE GOT CONSENT ON THIS AXIS. WE CAN HOPEFULLY FORGET ABOUT THAT JUST FOR A MINUTE. PROHIBITION ON EMBRYOS FROM PAID OOCYTE DONORS. AGAIN, CAN YOU USE A STEM CELL LINE FOR WHICH THE CONTRIBUTION -- AT SOME POINT SOMEWHERE IN ITS LIFE CYCLE A PAID DONOR CONTRIBUTED TO THE BLASTOCYST FROM WHICH THE STEM CELLS WERE DERIVED. UNDER OUR REGULATIONS IT'S PROHIBITED. SO IF YOU'RE IN THIS YES CATEGORY, IT MEANS YOU CANNOT USE IT. THAT'S CONSISTENT WITH THE CANADIAN GUIDELINES AND THE JAPANESE GUIDELINES. SO THERE IS A SORT OF PRECEDENT FOR THIS FAIRLY STRICT STANDARD.

NOW, IF YOU LOOK AT THE ISSCR, NAS, AND A NUMBER OF STATES, PARTICULARLY THE STATE OF CONNECTICUT AND MASSACHUSETTS, THESE ARE INTERESTING EXAMPLES BECAUSE IN THESE STATES THEY

HAVE EXPLICIT STATEMENTS FROM THEIR ATTORNEY GENERALS SAYING THAT YOU CAN USE A PAID IVF EMBRYO THAT WAS CREATED FOR REPRODUCTIVE PURPOSES TO DERIVE STEM CELLS. AGAIN, I DON'T HAVE AN OPINION ON SORT OF THE EFFICACY OR THE ETHICAL SORT OF JUDGMENT ON THESE POLICIES, BUT IT'S REALLY JUST TO POINT OUT WHAT'S SHAPING UP IS A PLAYING FIELD WITH A LITTLE BIT OF UNEVENNESS IN TERMS OF HOW PEOPLE VIEW DERIVED STEM CELL LINES.

AND I THINK IT'S AN OPEN QUESTION TO THE COMMITTEE AS TO WHETHER -- HOW YOU FEEL ABOUT THAT UNEVENNESS AND SORT OF WHAT THE FEELING IS WITH REGARD TO USE OF THOSE STEM CELLS LINES. IS THAT ISSUE CLEAR?

LET ME MOVE ON.

DR. TAYLOR: GEOFF, I'M JUST CURIOUS. IN MASSACHUSETTS, CONSENT ALSO ISN'T PREREQUISITE TO --

DR. LOMAX: WHAT THEY ORIGINALLY DID IS THEY TIED TO THE COMMON RULE. AND THIS GETS INTO SORT OF PREVIOUS LAW. AND, ALTA, IF I MISSPEAK HERE, PLEASE HELP ME OUT. THERE'S SORT OF HISTORICALLY RULES ABOUT STORED EMBRYOS HAVE FALLEN UNDER THE -- LEGALLY THERE'S THIS CONCEPT OF WHO HAS DISPOSITIONAL AUTHORITY. SO THE

MASSACHUSETTS LAW DIDN'T EXPRESSLY SORT OF MAKE A STATEMENT ABOUT CONSENT, BUT IT DEFERRED TO A SET OF LAW WHERE DISPOSITIONAL AUTHORITY LAY NOT WITH THE GAMETE DONORS, BUT IT LAID WITH THOSE INDIVIDUALS WHO HAD LEGAL CUSTODY OF THE EMBRYO. AS YOU MAY BE AWARE, IN AN IVF SETTING, IF YOU HAVE A DONOR RELATIONSHIP, IN THIS CASE A PAID DONOR, THEY TRANSFERRED DISPOSITIONAL AUTHORITY TO THE COUPLE OR THE WOMAN WHO THEN MAINTAINS THAT AUTHORITY FOR THE EMBRYO. AND UNDER THE MASSACHUSETTS RULE, THEY SORT OF BROUGHT THAT WITH THEM, AND THEY ARE NOW LOOKING TOWARDS -- MY SENSE IS THERE'S GOING TO BE MIGRATION TOWARDS THIS CONSENT FROM ALL GAMETE DONORS.

AGAIN, KEEP IN MIND IN A LOT OF THESE CASES, IT ISN'T THAT THE LAW SAYS YOU DON'T NEED TO GET CONSENT. THE LAW REMAINS SILENT AND, THEREFORE, IT KICKS BACK TO SORT OF OTHER THINGS IN THE LAW, WHICH BASICALLY COMES DOWN TO THE FACT THERE'S NOT AN EXPLICIT REQUIREMENT TO GET CONSENT FROM ALL GAMETE DONORS. LIKE I SAY, THE MIGRATION TENDS TO BE IN THIS DIRECTION.

DR. KIESSLING: I'M ACTUALLY NOT FAMILIAR WITH THIS, BUT THE THREE ESCRO COMMITTEES THAT I SERVE ON IN BOSTON ALL REQUIRE -- IT

DOESN'T HAVE ANYTHING TO DO WITH COMPENSATION. THEY DON'T ADMIT OR THEY DON'T SANCTION STEM CELL DERIVATION FROM ANYTHING WITH AN ANONYMOUS DONOR, EITHER SPERM OR EGG.

DR. LOMAX: PERHAPS THEY'RE RELYING ON THE NATIONAL ACADEMIES GUIDELINES AS THEIR BENCHMARK. THAT COULD BE -- CERTAIN INSTITUTIONS HAVE TOLD ME EVEN THOUGH THE MASSACHUSETTS LAW FALLS INTO THIS QUADRANT, A LOT OF INSTITUTIONS ARE ABIDING -- ARE CALIBRATING TO THE NATIONAL ACADEMIES, SO THEIR INSTITUTIONAL POLICIES WILL BE IN THIS QUADRANT.

DR. KIESSLING: GEOFF, WHERE DID THIS INFORMATION ABOUT THE MASSACHUSETTS COMMON RULE COME FROM?

DR. LOMAX: THE ATTORNEY GENERAL'S OFFICE. I'VE BEEN IN CONTACT WITH THE ATTORNEY GENERAL'S OFFICE OF MASSACHUSETTS.

DR. KIESSLING: WERE THEY ASKED TO PROVIDE, WHAT, AN OPINION?

DR. LOMAX: THERE IS A LEGAL OPINION, WHICH I CAN FORWARD TO YOU.

DR. KIESSLING: IT'S AN OPINION FROM THE AG'S OFFICE?

DR. LOMAX: ON THE STATUS OF THE PAID

GAMETES. AND THAT'S AVAILABLE ON THE WEB.

DR. KIESSLING: I ACTUALLY THINK I HAVE THAT. SO THAT WAS JUST AN OPINION THAT CAME OUT OF THE AG'S OFFICE?

DR. LOMAX: THAT'S CORRECT.

CHAIRMAN LO: GEOFF, BEFORE YOU MOVE ON, I WANTED TO ASK A QUESTION. I DON'T KNOW WHO'S BEST SITUATED TO ANSWER IT. HOW BIG AN ISSUE IS THIS FOR CIRM? I MEAN IS CIRM GOING TO GET A LOT OF, GO BACK TO WHAT ALAN WAS CONCERNED WITH THIS MORNING, IS CIRM GOING TO GET A LOT OF GRANT APPLICATIONS SAYING I WANT TO DERIVE NEW STEM CELL LINES FROM FROZEN EMBRYOS WHERE SOMEPLACE ALONG THE PROCUREMENT OF THE GAMETES, THERE WAS PAYMENT INVOLVED? IS THIS A BIG ISSUE FOR CIRM OR FOR SCIENTISTS?

DR. LOMAX: QUICK ANSWER. I'VE GONE TO THE NATIONAL ACADEMIES AND A LOT OF OTHER DELIBERATIVE BODIES AND SORT OF POSED THE QUESTION. I THINK UP UNTIL NOW IT HASN'T BEEN ON PEOPLE'S RADAR, SO I THINK IT'S JUST BEEN THIS INITIAL PHASE OF CAN PEOPLE HELP US WITH THIS QUESTION. I THINK IT WOULD BE USEFUL TO PUT THAT OUT. SO WE DO NOT HAVE AT THIS TIME SORT OF AN EMPIRICAL BODY OF EVIDENCE TO SORT OF DETERMINE

THE MAGNITUDE, IF ANY, OF THE PROBLEM. WE'VE BEEN TAKING ADVANTAGE OF THESE FORUMS TO SORT OF START TO POSE THE QUESTION.

DR. EGGAN: IT COMES UP ABOUT ONCE A MONTH THAT WE HAVE PEOPLE WHO WOULD LIKE TO DONATE THEIR OOCYTES FOR OUR RESEARCH WHO GET INTO THE DONATION PROCESS AND ARE BEING ADMINISTERED INFORMED CONSENT, AND AT THAT POINT WE DISCOVER THAT EITHER THEIR EMBRYOS WERE CREATED FROM AN ANONYMOUS DONOR OR THERE WAS PAID GAMETE DONATION AND THEY'RE EXCLUDED FROM DONATING THEIR EMBRYOS. THIS LEADS TO PROFOUND DISAPPOINTMENT AMONGST THOSE COUPLES THAT THEY CANNOT PARTICIPATE IN RESEARCH. IT JUST FRANKLY IS. IT'S A MAJOR ISSUE.

AND FOR THOSE PEOPLE WE WISH THEY ALMOST HAD NEVER KNOWN ABOUT THE OPPORTUNITY IN THE FIRST PLACE BECAUSE THEY'RE SO DISAPPOINTED. AND FROM MY PERSPECTIVE, IF THERE WAS SOMETHING -- ALTHOUGH IT IS TRUE THAT I RESPECT THAT WE ARE PROTECTING THOSE ANONYMOUS DONORS FROM PARTICIPATING IN SOMETHING THAT THEY DIDN'T IMAGINE THEY MIGHT HAVE PARTICIPATED IN AT THE END OF THE DAY, I, FOR ONE, FEEL MORE FOR THOSE COUPLES WHO FEEL LIKE THOSE ARE THEIR EMBRYOS, AND IN EVERY OTHER WAY THE

DISPOSITION OF THOSE EMBRYOS IS UNDER THEIR CONTROL EXCEPT FOR THEY CAN'T DO THIS.

I DO THINK IT IS GOING TO BE A MAJOR CONCERN. I DO THINK THAT THERE IS A POSSIBILITY, IF WE DON'T PAY ATTENTION TO THIS, MANY CELL LINES COULD BE DERIVED FROM THESE DIFFERENT TYPES OF EMBRYOS, AND THEN WHAT YOU DID ABOUT THEM AFTER THE FACT IS GOING TO BE A SIGNIFICANT QUESTION TOO. I THINK THIS IS AN IMPORTANT THING TO PAY ATTENTION TO.

MR. KLEIN: I THINK THAT RESPECTING THE INDIVIDUAL HERE AND WHERE THEY ARE LIVING, I MEAN I DON'T THINK -- WE DON'T WANT TO GET INTO THE POSITION OF TELLING ENGLAND THAT WE WON'T USE ANY OF THE LINES IN THEIR STEM CELL BANK BECAUSE THEY HAVE SOME RULES THAT ARE PUBLICLY DEBATED AND ACCEPTED IN ENGLAND AND THEY'RE DIFFERENT FROM WHAT THEY ARE HERE, PARTICULARLY WHEN THE NATIONAL ACADEMY OF SCIENCE AND RESPECTED GROUPS ALL OVER THE WORLD HAVE ACCEPTED THEIR STANDARDS AS IN MANY CASES BEING REALLY LEADING STANDARDS IN MEDICAL AND ETHICAL APPROACHES AND BENCHMARKS.

SO WHETHER SOMEONE LIVES IN NEW JERSEY OR WHETHER THEY LIVE IN ENGLAND, AND IF THERE'S A STEM CELL LINE THAT'S DEVELOPED OR EMBRYOS FROM

PAID OOCYTE DONORS, IF IT DOES NOT INVOLVE OUR FUNDS PAYING THEM, THAT'S SOMETHING OUTSIDE OF OUR JURISDICTION, AND IMPOSING OUR RULES ON OTHER COUNTRIES, AS LONG AS THEY ARE TRANSPARENT, LEGITIMATE, CONSENSUALLY AND PUBLICLY DEBATED AND PUBLICLY ACCEPTED RULES, I JUST DON'T THINK IT'S OUR PROVIDENCE TO BE IMPOSING THIS OUTSIDE OF OUR JURISDICTION. AND TO THE EXTENT THAT THERE IS IMPORTANT RESEARCH DONE AND WE NEED TO REPLICATE IT, WE MAY NEED TO GET ACCESS TO THOSE LINES TO BE ABLE TO DO SO IN CALIFORNIA.

CHAIRMAN LO: I KNOW FRANCISCO. I JUST WANT TO DRAW A DISTINCTION HERE BETWEEN A CIRM RESEARCHER COMING AND SAYING I WANT TO DERIVE A NEW STEM CELL LINE WITH CIRM FUNDING FROM AN EMBRYO FOR WHICH ONE OF THE GAMETE DONORS WAS PAID VERSUS I THINK, BOB, THE CASE YOU'RE RAISING IS A LITTLE BIT DIFFERENT, WHICH IS THE CIRM RESEARCHER SAYING I WANT FUNDING TO WORK ON A STEM CELL LINE THAT WAS DERIVED ELSEWHERE WITHOUT CIRM FUNDING IN MASSACHUSETTS, IN GREAT BRITAIN, OR WHATEVER, WHERE THAT JURISDICTION EXPRESSLY PERMITS THAT DERIVATION, THE SCIENCE IS THERE. NOW I WANT TO BUILD ON THEIR RESEARCH AND SHARE THE LINES. AT LEAST LOGICALLY ONE COULD SEPARATE THOSE TWO

CASES.

AND I GUESS I WANT TO RAISE THE QUESTION FOR THE OTHER ONE AS WELL. TO WHAT EXTENT IS THAT A PROBLEM CIRM NEEDS TO ADDRESS?

DR. LOMAX: I TRIED TO MAKE THAT DISTINCTION AT THE BEGINNING, AND I APOLOGIZE FOR NOT MAKING IT AS CLEARLY AS I MIGHT HAVE. THIS SLIDE IS SORT OF TRYING TO REINFORCE THE EXAMPLE OF, IN THIS CASE WE'RE ONLY TALKING ABOUT OUTSIDE LINES. AGAIN, I'LL REMIND YOU APRIL LAST YEAR THAT ISSUE DID GET TIME IN FRONT OF THE GROUP, AND WE SAID WE WANTED TO STICK WITH, IN TERMS OF CIRM-DERIVED LINES, USING EMBRYOS WITH PAID MATERIALS. THE SENSE OF THE COMMITTEE AT THE TIME WAS NOT TO REVISIT THAT QUESTION.

I'LL JUST FINISH UP HERE. I'VE SORT OF PARSED THESE THINGS PERHAPS A BIT TOO FINE. THIS IS SIMPLY BOB'S POINT HERE, THAT, AGAIN, WE HAVE, JUST TO REMIND YOU, IN THE REGULATIONS WE HAVE SORT OF TWO PARALLEL SETS OF CRITERIA. WE HAVE A SORT OF GENERIC SET OF CRITERIA ALLUDING TO CONSENT, OVERSIGHT, AND PAYMENT, WHICH DEFINES AN ACCEPTABLY DERIVED LINE, AND THEN WE HAVE A CATEGORY OF AUTHORIZED AUTHORITIES WHICH WE'VE SORT OF -- THE POINT OF IDENTIFYING AN AUTHORIZED

AUTHORITY IS THAT CELL LINES CAN COME IN WITHOUT THE FULL REVIEW. IT ALLOWS FOR THE MORE EFFICIENT EXCHANGE OF CELL LINES.

NOW, THERE ARE EXAMPLES WHERE THERE WILL BE MINOR VARIANCE IN THE LINES WE'VE IDENTIFIED AS FOLLOWING THE AUTHORIZED AUTHORITY CATEGORY. THERE WILL BE MINOR VARIATION IN THOSE REGULATIONS AS OPPOSED TO OUR OWN RULES.

BOB, YOU WERE, I THINK, REFERRING, AGAIN, THE BEST EXAMPLE IS THE HUMAN FERTILIZATION AND EMBRYOLOGY AUTHORITY'S EGG SHARING EXAMPLE, THAT LINES WILL COME THROUGH THAT MECHANISM. SO THEN WE HAVE A SITUATION WHERE AT FACE VALUE THE REGULATIONS SAY A HFEA-LICENSED, HFEA-DERIVED LINE CAN BE USED.

MR. KLEIN: I WAS ACTUALLY -- I WAS SAYING, LOOK, IF DOUG MELTON'S LAB AT HARVARD DEVELOPED LINES AND IT'S CONSISTENT WITH THE REGULATIONS OF THEIR IRB'S AND THEY WENT THROUGH THE RIGHT PROCESSES, OUR RESEARCHERS -- IT WASN'T OUR FUNDS THAT DERIVED THEM AND OUR RESEARCHERS SHOULD BE ABLE TO USE THOSE LINES RESPECTING OTHER SOURCES THAT ARE TRANSPARENT, GO THROUGH PUBLIC PROCESSES, HAVE THE RIGHT OVERSIGHT, OTHERWISE MEET REASONABLE -- AND MEET INFORMED CONSENT

GENERALLY ACCEPTED IN THAT JURISDICTION, YOU KNOW, I THINK THAT OUR RESEARCHERS SHOULD HAVE ACCESS TO THAT REGARDLESS OF WHETHER IT'S IN A STEM CELL BANK OR NOT.

AND ON THE HISTORIC ISSUE, I ACTUALLY THOUGHT THAT WE HAD GRANDFATHERED LINES CREATED BEFORE OUR OWN REQUIREMENTS ON THE SAME BASIS. THEY WEREN'T CREATED WITH OUR MONEY.

DR. LOMAX: LET ME GO TO THAT LAST EXAMPLE. ON YOUR PREVIOUS POINT, IF THAT'S THE SENSE OF THE COMMITTEE, I WOULD SUGGEST IT MIGHT BE AN ITEM WE WANT TO GO THROUGH IN A FUTURE SESSION AND LOOK AT THE LANGUAGE. AND I'D CERTAINLY BE HAPPY TO PROVIDE SORT OF A DETAILED ANALYSIS OF WHERE THE REGULATIONS STAND ON THAT ISSUE. I THINK THERE ARE A LOT OF EXAMPLES WHERE WE DO BRING IN LINES FROM OTHER JURISDICTIONS, BUT IF THEY'RE NOT LISTED ON THAT LIST OF APPROVED LINES AND THEY DON'T MEET THAT CRITERIA, THEN THEY WOULDN'T BE ELIGIBLE. SO THERE'S A SPACE IN THERE. IF IT'S A SENSE OF THE COMMITTEE TO REVISIT, THAT'S THE COMMITTEE'S PREROGATIVE.

CHAIRMAN LO: AGAIN, THIS IS WHAT I'M TRYING TO DO HERE, TO SORT OF PUT OUT ON THE TABLE ISSUES FOR US TO DEAL WITH. SOME OF THESE MAY NOT

BE AS BIG OR CONTROVERSIAL, BUT THEY MAY BE IMPORTANT FOR --

MR. KLEIN: I THINK THIS IS PRETTY FUNDAMENTAL SO THE RESEARCHERS DON'T GET CAUGHT UP IN THIS AND HAVE A CLEAR PATH TO BE ABLE TO SELECT THE LINES THEY CAN USE.

DR. LOMAX: I'LL GIVE YOU THE LAST EXAMPLE BECAUSE, AGAIN, I'M TRYING TO PARSE THIS IN AS SMALL A PIECE AS POSSIBLE SO YOU CAN SEE EACH OF THE SORT OF EXAMPLES HERE AND THEN DECIDE HOW YOU WANT TO PROCEED.

WE HAD A COMMUNICATION FROM A PRIVATE COMPANY THAT IS IN POSSESSION OF A CLINICAL GRADE LINE, WHICH THERE AREN'T A LOT OF CLINICAL GRADE LINES AT THE MOMENT, AND THIS IS CONSIDERED QUITE VALUABLE TO RESEARCH. IT WAS DERIVED BEFORE THE EFFECTIVE DATE OF OUR REGULATIONS. AND, IN FACT, APART FROM THE NIH LINES, WHICH WE GRANDFATHERED IN, WE ACTUALLY DO NOT HAVE A PROVISION THAT WOULD ALLOW THEM. IN THIS PARTICULAR EXAMPLE, THEY CANNOT CONFORM TO THE CONSENT REQUIREMENTS WHICH I DESCRIBED EARLIER. AND THERE'S NO PROVISION WITHIN THE REGULATIONS TO ENABLE THEM AROUND THAT EVEN THOUGH IT WAS DERIVED BEFORE THE EFFECTIVE DATE OF THE REGULATIONS.

SO, AGAIN, A FACE-VALUE READ OF THE REGULATIONS CREATES A CIRCUMSTANCE WHERE AT LEAST ONE COMMERCIAL GRADE LINE, THAT IS A CLINICAL GRADE COMMERCIAL LINE, HAS BEEN DETERMINED BY THE COMPANY CALLING IN TO NOT BE ELIGIBLE FOR USE BY CIRM GRANTEES. AND IN THIS CASE THEY EXPRESSED SORT OF INTEREST IN, IF IT WAS THE WISH OF THE WORKING GROUP, TO COME BEFORE THE WORKING GROUP AND EXPLAIN WHAT THEY CONSIDER TO BE THE VALUE OF THIS LINE AND MAKE THE CASE FOR THIS LINE.

I THINK THESE ARE VERY DIFFERENT THAN SOME OF THE ISSUES WE WERE TALKING ABOUT THIS MORNING. THEY TEND TO BE SORT OF DETAIL IMPLEMENTATION ISSUES. THERE ARE THINGS PERHAPS WE DIDN'T ANTICIPATE IN THE ORIGINAL DRAFTING OF THE LEGISLATION, BUT HAVE COME FORWARD THROUGH GETTING EXPERIENCE AND INTERACTING WITH AFFECTED PARTIES. SO I LEAVE THE LIST BEFORE YOU.

DR. KIESSLING: I HAVE A QUESTION. NOW, WHEN THEY TELL YOU THAT THEY -- I MEAN I THINK THE ISSUE OF PAYMENT IS NOT OF CONCERN TO ME PARTICULARLY AS THE ISSUE OF INFORMED CONSENT. AND I KNOW IN SOME OF THE CIRCUMSTANCES THAT TAKE PLACE IN SOME OF THE HARVARD INSTITUTIONS, THEY HAVE BEEN ABLE GO BACK AND IDENTIFY THE EGG DONOR

AND GET HER CONSENT BECAUSE EGG DONORS ARE ALL KNOWN.

NOW, HAS THIS PARTICULAR GROUP, HAVE THEY TRIED TO DO THAT?

DR. LOMAX: THEY INDICATED THAT LEGALLY THEY COULD NOT DO THAT, AND I DON'T -- YOU KNOW, THAT WAS -- THEY --

DR. KIESSLING: I THINK IT'S OF CONCERN IF SOMEBODY DONATED THEIR EGGS AND DIDN'T REALIZE THEY MIGHT BECOME AN IMMORTAL CELL LINE FOREVER AND EVER. I THINK THERE'S CONCERN THERE. IF IT WAS THE EGG THAT WAS DONATED, YOU CAN FIND THOSE PEOPLE AND MAKE AN ATTEMPT TO SAY WOULD THIS BE ALL RIGHT. THEN THE PROBLEM GOES AWAY. THE PROBLEM OF COMPENSATION DOESN'T GO AWAY, BUT THE PROBLEM OF INFORMED CONSENT GOES AWAY.

DR. LOMAX: IF YOU WERE TO SORT OF LOOK BACK AT THE RECORD OF THIS WORKING GROUP'S DELIBERATIONS, I THINK THE POINT YOU JUST STATED WAS A FAIRLY STRONG SENTIMENT ON THE WORKING GROUP, THIS SORT OF A CONSENT AS A DRIVER. AGAIN, I'M JUST SORT OF KIND OF BRINGING TO YOU SORT OF WHAT I PICKED UP, BUT I WILL REMIND YOU YOU FELT VERY STRONGLY ABOUT THIS. WHAT I'M SORT OF SAYING, THAT TOP SET OF CONSENT PROVISIONS, YES,

YOU FELT VERY STRONGLY ABOUT.

DR. KIESSLING: THAT'S PAID. I DON'T FEEL SO STRONGLY ABOUT THAT.

DR. LOMAX: IF YOU SET ASIDE THE PAID PART, THOUGH, THE CONSENT FROM ALL GAMETE DONORS, YEAH. I'M GIVING YOU TWO AXES HERE, SO IT'S THIS PART HERE. A LOT OF THE REGULATIONS ARE COALESCING AROUND THIS, YOU KNOW, EVERYONE IS SORT OF MIGRATING INTO THIS CATEGORY OF SORT OF STRONG CONSENT. THAT APPEARS TO BE BOTH SOMETHING YOU ALL DISCUSSED AND FELT QUITE STRONGLY ABOUT, AND, IN FACT, MOST EVERYONE WHO'S THINKING ABOUT THIS FEELS VERY STRONGLY ABOUT, SO THAT APPEARS TO BE AN EMERGING CONSENSUS POSITION.

DR. KIESSLING: SPERM DONORS ARE FREQUENTLY ANONYMOUS, AND YOU CAN'T NECESSARILY GO BACK AND IDENTIFY THEM. BUT THIS COMPANY THAT SAYS THEY HAVE A CLINICAL GRADE LINE FEELS THAT THEY CANNOT GO BACK AND GET CONSENT.

DR. LOMAX: THEIR INDICATION WAS THAT LEGALLY THEY COULD NOT, THAT THEY WERE FIREWALLED FROM ACCESSING THE ORIGINAL DONOR. THAT WAS THEIR CLAIM.

DR. KIESSLING: BECAUSE IT MIGHT BE ANONYMOUS TO THEM.

MR. KLEIN: HOW COULD THAT BE WITH A CLINICAL GRADE LINE? ON A CLINICAL GRADE LINE, YOU HAVE TO GO BACK AND --

DR. KIESSLING: YOU HAVE TO KNOW SOMETHING ABOUT THE HISTORY OF THE PEOPLE.

MR. KLEIN: THAT'S RIGHT. EITHER YOU HAVE CONSENT -- YOU HAD TO HAVE A DISCLOSURE ON THE HEREDITARY DISEASE PROFILE TO GET A CLINICAL LINE.

DR. LOMAX: MY UNDERSTANDING IS THAT THAT WAS DONE WITHIN THE IVF CONTEXT. THAT WAS PART OF THE IVF PROCEDURE. DOES THAT SOUND RIGHT?

DR. KIESSLING: WELL, I THINK THAT THAT'S A PRETTY GRAY AREA. I DON'T THINK THE FDA EVEN HAS REALLY GOOD GUIDELINES ON WHAT KIND OF INFORMATION YOU WANT ABOUT THE PEOPLE. CLINICAL GRADE LINE PROBABLY HAS MORE TO DO WITH THE DERIVATION AND HOW THEY HAVE TRACKED THE CELLS SINCE THEN.

DR. LOMAX: CORRECT.

DR. KIESSLING: BUT THE DONOR, I MEAN IT'S VERY POSSIBLE THAT, CERTAINLY IN THE HARVARD LABS, THE INFORMATION ABOUT WHO OWNS THE EMBRYO OR WHO THE EMBRYOS CAME FROM IS NOT PRIVILEGE. IT'S NOT GENERAL INFORMATION IN THE LABORATORY. AND SO

IT'S BLINDED AS TO WHO THE PEOPLE WERE. BUT I WOULD THINK -- BUT I KNOW THAT COUPLES WHO HAVE CONTACTED SOME OF THE HARVARD RESEARCH GROUPS WHO WANTED TO DONATE THEIR EMBRYOS AND HAD USED AN EGG DONOR WENT TO THE TROUBLE TO GET THAT EGG DONOR TO RECONSENT THAT THOSE EMBRYOS COULD BE USED FOR STEM CELL DERIVATION. I DON'T KNOW HOW COMMON THAT IS, AND IT WAS NOT DONE BY THE INVESTIGATORS. IT WAS DONE BY THE COUPLE WISHING TO DONATE THEIR EMBRYOS.

DR. EGGAN: I CAN COMMENT ON THAT LAST POINT BRIEFLY. I THINK THIS GOES TO HOW PALATABLE THE IVF DOCTORS FEEL ABOUT THAT. SOME OF OUR COLLABORATORS HAVE BEEN WILLING TO DO THAT AND OTHERS HAVE BEEN TOTALLY UNWILLING TO DO THAT JUST BASED ON CLINICAL PRACTICE AND SORT OF FEELING THAT THEY MIGHT NOT WANT TO REVISIT THOSE ISSUES, THOSE COUPLES.

DR. KIESSLING: THIS IS ACTUALLY A COUPLE FROM OUTSIDE OF BOSTON. THEY JUST REALLY WANTED TO DONATE THEIR EMBRYOS AND THEY DID IT.

DR. CARSON: HIPAA -- FDA HAS SAID THAT THEY WOULD FOLLOW THE HIPAA GUIDELINES IN TERMS OF THE IDENTITY CRITERIA THAT ARE REQUIRED FOR STORAGE OF ANY TISSUE. AND SO THERE ARE IDENTITY

CRITERIA, SUCH AS THE BIRTHDATE, THE NAME, SOCIAL SECURITY NUMBER, I THINK EVEN A TELEPHONE NUMBER THAT ARE NOT ALLOWED TO BE RECORDED. AND SO THE ABSENCE OF THOSE CRITERIA ARE -- AS LONG AS THOSE CRITERIA ARE ABSENT, THEN EVERYTHING ELSE IS OKAY. AND DISEASE AND DIAGNOSIS, LENGTH OF INFERTILITY ARE NOT ANY OF THOSE IDENTIFYING CRITERIA.

CHAIRMAN LO: JUST TO TRY AND KEEP US ON TRACK. DO WE NEED A BREAK? LET'S TAKE A TEN-MINUTE BREAK. WHEN I COME BACK, I'M GOING TO PUT A SLIDE UP WITH THE OPTIONS I'VE HEARD FOR THINGS WE COULD WORK ON. I'M GOING TO SORT OF HOLD OUR FEET TO THE FIRE AND SAY WHICH ONE SHOULD WE BE WORKING ON.

(A RECESS WAS TAKEN.)

CHAIRMAN LO: LET'S RECONVENE. AS I SAID, I THINK WHAT WE NEED TO DO NOW IS REALLY SET PRIORITIES AND SORT OF GIVE OURSELVES DIRECTION FOR THE NEXT SEVERAL MEETINGS. AND SO WHAT I DID TO TRY AND SYNTHESIZE THE VERY SORT OF RICH DISCUSSION WE'VE HAVE HAD TODAY IS JUST BULLET SOME POSSIBILITIES OF POSSIBLE ISSUES FOR US TO ADDRESS. I'M GOING TO SORT OF WORK BACKWARDS ACTUALLY.

RIGHT BEFORE THE BREAK, GEOFF LOMAX GAVE

US SEVERAL FAIRLY SPECIFIC ISSUES THAT I WOULD CHARACTERIZE, I HOPE THIS ISN'T INACCURATE, GEOFF, SAYING THAT THESE ARE AMBIGUITIES, PERHAPS IN ONE INSTANCE AN INTERNAL CONTRADICTION IN OUR REGULATIONS, BUT THINGS THAT NEED CLARIFICATION OF OUR CURRENT MES REGULATIONS. AND THESE, I TAKE IT, HAVE ALSO CAUSED SOME CONFUSION FOR SCRO'S AND POTENTIAL GRANTEES.

FIRST IS GRANDFATHERING OF HSC LINES DERIVED BEFORE OUR REGULATIONS WERE ADOPTED, BUT THESE LINES DO NOT MEET REQUIREMENTS FOR EITHER CONSENT OR PAYMENT.

NEXT ISSUE GOING UP, CIRM RESEARCHER WANTING TO WORK WITH HESC LINES DERIVED ELSEWHERE, ANOTHER COUNTRY, ANOTHER STATE, WITH GAMETES FROM PAID DONORS. CIRM WOULD NOT BE FUNDING THE DERIVATION, BUT FUNDING THE SECOND ORDER RESEARCH. AND, AGAIN, GIVEN THAT SHARING OF LINES ACROSS JURISDICTIONS IS A WAY TO KIND OF ACCELERATE RESEARCH, THIS WILL INCREASINGLY BECOME AN ISSUE.

THIRD ISSUE IS A CIRM RESEARCHER REQUESTING FUNDING TO DERIVE HESC LINES FROM EMBRYOS THAT HAD A PAID DONOR, WHETHER WE WANT TO REVISIT THAT ISSUE.

GOING BACKWARDS, ETHICAL ISSUES,

GUIDELINES REGARDING PHASE I CLINICAL TRIALS, PICKING UP ON SOME OF THE ISSUES JOHN WAGNER RAISED IN HIS PRESENTATION THIS MORNING.

AND, FINALLY, THE ISSUE THAT WE HAD A LOT OF DISCUSSION ON THIS MORNING AND OBVIOUSLY HAS BEEN DISCUSSED IN THE STATE AROUND PROP 71 AND AROUND SB 1260, ISSUES REGARDING OBTAINING OOCYTES FOR RESEARCH, PARTICULARLY SUGGESTIONS THAT WE MAY WANT TO RECONSIDER ALLOWING OOCYTE SHARING BY WOMEN IN IVF, AS SHERRY POINTED OUT, NOT THAT A WOMAN CAN'T DO THAT NOW PROVIDED SHE GIVES CONSENT AND HER REPRODUCTIVE INTERESTS AREN'T COMPROMISED, BUT TO ALLOW PARTIAL REIMBURSEMENT OF HER IVF EXPENSES. THAT WOULD BE SOMETHING DIFFERENT AND WOULD REQUIRE US TO REVISIT THAT ISSUE THAT ALTA CHARACTERIZED AS A FINALLY WROUGHT POLITICAL COMPROMISE A NUMBER OF YEARS AGO.

AND THE OTHER ISSUE WE MIGHT WANT TO ADDRESS, WHICH WAS THE SUBJECT OF SANDRA AND ROB'S REPORT, WAS DONATION SOLELY FOR RESEARCH. WE HEARD FROM KEVIN EGGAN AND OTHERS THAT, AT LEAST IN OTHER LOCATIONS, IT'S NOT BEEN POSSIBLE TO RECRUIT WOMEN DONATING OOCYTES SPECIFICALLY FOR RESEARCH AND NOT COMPENSATE THEM.

NOW, I MUST SAY, AS I TRY TO SYNTHESIZE

THE DISCUSSION, IT SEEMS CLEAR THAT IF WE TACKLE THAT FIRST TOPIC, THERE ARE A LOT OF PRELIMINARY STEPS. FIRST IS THAT WE NEED TO MAKE THE CASE -- WE MAY NEED TO DO THAT REGARDLESS OF WHAT WE DO, BUT THE CASE NEEDS TO BE MADE FOR THE NEED FOR FRESH OOCYTES TO DERIVE NEW STEM CELL LINES, PARTICULARLY WITH REGARD TO THE HYPE AROUND IPS CELLS. THE VERY CAREFUL REASONING THAT KEVIN EGGAN LED US THROUGH WITH THE LIMITATIONS OF THE IPS LINES IS NOT SOMETHING THAT'S WIDELY APPRECIATED IN THE PUBLIC AND PERHAPS NOT CONSISTENT WITH WHAT NIH IS TRYING TO DO UNDER THE PRESIDENT'S DIRECTION.

SECONDLY, I THINK THERE'S A THREAD RUNNING THROUGH THE CONVERSATION BEFORE LUNCH THAT IF WE ADDRESS THIS ISSUE, AND I SAY IT'S AN IF, WE NEED TO DO A LOT OF FACT-FINDING AND DATA GATHERING ABOUT WHAT HAS BEEN DONE IN TERMS OF APPROACHES TO RECRUITING WOMEN TO DONATE OOCYTES. WHAT ARE THEIR ATTITUDES? IS CALIFORNIA DIFFERENT THAN MASSACHUSETTS? IS CALIFORNIA DIFFERENT THAN THE UNITED KINGDOM, FOR EXAMPLE? THERE'S A LOT OF BACKGROUND WORK WE NEED TO DO TO ADDRESS THIS.

I JUST WANTED TO LAY THOSE OUT. I MAY HAVE OVERLOOKED SOME ISSUES, BUT LET'S THROW THAT

OPEN. AT THE END OF -- BEFORE THE END OF THIS MEETING, ACTUALLY WELL BEFORE THE END OF THE MEETING, I WANT TO SORT OF PRIORITIZE THESE ISSUES AND THE ISSUES IN THE PREVIOUS SLIDE; AND ONCE WE SET OUR PRIORITIES, THEN WE NEED TO DEVELOP SOME PLANS ON HOW WE'RE GOING TO GET TO THE NEXT MEETING AND BEYOND. SO LET ME JUST THROW IT OPEN FIRST TO THE COMMITTEE FOR DISCUSSION. I DO WANT TO GET SOME -- ALLOW THE PUBLIC TO COMMENT.

MS. CHARO: IF YOU CAN GO BACK TO THE PREVIOUS SLIDE PERHAPS, BERNIE. IT DOES SEEM TO ME THAT THERE ARE TOPICS ON WHICH IT MIGHT BE TEMPTING TO START TRYING TO WRITE NEW RULES, BUT IT MIGHT MAKE MORE SENSE TO HANG BACK UNTIL YOU ACTUALLY HAVE HAD SOME FOCUSED RESEARCH. I THINK IT WAS EXTREMELY, EXTREMELY REVEALING TO HAVE THE REPORT ON THE KIND OF PROTOCOLS THAT ARE NECESSARY IN ORDER TO SCREEN OOCYTE DONORS IN ORDER TO MINIMIZE RISKS, FOR EXAMPLE. IT WAS THE PERFECT BACKGROUND FOR RECONSIDERING IF ANYBODY EVER DID WANT TO RECONSIDER THE WHOLE ISSUE OF OOCYTE DONATION.

I CAN IMAGINE A FEW DIFFERENT THINGS THAT MIGHT BE HELPFUL BEFORE ONE GOT INTO DEBATING THESE TOPICS AS A GROUP. FOR EXAMPLE, WE HAVE YET

IN THE UNITED STATES TO HAVE ANYPLACE THAT JUST COLLATES A LIST OF THE LINES THAT ARE AVAILABLE TO RESEARCHERS AND THE KEY ASPECTS OF THEIR DERIVATION THAT MIGHT MAKE A DIFFERENCE IN WHETHER OR NOT YOU WOULD WANT YOUR GRANTEES TO USE THEM WITH CIRM MONEY. THAT WOULD MEAN THIS GROUP MIGHT WANT TO FIGURE OUT WHAT THAT LIST OF CHARACTERISTICS MIGHT BE, MINIMAL LIST BECAUSE IT'S GOING TO BE TRICKY, BUT WHOSE RULES THEY WERE DERIVED UNDER, AND THEN KEY THINGS IN OUR LIST OF CORE VALUES HAVING TO DO WITH CONSENT AND PAYMENT, ETC.

THERE HAVE BEEN A NUMBER OF PEOPLE WHO HAVE PROPOSED IT. THERE HAVE BEEN A COUPLE OF ATTEMPTS BY FOR-PROFIT COMPANIES TO DO IT AND SELL THE SERVICE THAT HAVE FAILED. AT LEAST WITHIN THE STATE OF CALIFORNIA YOU COULD START DOING THAT. I KNOW WE TALKED ABOUT IT, BUT I DON'T KNOW THAT WE'VE EVER ACTUALLY TACKLED IT. AND THEN YOU KNOW WHAT YOU'RE DEALING WITH IN TERMS OF AVAILABILITY OF LINES, THEIR CHARACTERISTICS, AND WHICH ONES WOULD BE USABLE OR NOT UNDER VARIOUS KINDS OF RULES YOU MIGHT IMAGINE.

A SECOND KIND OF FOCUSED INVESTIGATION MIGHT BE UNDERSTANDING HOW IT IS THAT A CALIFORNIA

COMPANY DID SUCCESSFULLY MANAGE TO RECRUIT AN OOCYTE DONOR OR OOCYTE DONORS UNDER PURELY ALTRUISTIC PROTOCOLS AND SUCCEED TO THE POINT OF BEING ABLE TO DO SCNT UP TO A HUMAN EMBRYO STAGE. THIS MAY HAVE BEEN A ONE-OFF IN WHICH YOU COULDN'T POSSIBLY REPEAT IT, OR IT COULD BE THAT THEY FOUND SOME REALLY WONDERFUL WAY OF RECRUITING. THEY WOULD HAVE SOME EXPERIENCE TO SHARE ON HOW THEY ADVERTISE, HOW MANY PEOPLE CAME FORWARD, HOW MANY PEOPLE GOT SCREENED OUT, WHAT DID THEY USE TO SCREEN THEM OUT, ETC., TO SEE WHETHER THERE'S ANYTHING TO BE LEARNED THERE BEFORE ONE PROCEEDS WITH ANOTHER CONVERSATION.

I WAS TALKING EARLIER ABOUT SOME OF THE ESCRO STRUGGLES WITH CHIMERIC RESEARCH. AND, AGAIN, BEING ABLE TO SIMPLY GET THE ESCRO'S IN THE STATE OF CALIFORNIA, AT LEAST THE ESCRO'S THAT HAVE CIRM GRANTEES AT THEIR INSTITUTIONS, TOGETHER TO TALK ABOUT THE PROTOCOLS THAT THEY HAVE ACTUALLY NOW REVIEWED AND WHERE THEY HAVE FOUND PROBLEMS AND WHERE THEY HAVE -- SHARING SOLUTIONS OR SHARING A SENSE OF WHAT THEY FOUND TROUBLESOME IN THE PROTOCOL OR IN THE BUREAUCRACY. ALL OF THESE THINGS, I THINK, MIGHT BE POTENTIALLY HELPFUL BEFORE ONE DECIDED WHETHER YOU WANTED TO

RETHINK THE GRANDFATHERING OR RETHINK THE ISSUES SURROUNDING DEBATABLE FORMS OF REIMBURSEMENT. THAT'S IT.

CHAIRMAN LO: IF I CAN INTERPRET, ALTA, IT SOUNDS LIKE YOU ARE SAYING THERE'S SOME INFORMATION GATHERING WE SHOULD DO BEFORE WE START COMMITTING OURSELVES TO PRIORITIES.

MR. SHEEHY: I WAS INTERESTED THAT ALTA BROUGHT UP THE IDEA OF A REGISTRY. I WONDER IF AT THIS POINT WE MIGHT WANT TO CONSIDER CARIS THOMPSON'S IDEA, WHICH DOES KIND OF DEAL WITH SOME OF THE DONOR ISSUES, WHICH IS IN TERMS OF TALKING ABOUT A STEM CELL BANK, STEM CELL REGISTRY, THERE WAS THIS NOTION ACTUALLY INVOLVING DONORS AS PARTNERS AND DECISION MAKERS IN THAT PROCESS.

NOW, SHE'S AT ONE OF YOUR HOMES, AND THEY HAVE A FAIRLY FLESHED OUT CONCEPT THAT MAY BE -- IT'S A LOT DIFFERENT, FRANKLY, FOR SCIENTISTS TO GET UP THERE AND SAY WE NEED TO PAY DONORS THAN FOR THE DONOR COMMUNITY TO STAND UP AND SAY WE'RE PARTICIPATING AS PARTNERS IN THIS, WE'RE STAKEHOLDERS, WE'RE INVOLVED WITH THE MANAGEMENT OF THE INFORMATION THAT'S BEING COLLECTED AND THE LINES THAT ARE BEING SHARED, AND WE BELIEVE, AS STAKEHOLDERS IN THIS PROCESS, THAT

THERE'S AN EQUITY ISSUE THAT NEEDS TO BE ADDRESSED. AND THAT JUST PUTS THIS IN A WHOLE DIFFERENT CONTEXT.

I WONDER IF WE WANT TO MAYBE MAKE A BOLD LEAP AND ACTUALLY START TO, INSTEAD OF VIEWING THESE AS ALL DISCRETE ISSUES, AND ACTUALLY -- AGAIN, I'M FROM HIV. I THINK WE'VE ALWAYS BEEN PARTNERS IN THE PROCESS WHENEVER WE COULD KICK THE DOOR IN TO MAKE PEOPLE LET US. MAYBE THIS IS ONE WAY TO REFRAME THIS DISCUSSION BECAUSE I DO SOMEHOW THINK -- I'M VERY SENSITIVE TO KEVIN'S ISSUE, THAT THIS IS IMPORTANT SCIENCE. I DON'T KNOW IF IT'S NECESSARILY FAIR NOT TO COMPENSATE PEOPLE FOR WHAT IS A RATHER ARDUOUS PROCESS, BUT I THINK THAT THEY NEED TO BE FULLY EMPOWERED STAKEHOLDERS IN THE PROCESS BEFORE WE START -- IF WE CAN START AT THE FRONT END AND GIVE THE POWER AND GIVE THE INVOLVEMENT AND MAKE THEM STAKEHOLDERS AND WE HAVE A MODEL THAT'S STARTING TO BE FLESHED OUT OF ONE OF OUR GRANTEES AT BERKELEY. THEY'VE GOT A GREAT PROGRAM THAT BROUGHT YOU HERE. I WONDER IF THAT'S ONE WAY THAT WE CAN START TO ADDRESS SEVERAL OF THESE ISSUES IS TO START DIALOGUING ALONG THOSE LINES. IT'S JUST A THOUGHT.

MS. LANSING: I THINK THAT THERE ARE STAGES THAT ONE DOES THINGS IN, I GUESS. FOR ME I THINK WE HAVE A LOT OF ISSUES THAT WE CAN DEAL WITH AS A GROUP THAT WILL OCCUPY OUR TIME FOR THE NEXT CERTAINLY SEVERAL MONTHS. LET'S SAY IT THAT WAY. WHAT I WOULD LIKE TO SUGGEST IS THAT IN THE AREA OF COMPENSATION, I STILL THINK THAT THERE IS CONFUSION AS TO WHAT WE AGREED TO DO. SO I THINK WE NEED TO BE VERY, VERY SPECIFIC AS TO WHAT EXPENSES REALLY MEANS. I THINK THAT ALAN WAS CONFUSED. WHEN WE WERE TALKING ABOUT IT, THERE WAS A SLIGHT CONFUSION. SO I WOULD LIKE TO SAY THAT PERHAPS WE CAN DRILL DOWN ON THAT.

AND THEN I THINK THAT CIRM, DO YOU KNOW, COULD DO SOME RESEARCH THAT HAS NOTHING TO DO WITH US IN THE SENSE OF, YOU KNOW, WHAT KEVIN IS SAYING, WHAT ALAN WAS SAYING, WHAT DIFFERENT PEOPLE ARE SAYING, THAT I'M NOT SAYING THEY'RE WRONG AND I'M NOT SAYING THEY'RE RIGHT. BUT I'M JUST SAYING LET'S SEE WHAT WE KNOW FROM THE STATE OF CALIFORNIA. LET'S SEE WHAT WE KNOW FROM OTHER PLACES, AND THEN COME BACK TO US. I THINK THIS IS A PROGRESS, AND I DON'T NECESSARILY KNOW, GIVEN HOW DIFFICULT THIS ISSUE IS, I DON'T NECESSARILY KNOW THAT WE SHOULD DO IT. YOU MAY BE SURPRISED

AT WHAT YOU FIND OUT. YOU MAY NOT BE. I DON'T KNOW, BUT I WOULD LIKE TO SUGGEST THAT THIS IS THE WORK OF CIRM FOR A WHILE TO COME BACK TO US IF THERE IS A PROBLEM.

MR. KLEIN: I WOULD JUST LIKE TO SAY I AGREE WITH SHERRY. I'M NOT PREPARED TO DEAL WITH PAID DONORS. I DON'T HAVE ENOUGH INFORMATION. I DON'T KNOW HOW TO FULLY EVALUATE THE ISSUE. IT'S A VERY IMPORTANT ISSUE. WE OWE IT SOME REAL THOUGHT, BUT WE NEED SOME RESEARCH AND WE NEED SOME INDEPENDENT EXPERTS TO GET SOME INFORMATION ON THE TABLE.

I THINK WHEN SOMEONE LIKE KEVIN EGGAN PUTS IT ON THE TABLE, I'M EXTREMELY FOCUSED BECAUSE OF HOW CRITICAL HE IS TO THE ENTIRE MOVEMENT, AND HIS RESEARCH IS EXTRAORDINARY. SO IF HE THINKS IT'S AN ISSUE, IT'S SOMETHING WE NEED TO LOOK AT. FIRST, WE NEED A FUNDAMENTAL BODY OF INFORMATION TO FIGURE OUT WHERE WE'RE GOING. AND I DON'T THINK -- WE'RE NOT READY RIGHT NOW BECAUSE WE DON'T HAVE THAT INFORMATION.

THESE NEW LINES, THE NEW CELL LINES, MAY GIVE US SOME INFORMATION PRETTY RAPIDLY, BUT WE DON'T HAVE IT RIGHT NOW. SO I'M NOT PREPARED TO GO ANYWHERE CLOSE TO PAID DONORS UNTIL WE GET THIS

INFORMATION IN HAND.

MS. LANSING: COULD I RESPOND? SO I THINK WHAT WE'RE SAYING, I THINK WE'RE SORT OF GATHERING UNANIMITY. I THINK WHAT WE'RE SAYING IS THAT WE'RE GRATEFUL THAT ALAN BROUGHT UP THIS ISSUE. THAT'S THE WONDERFUL THING ABOUT HAVING A NEW LEADER, SOMEONE WITH AN OUTSIDE PERSPECTIVE. AND NOW LET'S DO SOME RESEARCH AND SEE IF IT'S AN ISSUE THAT WE SHOULD DEAL WITH. BUT THAT DOESN'T STOP US, I THINK, FROM GETTING CLARITY AS TO WHAT ACTUALLY EXPENSES MEANS BECAUSE IS IT YOUR CAB FARE. I DON'T KNOW. I COULDN'T DRILL DOWN.

CHAIRMAN LO: SO I'D LIKE TO GET MORE COMMITTEE COMMENT. I'M HEARING A NUMBER OF PEOPLE SAYING THAT WHAT WE SHOULD BE FOCUSING ON IS GATHERING PERTINENT INFORMATION ON THE TOPICS WE DISCUSSED THIS MORNING AND TO REALLY CLARIFY WHAT POTENTIAL EGG DONORS, HOW THEY FEEL ABOUT THIS ISSUE. ALTA'S SUGGESTION THAT WE SHOULD LOOK IN-DEPTH AT APPROACHES VARIOUS ORGANIZATIONS HAVE TAKEN TRYING TO RECRUIT DONORS, PARTICULARLY SUCCESSFUL ONES AS WELL AS UNSUCCESSFUL ONES. AND THEN BOB AND SHERRY POINTING OUT THAT WE JUST NEED A LOT OF INFORMATION ON THE SCOPE OF THE PROBLEM, THE NEED FOR NEW LINES AND SO FORTH, AND THAT

SHOULD BE PRELIMINARY TO A DECISION AS TO HOW MUCH IN-DEPTH WE WANT TO PURSUE IT.

MY OWN THOUGHT IS THAT THAT INFORMATION WILL BE USEFUL JUST TO GATHER, DISSEMINATE, AND SHARE WITH THE PUBLIC BECAUSE IF WE'RE CONFUSED, MY GUESS IS A LOT OF OTHER PEOPLE ARE CONFUSED AS WELL.

DR. PRIETO: I THINK I'D ALSO LIKE TO HEAR FROM EGG DONORS, AND I'D LIKE TO HEAR FROM OTHER GRANTEES, CIRM SCIENTISTS, AS TO WHETHER THEY'RE HAVING OR ANTICIPATE THAT THEY'RE GOING TO HAVE DIFFICULTIES. THESE ARE PEOPLE WHO ARE VERY INTIMATELY INVOLVED IN OUR PROCESS, AND WE NEED TO HEAR FROM THEM.

DR. KIESSLING: IF WE GO BACK TO DEFINITIONS HERE, WHAT IS THIS 100020, AND IT SAYS PERMISSIBLE EXPENSES. YOU KNOW, I THINK THAT ONE OF THE THINGS THAT I'M STILL CONFUSED ABOUT NOW IS THE PERMISSIBLE EXPENSES INCLUDE COSTS ASSOCIATED WITH TRAVEL, HOUSING, CHILDCARE, MEDICAL CARE, HEALTH INSURANCE, AND ACTUAL LOST WAGES. HOW DOES THAT SENTENCE APPLY TO A WOMAN GOING THROUGH INFERTILITY TREATMENT WHO WANTS TO DONATE HER EGGS?

CHAIRMAN LO: THAT'S, I THINK, THE KIND

OF AMBIGUITY THAT WE HAVE NOT ADDRESSED, BUT I THINK BOTH YOU AND SHERRY ARE SAYING IT'S SOMETHING WE NEED TO SORT OF CLARIFY.

DR. KIESSLING: CAN WE DO THAT THIS AFTERNOON?

CHAIRMAN LO: I'M NOT SURE.

DR. KIESSLING: IT'S JUST A SENTENCE, AND WE'VE MADE THIS REALLY CLEAR. WE HAD IN MIND PEOPLE WHO WERE GOING TO DONATE EGGS JUST FOR RESEARCH. BUT NOW IF YOU WANT TO EXTEND THAT TO INFERTILITY PROGRAMS WHO MIGHT BE WILLING TO COUNSEL PATIENTS THAT THEY COULD DONATE SOME NUMBER OF EGGS ABOVE SOME THRESHOLD NUMBER -- IN ENGLAND THE NUMBER 12 IS THE MAGIC NUMBER -- ABOVE 12 EGGS, THEN HOW DOES THIS SENTENCE APPLY TO THAT WOMAN WHO SAYS, YES, I WOULD LIKE TO DO THAT?

CHAIRMAN LO: WELL, IT'S NOT CLEAR WHETHER THEY SAY AND WE'LL GIVE YOU 50 PERCENT OFF YOUR IVF CYCLE, WHICH IS BASICALLY WHAT THEY DO IN THE UK. THAT'S A COMPLICATED ISSUE.

MS. LANSING: THAT'S MUCH MORE COMPLICATED. THAT WE'RE NOT SAYING WE SHOULD DO.

CHAIRMAN LO: NOT TODAY, BUT WE CAN CERTAINLY RAISE THAT AS AN ISSUE. THAT'S, I

THINK, THE QUESTION.

MR. KLEIN: I DON'T THINK WE CAN GET THERE AT THIS POINT. BUT IN TERMS OF THAT SENTENCE, WE HAVE REGULATIONS IN PLACE, AND WE HAVE THE PREVIOUS TRANSCRIPTS THAT LED TO THOSE REGULATIONS. AND PROBABLY ONE OF THE THINGS WE NEED TO DO IS GET JAMES HARRISON, WHO WAS THE COUNSEL TO US DURING THOSE REGULATIONS, TO GET US A LEGAL OPINION SO WE'RE CRYSTAL CLEAR.

DR. KIESSLING: BECAUSE SOME OF THIS MIGHT APPLY TO HER.

MR. KLEIN: I DON'T KNOW OF ANYTHING THAT SAYS YOU CAN'T, IF YOU'RE IN IVF, DONATE PART OF YOUR EXCESS EGGS. THERE'S NOTHING THAT SAYS THAT YOU CAN'T.

DR. KIESSLING: PART OF THIS SENTENCE MIGHT APPLY TO HER.

MS. CHARO: ANN, I BELIEVE I DO APPRECIATE WHAT YOU ARE ASKING, WHICH IS WHY, BASED ON THAT SENTENCE, WHICH TALKS ABOUT MEDICAL EXPENSES, COULD SOME OF HER IVF MEDICAL EXPENSES NOT BE COVERED AS A REIMBURSEMENT. I THINK WE'VE GOT TWO QUESTIONS HERE. ONE IS A VERY KIND OF HYPER TECHNICAL INTERPRETATION OF THE PROVISION QUESTION BECAUSE THERE IS A GENUINE AMBIGUITY IN

THERE.

THE SECOND IS TRYING TO REALLY GET BACK AT WHAT PEOPLE THOUGHT THEY WERE WRITING AT THE TIME AND THE PURPOSE OF IT. AND I SUSPECT, I'M SPEAKING FOR MYSELF, I SUSPECT THAT THE PURPOSE WAS TO LEAVE PEOPLE NO BETTER OFF AND NO WORSE OFF THAN THEY WOULD BE IF THEY HAD NEVER DECIDED TO HAVE SOME OF THEIR EGGS GO INTO RESEARCH. AND DISCOUNTING AN IVF PROCEDURE COULD REASONABLY BE INTERPRETED AS LEAVING THEM BETTER OFF.

NOW, THAT'S NOT TO SAY THAT I'M HAPPY WITH COMPROMISE. I THINK I'VE SAID SEVERAL TIMES THAT I FIND THIS MORE RESTRICTIVE THAN I WOULD PERSONALLY CARE TO HAVE IT, BUT I DO APPRECIATE THAT THE COMPROMISE WAS TO ELIMINATE ALL POSSIBLE FINANCIAL INCENTIVES TO DONATE SO THAT EACH DONATION WAS VIEWED AS COMPLETELY AND TOTALLY INDEPENDENTLY VOLUNTARY.

MS. LANSING: YOU'RE ABSOLUTELY RIGHT, ALTA. I REMEMBER THIS VERY CLEARLY. I ALSO REMEMBER THAT WE SAID, WHICH IS WHY I THINK IT WILL BE GREAT TO HAVE SOME RESEARCH ON THIS, WE ALSO SAID WE ARE GOING TO TAKE THE MOST CONSERVATIVE POINT OF VIEW. THIS IS INCREDIBLY CONTROVERSIAL. THIS IS AN ISSUE THAT LINES PEOPLE

UP, AND RIGHTFULLY SO. WE'RE GOING TO TAKE THE MOST CONSERVATIVE THING. WE SAID WE'RE A WORK IN PROGRESS. WE'RE CONSTANTLY GOING TO MODIFY AND REMODIFY. LET'S SEE WHAT EFFECT THERE WAS, IF ANY, AND LET'S GATHER THROUGH CIRM SOME DATA.

CHAIRMAN LO: SO LET'S SEE IF WE'RE COMING TO AGREEMENT HERE TO CHARGE, I GUESS IT'S GOING TO BE, GEOFF AND CIRM STAFF, BUT GEOFF TO WORK WITH BOB AND ALAN TO GET US INFORMATION ON THE NUMBER OF ISSUES THAT HAVE BEEN RAISED, COME BACK TO US NEXT MEETING WITH BOTH INFORMATION AND PERHAPS INVITE PEOPLE TO COME AND PRESENT TO US THEIR OWN EXPERIENCES. WE'VE HAD A NUMBER OF SUGGESTIONS HERE. AND REALLY TO PUT OURSELVES MORE IN INFORMING OURSELVES AND THEREBY INFORMING SORT OF PEOPLE IN CALIFORNIA WHAT SOME OF THESE ISSUES ARE, AND THEN WE'LL BE IN A BETTER POSITION TO SAY WHERE DO WE GO NEXT.

DR. CIBELLI: I'M NOT SURE BECAUSE I WASN'T HERE BEFORE, BUT HAVE WE EVER TALKED ABOUT GETTING CELL LINES FROM GROUPS THAT THEY, INDEED, HAVE COMPENSATED THE DONORS AND USED THEM FOR CIRM FUNDING?

MS. CHARO: THE REGULATIONS ACTUALLY PREVENT CIRM GRANTEES FROM DOING THAT RIGHT NOW.

DR. KIESSLING: USING CELL LINES.

MS. CHARO: USING CELL LINES THAT WERE MADE ELSEWHERE UNDER DIFFERENT RULES THAT PERMITTED PAYMENT TO THE DONORS.

CHAIRMAN LO: THAT'S NOT ACCEPTABLE, BUT WE HAVE THAT AMBIGUITY SAYING WE ARE DEEMING UK -- HFEA OR UK STEM CELL BANK APPROVAL TO BE AN ACCEPTABLE LINE. SO THERE'S THAT INTERNAL CONTRADICTION, BUT WE DID DISCUSS THAT. SO THE ISSUE IS DO WE WANT TO RECONSIDER IN LIGHT OF WHAT WE HEARD THIS MORNING.

DR. CIBELLI: THAT'S HAPPENING RIGHT NOW. THERE ARE CELL LINES THAT ARE EXTREMELY VALUABLE LIKE THE ONES PRODUCED BY PARTHENOGENESIS. ALL OF THOSE ARE BEING PRODUCED, AS FAR AS I KNOW, WITH SOME SORT OF COMPENSATION.

CHAIRMAN LO: AGAIN, THE ARGUMENT WOULD BE DO WE ALSO NEED, BEFORE WE MAKE THE DECISION, TO HEAR A LOT MORE ABOUT THE IMPORTANCE OF THOSE PARTHENOGENIC LINES AND HOW THERE REALLY WAS NO ALTERNATIVE. ALTA AND THEN I DO WANT TO OPEN UP TO PUBLIC COMMENT AS WELL.

MS. CHARO: I DO THINK IT'S WORTH PUTTING INTO PLAY AT A FUTURE TIME A DISCUSSION ABOUT THIS PARTICULAR DISCONNECT; THAT IS, THERE

ARE COUNTRIES THAT HAVE VERY ROBUST REGULATORY OVERSIGHT SYSTEMS. AND THE UK'S HFEA IS AN EXAMPLE. WHERE THEIR ACTUAL RULES DIFFER FROM THE CIRM SOMEWHAT, BUT THOSE DIFFERENCES, WHICH IN CALIFORNIA WERE DEEMED TO BE -- THOSE RULES, FOR EXAMPLE, ABOUT SOME DEGREE OF DISCOUNT, WHICH IN CALIFORNIA WERE DEEMED TO BE UNACCEPTABLY LIBERAL, WHATEVER, EXIST THERE WITHIN THIS ROBUST OVERSIGHT SYSTEM THAT MAYBE CORRECTS FOR ANY OF THE FEARS THAT DROVE THE DECISION-MAKING IN CALIFORNIA. IT'S A LEGITIMATE DISCUSSION TO ASK WHETHER, EVEN IF YOU WOULDN'T ACCEPT LINES FROM ANY RANDOM COUNTRY, IF YOU WOULDN'T ACCEPT LINES FROM CHINA AND THE UKRAINE THAT CAME FROM PAID DONORS WHERE YOU MIGHT NONETHELESS WANT TO BE ABLE TO SAY THAT AN APPROVAL BY THE HFEA OR AN APPROVAL BY THE JAPANESE AUTHORITIES OR AN APPROVAL BY THE ISRAELIS WOULD TRUMP BECAUSE IT'S AGAINST THE BACKDROP OF A DIFFERENT SOCIETY AND A DIFFERENT SET OF RULES. THAT, I THINK, IS A WAY TO STRUCTURE OUR CONVERSATION.

DR. CIBELLI: THE REASON I BROUGHT UP THE PARTHENOGENESIS IS BECAUSE ALL THE OTHER LINES THAT WE'RE TALKING ABOUT, YOU CAN HAVE THEM, YOU CAN HAVE BIPARENTAL LINES. WE ALREADY HAVE THEM

EVERYWHERE, BUT THERE ARE CERTAIN LINES LIKE THIS ONE THAT MAY NOT HAPPEN FOR A WHILE. WE MAY NOT EVER GET THEM IN CALIFORNIA IF WE DON'T CHANGE THE RULES.

DR. PRIETO: JUST THAT I WAS THINKING THAT IN THE UK, ONE OF THE ISSUES THEY DON'T FACE THAT WE DID AND DISCUSSED IS THAT PRESUMABLY ANY WOMAN DONATING FOR WHATEVER REASON WOULD HAVE ANY FUTURE MEDICAL COMPLICATIONS AND, YOU KNOW, MEDICAL NEEDS MET THROUGH THE NATIONAL HEALTH SERVICE.

CHAIRMAN LO: ANY OTHER COMMENTS ON THE COMMITTEE? PUBLIC COMMENT?

MS. MILSAP: MY NAME IS KATHERINE MILSAP. I'M FROM THE STEM CELL RESEARCH OVERSIGHT COMMITTEE AT STANFORD. I MANAGE THE COMMITTEE. YOU'RE REQUESTING INFORMATION ABOUT THE SUCCESS OR NOT SUCCESS OF ALTRUISTIC OOCYTE DONATION, AND THAT GOES IN LINE WITH ALTA'S SUGGESTION OF ASKING ESCRO COMMITTEES FROM THE STATE TO PROVIDE THAT INFORMATION.

I SUGGEST THAT THE CIRM GET THOSE ESCRO COMMITTEES TOGETHER TO GIVE YOU THAT INFORMATION.

CHAIRMAN LO: OTHER COMMENTS?

MR. REED: JEFF SAID SOMETHING THAT

RESONATED WITH ME WHEN HE TALKED ABOUT THE STAKEHOLDERS. AND WHEN WE'RE GOING TO THE CLINICAL TRIALS AND WE'RE TALKING ABOUT WHICH SHOULD GO FIRST, WHAT ARE THE ACCEPTABLE RISKS, I THINK IT WOULD BE REALLY HELPFUL IF THE PATIENT ADVOCATES GROUPS WERE POLLED. JUST SEND OUT A QUESTIONNAIRE: WHAT DO YOU THINK IS ACCEPTABLE? SOME THINGS THAT WE ON THE OUTSIDE MAY LOOK AT MAY BE ONE THING. OKAY. I WOULD AGREE IN THEORY THAT AN AT RISK OF DEATH GROUP WOULD BE MORE LIKELY TO BE AN APPROPRIATE THING FOR A CLINICAL TRIAL THAN PARALYSIS. HOWEVER, I ALSO KNOW A PERSON WHO IS SERIOUSLY PLANNING TO COMMIT SUICIDE BECAUSE SHE CAN'T STAND IT ANY LONGER.

I THINK IT WOULD BE IMPORTANT THAT THE STAKEHOLDERS, WHICH INCLUDE THE PATIENTS, AND I KNOW WE HAVE PATIENT ADVOCATES HERE, THIS IS A GREAT PATIENT ADVOCATES BOARD, BUT I WISH -- SEEMS LIKE IF WE COULD SEND OUT A QUESTIONNAIRE: WHAT DO YOU CONSIDER ACCEPTABLE RISKS? WHAT DO YOU THINK SHOULD BE TAKEN INTO CONSIDERATION ON THE CLINICAL TRIALS? GET MORE PATIENT ADVOCATE INVOLVEMENT THAT WAY.

MR. KLEIN: I THINK THAT IS A REALLY IMPORTANT ISSUE. I MEAN THERE'S A PHILOSOPHICAL

ISSUE HERE, WHICH IS ARE PATIENTS EMPOWERED TO CONTROL THEIR LIVES, OR ARE WE GOING TO CONTROL THEIR LIVES AND DICTATE TO THEM ACCEPTABLE RISK? FROM A PATIENT PERSPECTIVE, I FIND IT UNACCEPTABLE TO SAY THAT WE'RE GOING TO SET OUR STANDARDS ON ACCEPTABLE RISK WHEN I REALLY THINK IT SHOULD BE WITH THE PATIENT AND THEIR PHYSICIAN AND THE SCIENTISTS THAT ARE ADVISING THEM.

SO I WOULD THINK, BECAUSE IT'S GOING TO TAKE SOME TIME TO GET DOWNSTREAM ON THIS AND GET THE PROPER INPUT FROM PATIENT GROUPS AND CIVIC GROUPS, THAT IS A REALLY CENTRAL ISSUE THAT WE'VE GOT TO GET OUT OF THE WAY IN CLINICAL TRIALS BECAUSE THERE ARE A LOT OF PATIENT GROUPS THAT BELIEVE THAT THIS PATERNALISTIC VIEW THAT THEY SHOULD NOT BE ALLOWED TO HAVE CLINICAL TRIALS BECAUSE OF THE RISK TO THEM IS TOTALLY UNACCEPTABLE AND DENIAL OF THE INDIVIDUAL VALUE OF THEIR LIVES AND THE INDIVIDUAL RIGHT FOR THEM TO MAKE DECISIONS.

SO I THINK THIS IS A MAJOR PHILOSOPHICAL ISSUE THAT WE SHOULD PUT ON THE TABLE.

DR. TAYLOR: BERNIE, THIS IS MAYBE COMING A LITTLE BIT OUT OF LEFT FIELD, BUT IF YOU'RE GETTING READY TO LEAVE THIS SLIDE, ONE OF

THE QUESTIONS THAT I HAVE, AND IT'S REALLY FROM A DIMENSION THAT I HAVE VERY, VERY LIMITED INSIGHT INTO, ARE SOME OF THE BUSINESS ASPECTS OF PROP 71 AND ESSENTIALLY LOWERING THE BAR FOR OUTSIDE -- FOR LINES DERIVED PARTICULARLY OUTSIDE OF THE STATE.

SO THE QUESTION THAT I HAVE IS THAT A BIG PART, I THINK, OF WHAT PROMPTED VOTERS TO PASS PROP 71 WAS THIS IDEA THAT IT WAS GOING TO BE KIND OF AN ENGINE FOR BIOMEDICAL INVESTIGATION AND POTENTIALLY PROFIT. SO IF WE KIND OF LOWER THE BAR TO ALLOW CELL LINES AND MAKE IT ACTUALLY, FRANKLY, EASIER FOR CIRM INVESTIGATORS TO USE CELL LINES THAT AREN'T DERIVED HERE, THAT AREN'T DERIVED UNDER OUR STRICT REGULATIONS, ARE WE GOING TO BE KIND OF DEPRIVING INSTITUTIONS WITHIN CALIFORNIA, BOTH ACADEMIC AND PRIVATE, THE IP OPPORTUNITIES THAT WE SORT OF BUILT IN, I THINK, TO THE PROMISE OF PROP 71?

I CAN ACTUALLY SEE HOW WE COULD GO -- FROM WHAT ALAN SAID EARLIER TODAY, WE COULD DECIDE IT'S TOO INEFFICIENT TO DERIVE CELL LINES FROM SCNT. WE COULD GET CELL LINES THAT CAME FROM OTHER COUNTRIES, EVEN IF THEY WEREN'T DERIVED UNDER OUR STRICT REGULATIONS, AND WE'D FIND THAT

WE'D BE USING CIRM FUNDS TO FUND GREAT RESEARCH, BUT NOT GENERATING LINES PERHAPS THAT WOULD BE ECONOMICALLY BENEFICIAL.

DR. CIBELLI: I APPRECIATE ROBERT'S COMMENTS, BUT I ALSO WANT TO SAY THAT THE REASON I'M HERE AND TAKING TIME TO FLY OUT OF BEAUTIFUL MICHIGAN IS TO -- THE REASON I'M HERE IS BECAUSE THE ULTIMATE GOAL IS TO HELP PATIENTS. A BY-PRODUCT MAY BE ECONOMIC DEVELOPMENT OR JOBS OR YOU NAME IT, BUT I THINK THE MAIN GOAL WE'RE ALL HERE, LET'S NOT FORGET, IS TO HELP PEOPLE THAT NEED HELP. AND IF THEY'RE REQUIRED TO BRING CELL LINES FROM ISRAEL, FROM SPAIN THAT ARE THE BEST CELL LINES THAT WE CAN GET OR THEY HAVE THESE UNIQUE CHARACTERISTICS THAT REALLY IS GOING TO TAKE THINGS FASTER TO THE PATIENT, I THINK WE HAVE THE OBLIGATION TO DO IT AND MAKE IT EASIER FOR THE PEOPLE THAT ARE DOING THE RESEARCH IN CALIFORNIA.

CHAIRMAN LO: LET ME TRY AND MOVE US TOWARDS --

MR. KLEIN: CAN I MAKE ONE MORE COMMENT ABOUT THIS POINT THAT WAS RAISED? I THINK IT'S REALLY IMPORTANT THE POINT JOSE JUST MADE. DURING THE CAMPAIGN I DIDN'T ACCEPT ANY BIOTECH OR PHARMA MONEY, AS IN ZERO. MAY HAVE BEEN INDIVIDUAL

SCIENTISTS THERE THAT GAVE A VERY SMALL AMOUNT OF MONEY, I THINK LESS THAN $30,000 OUT OF 34 MILLION. BUT THE MISSION IS WHAT'S IMPORTANT TO THE PUBLIC. WE DID HUNDREDS OF THOUSANDS OF DOLLARS OF POLLING. SO WE HAVE A PRETTY GOOD IDEA WHAT PEOPLE WERE VOTING ON, AND THEY WERE VOTING US ADVANCING THERAPIES FOR THE BENEFIT OF PATIENTS.

THE BUSINESS ISSUES ARE A PURE BY-PRODUCT, AND EVEN IN SUPPLIERS, WE HAVE A GOAL STATEMENT THAT APPROXIMATELY 50 PERCENT OF THE SUPPLIERS SHOULD HAVE AN IN-STATE SOURCE. BUT IF WE NEED TO GO TO ENGLAND OR SWEDEN OR ISRAEL OR WHEREVER WE NEED TO GO TO GET THE RIGHT CELL LINES TO ADVANCE MEDICAL MISSIONS, WE HAVE AN OBLIGATION TO PEOPLE WHOSE LIVES ARE BEING DEVASTATED EVERY DAY WITH CHRONIC DISEASE TO FOLLOW THAT SCIENTIFIC MISSION, FOLLOWING IT ETHICALLY, SAFELY, AND CAREFULLY MEDICALLY, BUT FOLLOWING THAT MISSION WITH THAT HIGH FOCUS. AND IT IS VERY IMPORTANT THAT WE LOOK AT OUR MISSION IN THAT CONTEXT.

CHAIRMAN LO: I WANT TO TRY AND SEE IF I CAN MOVE US TOWARDS CLOSURE HERE BECAUSE THE HOUR IS GETTING ON. WHAT I THOUGHT I HEARD WAS SOME AGREEMENT, CORRECT ME IF I'M WRONG, THAT WE SHOULD

ON THE SWG GO INTO SORT OF AN INFORMATION GATHERING MODE. AND THERE ARE A NUMBER OF IDEAS PUT OUT OF SPECIFIC ISSUES WE SHOULD ADDRESS, PEOPLE TO TALK TO. MY COMPUTER JUST CRASHED, SO I DON'T HAVE THAT LIST.

I THINK GEOFF AND ALTA AND SHERRY AND OTHERS HAVE SUGGESTED SPECIFIC THINGS FOR US TO LOOK AT IN TERMS OF GOING BACK TO SCRO'S, ASKING THEM WHERE THEY'RE HAVING PROBLEMS PARTICULARLY WITH USING LINES DERIVED ELSEWHERE, GOING TO ADVOCACY GROUPS AND PARTICULARLY WOMEN WHO MIGHT BE INTERESTED IN DONATING, AND SORT OF FINDING OUT WHAT THEIR VIEWS ARE.

SO I THINK -- AND FINDING OUT BASIC INFORMATION OF HOW PEOPLE HAVE TRIED TO RECRUIT OOCYTE DONORS IN CALIFORNIA PARTICULARLY WHERE THERE'S BEEN SUCCESS AND GET MORE INFORMATION FROM PEOPLE LIKE KEVIN AND ANN WHO HAVE TRIED TO DO THAT IN OTHER SETTINGS, AND TO REALLY HAVE THAT BE OUR FIRST ORDER OF BUSINESS. AND THEN BASED ON THAT INFORMATION, WE WILL ABLE TO MAKE A MORE KIND OF ENLIGHTENED DECISION ON WHAT POLICY SORT OF ISSUES WE SHOULD TRY AND PUSH TOWARDS. I THINK IT WOULD BE UP TO GEOFF, AND I'LL WORK WITH GEOFF, AS I THINK BOB AND ALAN WILL AS WELL, TO SORT OF

INVITE THE RIGHT PEOPLE. AND WE'LL CONSULT WITH ALL OF YOU TO SORT OF MAKE SURE WE'VE GOT THE TOPICS COVERED AND THE RIGHT PEOPLE TO THE NEXT MEETING.

DOES THAT SOUND LIKE A REASONABLE WORKING PLAN FOR AT LEAST THE NEXT MEETING? WE ALWAYS WANT TO KEEP OUR EYE ON THE POLICY IMPLICATIONS OF WHAT WE DO.

MS. FOGEL: JUST TWO POINTS. INFORMATION GATHERING IS REALLY IMPORTANT. I DO THINK YOU HAVE TO BE CAREFUL THAT YOU DON'T GO ASK QUESTIONS OF A SLANTED GROUP. SO IF YOU GO TO CURRENT EGG DONORS WHO ARE USED TO BEING PAID FOR FERTILITY, YOU'RE GOING TO GET VERY DIFFERENT ANSWERS THAN IF YOU TRY TO DO SOME BROADER SURVEY OF PERHAPS THE TARGET GROUP OF WOMEN WHO YOU MIGHT BE WANTING TO ASK FOR RESEARCH EGGS. SO WE HAVE TO BE CAREFUL WE DON'T PRESUPPOSE THE ANSWER.

THE OTHER THING I WANTED TO SAY ABOUT THE CHART SHOWING TRENDS OF WHERE THINGS ARE GOING, CALIFORNIA'S PROMISE WAS THAT WE WERE GOING TO BE A LEADER. WE WERE GOING TO SET THE HIGHEST ETHICAL STANDARDS. WE WERE GOING TO BE THE BIG GUERILLA. WE PUT THE MOST MONEY INTO THIS. AND I THINK WE NEED TO KEEP REMEMBERING THAT, NOT TO BE

LOWERING THE BAR BECAUSE OTHER PEOPLE ARE LOWERING THE BAR, BUT RATHER SETTING THE EXAMPLE. WE ALREADY ARE HEARING ABOUT RESEARCHERS COMING TO CALIFORNIA TO DO WORK HERE. AND I THINK IT'S IMPORTANT FOR US TO SAY TO THEM, GREAT, WE WANT YOU HERE, AND HERE ARE OUR HIGHER ETHICAL STANDARDS. SO LET'S NOT BE TEMPTED TO LOWER THOSE.

CHAIRMAN LO: ANY OTHER PUBLIC?

MS. LANSING: I JUST WANT TO ACTUALLY RESPOND TO WHAT YOU ARE SAYING, WHICH I AGREE WITH. ALSO, THE RESEARCH ISN'T JUST GOING TO BE ON THAT. THE RESEARCH HAS TO BE ON ARE WE NOT GETTING EGGS? ARE WE NOT GETTING THIS? THAT REALLY TO ME IS THE REAL SEMINAL QUESTION, DO YOU KNOW, THAT YOU RAISED, THAT WE WON'T GET THEM.

MR. JANUS: JUST ONE COMMENT ON THE IP ISSUE, IF I UNDERSTOOD IT CORRECTLY. EVEN IF THE LINES CAME FROM OUTSIDE OF THE CALIFORNIA, THE BIOTECH INDUSTRY THROUGH CIRM-FUNDED GRANTS, ANY METHODS THAT WERE DEVELOPED WITH THOSE LINES OR COMPOSITION OF MATTER FOR THE END DIFFERENTIATED PRODUCT WOULD ACCRUE TO CALIFORNIA. SO, IN FACT, I THINK WE'RE ENTHUSIASTIC ABOUT DEVELOPING IP EVEN WITH LINES FROM INSIDE OR OUTSIDE OF

CALIFORNIA THAT WOULD ACCRUE TO CALIFORNIA. I THINK THAT'S VERY IMPORTANT.

CHAIRMAN LO: OTHER QUESTIONS, COMMENTS?

MS. SMITH-CROWLEY: SHANNON SMITH-CROWLEY REPRESENTING THE AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS, DISTRICT 9, AND THE AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE. I'D LIKE TO HAVE YOU HAVE THE PERSPECTIVE THAT PERHAPS THE HIGHEST ETHICAL STANDARD COULD BE EQUITY IN HOW RESEARCH SUBJECTS ARE COMPENSATED.

CHAIRMAN LO: ALL RIGHT. SO I THINK, GEOFF, DO YOU HAVE A CLEAR IDEA? WE'RE AGAIN PLACING THINGS ON YOUR VERY CAPABLE SHOULDERS. BUT IN TERMS OF GOING INTO OUR INFORMATION GATHERING MODE, I THINK WE WILL BE CONSULTING WITH THE COMMITTEE TO MAKE SURE WE GET THE TOPICS RIGHT AND SUGGESTIONS FOR PEOPLE FOR OUR NEXT MEETING.

DR. LOMAX: I THINK WE WILL PROCESS THIS LIST AND SUGGEST PERHAPS WE MAY NEED TO CONVENE YOU ALL FOR A TELEPHONE CALL SO WE CAN SORT OF DO ANY FINAL PROCESSING IN PUBLIC AS WELL IF WE ARE MAKING SORT OF DECISIONS THAT ARE SUBSTANTIVE. SO WE WILL SORT OF CHECK ON THAT TO SEE THE BEST WAY TO PROCEED.

CHAIRMAN LO: I THINK WHAT WE'RE TALKING

ABOUT IS REALLY SORT OF ARRANGING THE AGENDA AND INVITING PEOPLE AS OPPOSED TO SUBSTANTIVE DECISION. I HEARD A LOT OF FEELING THAT WE NEED TO GET MORE INFORMATION BEFORE WE START MAKING DECISIONS.

DR. LOMAX: IF YOU ALL ARE COMFORTABLE THAT THE SUBSTANTIVE LIST, AND IT IS FAIRLY SUBSTANTIVE AS I HAVE IT RIGHT NOW, IS THE RIGHT LIST, THEN, YES, WE'RE IN A FINE POSITION TO MOVE FORWARD.

CHAIRMAN LO: ALL RIGHT. THEN IF THERE ARE NO OTHER COMMENTS, I'M GOING TO TAKE THE LIBERTY OF, FIRST OF ALL, THANKING YOU ALL FOR COMING, PARTICULARLY THOSE FROM OUT OF TOWN. AND I SORT OF WANT TO EXPRESS MY SYMPATHIES TO THOSE OF YOU WHO ARE GOING BACK TO COLD, SNOWY, ICY CLIMATES, BUT YOU CAN ALWAYS MOVE TO CALIFORNIA. IT'S LIKE THIS EVERY DAY OF THE YEAR.

MS. LANSING: IT'S EVEN BETTER IN LOS ANGELES.

CHAIRMAN LO: SOMEONE LIKE TO OFFER A MOTION FOR ADJOURNMENT?

MS. CHARO: I SO MOVE.

DR. PRIETO: SECOND.

CHAIRMAN LO: ALL IN FAVOR.

(THE MEETING WAS THEN ADJOURNED AT 04:17 P.M.)

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REPORTER'S CERTIFICATE

I, BETH C. DRAIN, A CERTIFIED SHORTHAND REPORTER IN AND FOR THE STATE OF CALIFORNIA, HEREBY CERTIFY THAT THE FOREGOING TRANSCRIPT OF THE PROCEEDINGS BEFORE THE SCIENTIFIC AND MEDICAL ACCOUNTABILITY STANDARDS WORKING GROUP TO THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE IN THE MATTER OF ITS REGULAR MEETING HELD AT THE LOCATION INDICATED BELOW

KABUKI HOTEL
1625 POST STREET
SAN FRANCISCO, CALIFORNIA
ON
FEBRUARY 28, 2008

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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