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

REGULAR MEETING

LOCATION: SAN FRANCISCO COURTYARD DOWNTOWN
299 SECOND STREET
SAN FRANCISCO, CALIFORNIA

DATE: FRIDAY, APRIL 6, 2012
9 A.M.

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

BRS FILE NO.: 91988

I N D E X

SAN FRANCISCO, CALIFORNIA; FRIDAY, APRIL 6, 2012

9 A.M.

CHAIRMAN LO: DELIGHTED YOU ALL COULD COME. WE HAVE AN INTERESTING AGENDA. COUPLE HOUSEKEEPING DETAILS. FIRST, BECAUSE THIS IS BEING TRANSCRIBED, I, AS SORT OF A REPEAT OFFENDER, HAVE BEEN TASKED WITH REMINDING EVERYBODY TO SPEAK INTO THE MIKE AND TO IDENTIFY YOURSELVES WHEN YOU ARE SPEAKING SO WE CAN HAVE ACCURATE AND FULL TRANSCRIPTS.

SINCE I HAVE BEEN INCORRIGIBLY REFRACTORY, I'M NOW MIKED WITH ONE OF THESE THINGS. SO DON'T COME UP TO ME AND WHISPER THINGS DURING BREAKS BECAUSE IF YOU FORGET TO TURN IT OFF, IT WILL BE BROADCAST TO THE ROOM, MUCH TO OUR EMBARRASSMENT.

I WANT TO WELCOME EVERYONE AND SAY, FIRST, THAT SHERRY LANSING, OUR CO-CHAIR, IS UNABLE TO BE HERE TODAY AND ASKED ME TO SEND HER REGRETS AND HER WELCOME. WE'VE TALKED OVER THE AGENDA AND THE THINGS WE'RE GOING TO DISCUSS WITH HER, AND SHE LOOKS FORWARD TO HEARING THE RESULTS OF OUR DELIBERATIONS.

I JUST WANT TO GIVE YOU A QUICK OVERVIEW OF THE MEETING. WE WILL NOT HAVE A QUORUM. SO WHAT

WE WILL DO IS NOT MAKE FORMAL RECOMMENDATIONS, BUT I THINK WE DO WANT TO COMMUNICATE TO THE ICOC A SENSE OF THE COMMITTEE AS TO HOW WE FEEL ABOUT THESE ISSUES.

I WANT TO PARTICULARLY WELCOME SOME NEW MEMBERS. JON THOMAS, IT'S HARD TO IMAGINE YOU AS NEW BECAUSE YOU REALLY SORT OF JUMPED RIGHT IN AND LEFT YOUR MARK ON THIS AGENCY. THIS IS ACTUALLY YOUR FIRST SWG MEETING. WELCOME YOU ON BEHALF OF THE MEMBERS AND HOW WE'RE LOOKING FORWARD TO WORKING WITH YOU.

AND THEN WE DO HAVE TWO NEW MEMBERS DOWN THATAWAY. JEFF BOTKIN FROM THE UNIVERSITY OF UTAH AND NICOLE LOCKHART FROM NIH. SPECIAL GREETINGS TO BOTH. WE HAD A SORT OF AN INTRODUCTORY MEETING LAST NIGHT, AND WE LOOK FORWARD TO YOUR EXPERTISE AND CONTRIBUTIONS.

I WANT TO FIRST JUST SAY THAT, AS WE DISCUSSED A BIT LAST NIGHT, THE SWG HAS EVOLVED OVER TIME. I THINK WHAT WE'RE TRYING TO DO IS KEEP UP TO AND AHEAD OF THE BREAKING ETHICAL ISSUES AND GIVE ADVICE TO THE ICOC AND TO THE LEADERSHIP, JON AND HIS TEAM. AND I THINK AS WE LOOK BACK OVER WHAT HAS HAPPENED IN THE PAST EIGHT YEARS, AND I THINK THIS REALLY CAME HOME LAST NIGHT WHEN WE WERE TALKING

ABOUT ALL THE WORK WE DID AT THE BEGINNING WITH CONSENT FOR OOCYTE DONORS DONATING OOCYTES EXPRESSLY FOR RESEARCH, ALL THE WORK WE PUT INTO WHAT CELL LINES WERE ACCEPTABLE FOR CIRM FUNDING, WE NOW ARE SORT OF LOOKING AT A NEW SET OF ISSUES. AND BECAUSE OF THE MISSION OF CIRM UNDER JON AND ALAN TO REALLY PUSH TOWARDS BRINGING STEM CELL DISCOVERIES INTO THE CLINIC AND REALLY THINKING ABOUT CLINICAL TRIALS, WE REALLY WANT TO MAKE SURE THAT WE HELP CIRM AS A STANDARDS WORKING GROUP THINK THROUGH THE ISSUES WITH REGARD TO, FIRST OF ALL, STEM CELL BANKING, WHICH WE'RE GOING TO DISCUSS AT SOME LENGTH LATER THIS MORNING, BUT ALSO EVENTUALLY TO CLINICAL TRIALS.

SO THERE'S A COUPLE OF GOALS I'D LIKE TO ACCOMPLISH TODAY. FIRST IS THERE ARE A NUMBER OF AMENDMENTS, PROPOSED AMENDMENTS, TO THE REGULATIONS I'D LIKE US TO THINK ABOUT AND GIVE OUR VIEWS TO THE ICOC ON. I WOULD REGARD THESE AS PRIMARILY TECHNICAL AMENDMENTS, BUT I THINK THEY WILL IMPROVE HOW THE AMENDMENTS WORK.

AND THEN I'D LIKE TO SPEND THE BULK OF THE MEETING TALKING ABOUT CIRM'S PROPOSAL FOR A BANKING INITIATIVE WITH INDUCED PLURIPOTENT STEM CELLS. AND WE'LL HEAR ABOUT SOME INTERESTING REQUESTS FOR

APPLICATIONS, SOME EXPERIENCE WITH THE CIRM REQUIREMENTS AND RECOMMENDATIONS FOR CONSENT FOR IPSC DERIVATION.

THEN WE'RE GOING TO ASK NICOLE TO REALLY HELP US THINK THROUGH ISSUES RELATED TO RETURN OF RESULTS FROM THIS RESEARCH BACK TO THE ORIGINAL DONORS. AND THAT'S A VERY COMPLICATED ISSUE THAT WE WANT TO TRY AND UNDERSTAND.

SO WITH THAT, I GUESS WE'VE OFFICIALLY CALLED THE MEETING TO ORDER. SINCE WE'RE NOT A QUORUM, GEOFF, YOU JUST WANT TO NOTE WHO'S HERE FOR THE RECORD.

DR. LOMAX: THANK YOU, BERNIE. FOR THE RECORD, BERNARD LO, DOROTHY ROBERTS, ROBERT TAYLOR, NICOLE LOCKHART, JEFFREY BOTKIN, JON THOMAS, I THINK I SAW FRANCISCO PRIETO, TED PETERS, AND JOHN WAGNER. I BELIEVE JEFF SHEEHY WILL BE HERE THIS MORNING AS WELL.

CHAIRMAN LO: GREAT. JON, WHY DON'T YOU GIVE US YOUR COMMENTS.

CHAIRMAN THOMAS: I WOULD JUST LIKE, ON BEHALF OF THE BOARD, TO WELCOME EVERYBODY HERE. THIS BODY HAS OVER THE YEARS HAD AN EXTREMELY IMPORTANT ROLE IN THE ABILITY OF CIRM TO FUNCTION. WHILE THE SCIENTIFIC CHALLENGES HAVE BEEN GREAT AND

CONTINUE TO BE AND ARE ABLY BEING LOOKED AFTER BY OUR SCIENCE STAFF, WE HAVE DR. FEIGAL AND DR. OLSON AND A NUMBER OF OUR OTHER FOLKS HERE DOING A WONDERFUL JOB, NONE OF THAT WOULD HAVE BEEN POSSIBLE HAD THIS GROUP NOT BEEN ABLE TO ESTABLISH A SET OF ETHICAL PARAMETERS THAT PASSED MUSTER AS LOOKED UPON BY THE OUTSIDE WORLD. AND THE ISSUES WERE MANY, THE ISSUES WERE THORNY, VERY COMPLICATED. AND UNDER THE LEADERSHIP OF BERNIE AND THE DRAMATIC ROLE THAT ALL MEMBERS OF THIS COMMITTEE PLAYED EARLY ON AND CONTINUE TO PLAY AT THIS POINT, YOU'VE REALLY SET THE TABLE. YOU GUYS ARE SORT OF THE SOUL OF THE WHOLE UNDERTAKING. YOU SET THE TABLE FOR CIRM TO DO WHAT IT'S DOING. AND I WANT TO CONGRATULATE YOU ON THAT WORK, LET YOU KNOW HOW VALUABLE THE BOARD FEELS THE WORK YOU'RE DOING IS.

WOULD LIKE TO ALSO GIVE A SPECIAL SHOUT OUT TO GEOFF LOMAX FOR ALL HE HAS DONE TO HELP RUN AND COORDINATE ALL OF THIS OVER THE YEARS. YOU GUYS MAKE A GREAT TEAM. WE'RE DELIGHTED TO SEE MEMBERS WHO HAVE BEEN HERE BEFORE. AND NEW MEMBERS, WELCOME. THERE ARE NO SHORTAGE OF ISSUES IN THIS AREA ON AN ONGOING BASIS, AND WE VERY MUCH APPRECIATE AND HIGHLY VALUE WHAT YOU'RE DOING.

SO ON BEHALF OF THE BOARD, WELCOME AND

THANK YOU VERY MUCH FOR ALL OF YOUR EFFORTS.

CHAIRMAN LO: THANKS, JON. LET'S GO AHEAD AND HEAR SOME STAFF REPORTS AND UPDATES. AND, GEOFF, I'M JUST GOING TO TURN IT OVER TO YOU TO SORT OF BRING US UP TO DATE ON A NUMBER OF ISSUES HERE.

DR. LOMAX: THANKS VERY MUCH. ONE OF THE THINGS I'D LIKE TO PRESENT TO YOU THIS MORNING IS A PROJECT WE HAD DONE LAST SUMMER. AND THIS WAS REALLY AN EFFORT TO TAKE ADVANTAGE OF SOME OF THE DATA AVAILABLE TO CIRM TO THEN EVALUATE THE WORK THAT WE'VE DONE HERE. WE THOUGHT IT WAS A NICE TOOL TO TAKE INFORMATION ABOUT WHAT OUR GRANTEES ARE DOING AND RELATE IT BACK TO THE STANDARDS. SO I WILL DESCRIBE TO YOU A PROJECT THAT WAS FOCUSED SPECIFICALLY ON LOOKING AT THE VALUE OF THE ESCRO COMMITTEES IN EVALUATING EMBRYONIC CELL LINE PROVENANCE.

I'D LIKE TO GIVE TREMENDOUS THANKS TO ROHUN PATEL, AN UNDERGRADUATE FROM UCLA, WHO APPROACHED CIRM AND SAID, "I REALLY WANT TO GET INVOLVED WITH YOU GUYS AND DO SOMETHING." AND HE WAS TERRIFIC. SO HE LEARNED ALL ABOUT ACCESS DATABASES IN ABOUT THREE WEEKS. THIS REMINDED ME HOW, WHEN UNDERGRADUATES DIG INTO A PROJECT, THE AMOUNT OF ENERGY AND DRIVE THEY BRING TO THINGS. I

STARTED TO FEEL A LITTLE OLD ACTUALLY. BUT IT WAS REALLY GREAT TO WORK WITH SOMEONE WITH SO MUCH ENERGY AND ENTHUSIASM.

BEHIND THE SCENES AT CIRM, WE HAVE A TREMENDOUS I.T. TEAM WHO WERE VERY GENEROUS IN TERMS OF BEING ABLE TO HELP PULL DATA FOR US, AND THEN A LOT OF FOLKS FROM SCIENCE AND COMMUNICATIONS WHO REALLY HELPED SORT OF MOVE THE PROJECT ALONG AND GIVE ROHUN A SENSE THAT WHAT HE WAS DOING WAS REALLY VALUED BY THE ORGANIZATION. THANKS EVERYONE FOR YOUR HELP.

SO THE GOAL OF THIS PROJECT WAS TO LOOK AT THE USE OF HUMAN EMBRYONIC STEM CELL LINES BY INDIVIDUAL GRANT NUMBER. AND TO MY KNOWLEDGE, NO ONE HAS BEEN ABLE TO REALLY LOOK AT EMBRYONIC CELL LINE UTILIZATION ON A SORT OF PROJECT-BY-PROJECT BASIS. AND, AGAIN, SINCE WE WERE DOING THIS SORT OF WITH OUR STANDARDS HAT ON, ONE OF THE THINGS THAT WE WERE REALLY INTERESTED IN UNDERSTANDING IS THE DIFFERENCE -- WHAT'S THE UTILIZATION RATE FOR NIH-APPROVED, THE BUSH LINES, SO THE EARLY NIH LINES, THE NEWER LINES, OR THE LINES THAT ARE NOW APPEARING ON THE NIH REGISTRY. AND THEN SOMETHING WE HAD A VERY STRONG INTEREST IN WAS THE LINES DERIVED BY OUR GRANTEES THROUGH OUR FUNDING.

WE HAD A SECONDARY GOAL OF TRYING TO CODE THE LINES BY SORT OF AREA OF RESEARCH, THE IDEA OF WHAT ARE THE LINES BEING USED FOR. WE'VE POSITIONED THE DATA THAT WAY, BUT THERE'S NO ANALYSIS IN TERMS OF OUR SECONDARY GOALS. IN THE AMOUNT OF TIME WE HAD, WE GOT THROUGH THE PRIMARY GOALS. AND ULTIMATELY ONE OF THE THINGS WE DO ON OUR WEBSITE IS WE REPORT ON CIRM FUNDING IN RELATION TO DISEASE AREAS. AND, AGAIN, IN SORT OF A DREAM WORLD, WE COULD RELATE CELL LINE UTILIZATION TO THOSE DISEASE AREAS. AGAIN, WE DIDN'T GET THERE, BUT WE SORT OF POSITIONED THE DATA IN A WAY WHERE THAT COULD BE DONE WITH MORE FOLLOW-UP.

ONE OF THE REASONS THAT I FELT THIS WAS ACTUALLY IMPORTANT FROM A REGULATORY POLICY PERSPECTIVE IS THERE HAVE BEEN A NUMBER OF PUBLICATIONS THAT WERE LOOKING AT CELL LINE UTILIZATION AND THEN DRAWING INFERENCE AS TO THE VALUE OF STATE FUNDING VERSUS NIH FUNDING. AND THE SORT OF GIST OF THOSE PUBLICATIONS WERE MOST OF THE WORK GOING ON COULD HAVE BEEN DONE WITH NIH FUNDING ANYWAY. AND WHEN I READ THESE PAPERS, THEY DIDN'T SIT RIGHT WITH ME BECAUSE REALLY THERE WAS A DISCONNECT BETWEEN WHAT I WAS SEEING IN TERMS OF WORK I WAS DOING AT CIRM AND REALLY LOOKING THROUGH

THE PROTOCOLS, BUT WE TO DATE HADN'T REALLY PUT ANYTHING OUT TO SUBSTANTIATE THAT. SO WHAT WE WERE LEFT WITH WAS WHAT I WOULD CHARACTERIZE AS A LITERATURE THAT SUGGESTED CERTAIN THINGS BASED ON THE BEST AVAILABLE DATA, AND CIRM HAVING THE BEST AVAILABLE HAD NOT YET CHIMED IN ON THE SUBJECT, SO IT WAS OUR TURN.

SO WHAT WE DID IS WE USED WHAT -- WE GET PROGRESS REPORTS FROM OUR GRANTEES WHICH ARE INCREDIBLY DETAILED IN TERMS OF THE MATERIALS THEY'RE USING, AND PARTICULARLY EMBRYONIC STEM CELL LINES. SO WHAT WE WERE ABLE TO DO IS, FROM THESE PROGRESS REPORTS, DUMP ALL THAT DATA INTO WHAT I'M GOING TO CALL THE HESC LINE UTILIZATION DATABASE. AND, AGAIN, I MENTION THE DISEASE PIECE. I'M NOT GOING TO SPEND A LOT OF TIME ON THAT BECAUSE THAT PIECE WASN'T DONE. SO THE CRITICAL THING IS THESE ARE ACTUAL REPORTS FROM THE GRANTEES BASED ON RESEARCH THAT WAS ACTUALLY DONE. AND THIS IS VERY IMPORTANT BECAUSE A LOT OF -- IN SURVEYS PEOPLE REPORT USING A LOT OF CELL LINES; BUT WHEN YOU ACTUALLY ASK -- THESE ARE LINES PERHAPS THEY ARE THINKING MIGHT BE USEFUL OR THEY MIGHT BE USING, BUT THEY DIDN'T GET INSTITUTIONAL APPROVAL, THESE ARE LINES THAT MADE IT INTO THE LAB AND WERE ACTUALLY

USED IN STUDIES. SO WE WERE ABLE TO CAPTURE THAT ON A PROTOCOL-BY-PROTOCOL BASIS.

SO WHAT WE WERE ABLE TO CAPTURE IS WHAT I'M DESCRIBING AS UTILIZATION EVENTS. THERE WERE 339 EVENTS OR PROTOCOLS WHERE LINES WERE USED. WE CREATED A UNIQUE RECORD FOR EACH OF THOSE EVENTS. SO IT WOULD BE GRANT NUMBER H9 OR GRANT NUMBER UCSF2. SO WE HAVE A UNIQUE RECORD FOR EVERY EVENT. IT ALSO GAVE US AN OPPORTUNITY TO GO THROUGH THE CIRM DATABASE, AND WE STANDARDIZED ALL THE CELL LINE NAMES BECAUSE THERE'S A LITTLE BIT -- OVER TIME THERE'S A LITTLE BIT OF SLIPPAGE IN HOW PEOPLE ARE NAMING LINES. SO IT WAS A NICE EXERCISE. WE WERE ABLE TO GIVE SOMETHING BACK TO THE DATA FOLKS, WHICH WAS A CONSISTENT NAMING SCHEME FOR ALL THE STEM CELL LINES.

AND THEN WE CREATED A SET OF TABLES, WHICH I'LL SHOW YOU IN A MOMENT. THE 339 EVENTS REPRESENT 97 GRANTS. IS THAT CLEAR? SO 339 USES OF STEM CELL LINES WITHIN 97 GRANTS. AND WHAT WE ACTUALLY SEE IS 138 UNIQUE STEM CELL LINES BEING USED WITHIN THE 97 GRANTS. DID THAT COME OFF CLEARLY? SO OBVIOUSLY THIS NUMBER, THERE'S A LOT OF DUPLICATION IN THE LINES BEING USED. WE REDUCE IT DOWN TO 97 GRANTS WHERE 339 BECOMES 138 UNIQUE.

SO, AGAIN, WE WERE THINKING WITH THE SORT OF STANDARDS HAT ON, WHAT SORT OF CATEGORIES DID THESE STEM CELL LINES FALL INTO? SO WHAT WE HAD TO DO IS CREATE A HIERARCHY IN PART BECAUSE WE KNOW THAT CERTAIN STEM CELL LINES WOULD APPEAR -- H9 IS A GOOD EXAMPLE. IT WAS IN THE NIH REGISTRY PRIOR TO 2009 AND IT'S ALSO A CURRENT REGISTRY LINE. SO THESE NUMBERS REPRESENT A HIERARCHY. SO H9 IS ONLY BEING COUNTED AS A CURRENT LINE AND NOT AS A PRIOR 2009 LINE. WE WANT TO AVOID DOUBLE COUNTING.

DR. ROBERT TAYLOR: IN THE 339 EVENTS THAT YOU HAVE -- I'LL TRY TO SCREAM. IT'S REALLY NOT THAT IMPORTANT A QUESTION. I WAS WONDERING OUT OF THE 339 EVENTS, WHAT'S THE GENERAL PROPORTION THAT ACTUALLY DIDN'T MAKE IT TO A -- SO THERE WOULD BE PROPOSALS TO USE HESC LINES, BUT I'M ASSUMING THAT SOME OF THOSE HAVEN'T GOTTEN TO THE POINT --

DR. LOMAX: WE WERE VERY DELIBERATE. WE WANT TO AVOID THAT PHENOMENON OF PHANTOM UTILIZATION. THAT'S WHY WE'RE RELYING ON PROGRESS REPORTS WHICH ARE ACTUAL CERTIFIED HERE'S WHAT WE DID. THAT'S WHAT'S UNIQUE ABOUT WHAT WE'RE DOING. OTHER PEOPLE HAVE USED THINGS LIKE MATERIAL TRANSFER AGREEMENTS, SURVEYS. NOT A BAD WAY TO GO. IF YOU DON'T HAVE ANYTHING BETTER, FINE METHODOLOGY. BUT

THIS IS WHAT I WOULD SUGGEST IS A GOLD STANDARD. CERTIFIED, HERE'S WHAT WE DID DATA.

SO WE DEVELOPED THE HIERARCHY IN ORDER TO, AGAIN, AVOID DUPLICATION WITH LINES THAT WOULD APPEAR IN MULTIPLE PLACES. AND, AGAIN, IT GIVES US A WAY OF LOOKING AT IT WITH A SORT OF REGULATORY LENS. SO THAT WE FOUND THAT CURRENT NIH REGISTRY LINES, 35 OF THE LINES THAT ARE IN THE REGISTRY WERE PART OF WHAT OUR GRANTEES USED, AND THAT WAS A QUARTER OF ALL LINES USED BY OUR GRANTEES IN THE STUDY PERIOD.

WE THEN HAD CIRM-DERIVED LINES THAT ARE NOT IN THE REGISTRY. I THINK THERE WERE 18 CIRM LINES DERIVED, BUT NINE OF THEM HAD ALREADY BEEN QUALIFIED FOR THE REGISTRY. A NUMBER OF THOSE FROM BOTH UCSF AND UCLA. SO THEY ACTUALLY ARE UP HERE, BUT THEN THERE'S ANOTHER NINE LINES THAT ARE EITHER IN THE PROCESS OR HADN'T MADE IT YET. SO 7 PERCENT OF THE LINES WERE CIRM-DERIVED LINES, AND WE'RE VERY PROUD ABOUT THOSE LINES BECAUSE WE HAVE DOCUMENTATION FROM THE GRANTEES THAT DERIVED THEM CERTIFYING THAT THEY WERE DERIVED ACCORDING TO OUR CONSENT PROTOCOLS. AND SO WE FEEL VERY GOOD ABOUT THE FACT THAT WE'VE CONTRIBUTED SOMETHING TO THE RESEARCH STREAM THAT IS CONSISTENT WITH WHAT WE WANT

TO SEE FROM CONSENT AND OVERSIGHT.

BUT THE BIG NUMBER THAT REALLY JUMPS OUT HERE FOR, AGAIN, UNDERSCORING THE IMPORTANCE, I THINK, OF THE REGULATIONS IS THE ESCRO-APPROVED LINES. THERE WERE 70 LINES THAT HAD TO BE EVALUATED IN SOME WAY BY AN OVERSIGHT COMMITTEE, AND THAT'S 51 PERCENT OF LINES ACTUALLY USED. SO THIS IS A PIECE THAT REALLY HADN'T -- SORT OF THE MAGNITUDE AND PROPORTION OF THIS HAS NOT REALLY SHOWN UP IN PREVIOUS STUDIES. AND WE THINK THIS IS AN IMPORTANT SORT OF INSIGHT INTO SORT OF THE VALUE OF RESEARCH OVERSIGHT.

AND THEN THE BUSH LINES, IF YOU WILL, 7 PERCENT, AND THEN THE UK STEM CELL BANK LINES ARE ANOTHER SIGNIFICANT PROPORTION. AND AS YOU MAY WELL KNOW, WE AUTHORIZE USE OF THESE LINES SORT OF AUTOMATICALLY. THEY'RE VIEWED TO BE SORT OF ETHICALLY DERIVED WITH NO FURTHER REVIEW. AND IT'S INTERESTING TO SEE THE VALUE OF A POLICY LIKE THAT. WE THINK WE SEE A LOT OF GRANTEES UTILIZING THE UK STEM CELL BANK FOR THAT REASON AS WELL. SO THIS IS REALLY SORT OF THE GUTS OF OUR FINDINGS.

I HAVE A COUPLE OF OTHER TABLES I CAN SHOW YOU. BUT I WANT TO PAUSE THERE AND SEE IF THERE ARE ANY OTHER QUESTIONS IN TERMS OF THIS. TERRIFIC.

SO ONE OF THE THINGS -- SO, AGAIN, TO REMIND FOLKS, WHILE THE DISTRIBUTION IS VERY BROAD, THERE STILL IS A FAIRLY HIGH CONCENTRATION OF UTILIZATION AMONGST SOME OF THE MOST FREQUENTLY USED -- SOME OF THE COMMON LINES. I THINK THESE NAMES WILL BE FAMILIAR TO MOST FOLKS. BUT IT IS WORTH NOTING THAT THERE ARE A NUMBER OF LINES THAT HAVE NOT YET BEEN NIH APPROVED THAT WE'VE STILL -- OUR GRANTEES ARE ABLE TO UTILIZE BECAUSE OF OUR REGULATIONS AND OUR POLICIES.

AND THEN I THINK I'VE CIRCULATED THIS. I CAN RECIRCULATE IT TO THE GROUP. WE'VE WRITTEN THIS UP AND WE WERE PUBLISHED IN 2011 IN *STEM CELL RESEARCH AND THERAPY*. AND THIS IS A NICE PUBLICATION BECAUSE IT'S AN OPEN ACCESS JOURNAL, SO FOLKS GET THE DATA RIGHT THERE. BUT WE TRIED NOT TO STOP THERE. ONE OF THE THINGS THAT'S REALLY BEEN A PLEASURE WORKING AT CIRM IS THERE'S A REAL INTEREST IN SORT OF GETTING THE INFORMATION OUT IN A MORE SORT OF PUBLIC WAY THAN OTHER SORTS OF COMMUNICATION. SO WE ALSO HAVE USED THESE FINDINGS IN A COUPLE OF OUR BLOG ENTRIES. AND THAT'S BEEN A REAL PLEASURE BECAUSE YOU KIND OF PUT THINGS INTO JOURNALS AND YOU OCCASIONALLY GO BACK AND LOOK AND SEE YOU'VE BEEN CITED THREE TIMES AND THAT'S GREAT.

WE ACTUALLY GET QUITE A FEW COMMENTS AND THINGS ON THE BLOG. SO THIS WAS A NICE OPPORTUNITY TO TALK ABOUT THE VALUE OF CIRM IN RELATION TO STEM CELL RESEARCH THAT YOU'RE SORT OF HOPEFULLY HITTING A DIFFERENT AUDIENCE THERE.

SO THAT COVERS THAT PIECE OF IT. AGAIN, I DON'T KNOW IF THERE'S ANY QUESTIONS AT THIS STAGE.

DR. BERNSTEIN: MY NAME IS DENISE BERNSTEIN FROM UCSF. I NOTICE THAT A LOT OF HUES LINES, THE HARVARD LINES THAT ARE RESTRICTED LINES. DO YOU CHECK AGAINST YOUR GRANT TO SEE WHETHER THE RESTRICTIONS ARE BEING FOLLOWED?

DR. LOMAX: WE DON'T. AND THE REASON WE DON'T IS THAT THOSE RESTRICTIONS ARE NIH RESTRICTIONS IMPOSED BY NIH BASED ON THEIR REVIEW. THE BOARD PASSED A -- THIS WAS PASSED BY THE ICOC SOMETIME IN 2009, I BELIEVE, I THINK MIDDLE OF 2009. THE RATIONALE WAS THAT WE HAD ALWAYS APPROVED THE BUSH LINES FOR RESEARCH. THERE HAD BEEN A SUBSTANTIAL INVESTMENT IN THOSE LINES WITH OUR GRANTS FUNDING. AND THE FEELING AT THAT POINT WAS IT WAS NOT APPROPRIATE TO THEN IMPOSE RETROACTIVE RESTRICTIONS ON THE UTILIZATION OF THOSE LINES AT A LATER DATE. WE WERE ALREADY HEAVILY INVESTED IN THOSE PROTOCOLS.

SO AS A POLICY DECISION, CIRM ALLOWS THE USE OF THOSE LINES AS YOU WOULD HAVE BEEN ABLE TO UTILIZE THEM IN 2008. DOES THAT MAKE SENSE?

DR. BERNSTEIN: IT DOES. I CAN'T REMEMBER THAT THEY WERE THERE BEFORE 2008.

DR. LOMAX: THEY WERE AVAILABLE FOR UNRESTRICTED USE PRIOR TO THE TIME THEY WERE LISTED ON THE NIH REGISTRY IN WHICH THEY WERE THEN LISTED WITH RESTRICTIONS.

CHAIRMAN LO: I WANT TO ASK YOU A QUESTION WITH REGARD TO THIS TABLE AND SOME OF THE ONGOING CONTROVERSY IN THIS COUNTRY REGARDING THE USE OF HUMAN EMBRYONIC STEM CELL LINES AND A BIG ELECTION COMING UP IN THE FALL.

SO THERE IS A SEGMENT OF THE POPULATION THAT SAYS WHY DO WE NEED TO HAVE ANY NEW LINES? WHY DON'T WE JUST USE THE ORIGINAL BUSH PRESIDENTIAL LINES? I WAS GOING TO ASK THE SCIENTISTS ON THE GROUP AND I GUESS JEFF BOTKIN AS WELL BECAUSE YOU CHAIR THE NIH WORKING GROUP THAT REVIEWS CANDIDATE NEW LINES. DO WE HAVE A WELL-ARTICULATED PIECE THAT THE PUBLIC CAN LOOK AT TO SORT OF UNDERSTAND WHY IT IS, EVEN THOUGH THE PREPONDERANCE OF GRANTS ARE PROPOSING TO USE THE NIH-APPROVED LINES, THAT OTHER LINES ARE IMPORTANT TO HAVE OPEN TO RESEARCHERS AND,

IN FACT, THIS GOES TO YOU, GEOFF, THAT THERE MAY ACTUALLY BE A NEED FOR NEWER LINES, FOR EXAMPLE, LINES THAT HAVE SPECIFIC GENOMIC OR PHENOTYPIC CHARACTERISTICS?

DR. LOMAX: I WOULD LIKE TO DEFER TO MY SCIENCE COLLEAGUES ON THIS QUESTION. ONE TECHNICAL NOTE JUST METHODOLOGICALLY, JUST SO YOU UNDERSTAND WHAT YOU'RE SEEING. THIS TABLE REPRESENTS A LOOK INTO ABOUT TWO AND A HALF TO THREE YEARS BACK. IT'S ALSO SOMETHING TO KEEP IN MIND. ONE OF THE THINGS ABOUT OUR METHODOLOGY IS BECAUSE WE RELIED ON PROGRESS REPORTS, IN ORDER TO MEET THE CRITERIA FOR BEING IN THIS STUDY, THEY HAD TO BE COMPLETED PROGRESS REPORTS. WE DID IT LAST SUMMER. PROGRESS REPORT HAD TO BE REPORTING ON SOMETHING THAT WAS A YEAR FURTHER BACK. SO, AGAIN, MY SENSE IS IN TERMS OF IMPERFECT FOLLOW-UP SUBSEQUENTLY, THIS IS BEGINNING TO CHANGE ALREADY. THIS IS A LITTLE BIT OF AN OLDER PICTURE; BUT IN TERMS OF THE BROADER QUESTION --

CHAIRMAN LO: THAT WOULD BE IMPORTANT IF YOU COULD UPDATE THAT. MY SENSE IS THAT THIS WILL COME UP AGAIN BETWEEN NOW AND NOVEMBER. AND DATA AS TO WHAT LINES ARE BEING USED COULD HAVE SOME IMPACT. WE HAVE ACCESS TO THAT DATA THAT OTHER PEOPLE DON'T.

IT WOULD BE PARTICULARLY USEFUL.

DR. ROBERTS: JUST TO CLARIFY, WHEN YOU SAY IT'S BEGINNING TO CHANGE, YOU MEAN THAT EVEN A HIGHER PERCENTAGE ARE NOT NIH-APPROVED LINES THAT ARE BEING USED? WHEN YOU SAY IT'S ALREADY BEGINNING TO CHANGE, WHAT DO YOU MEAN?

DR. LOMAX: WHAT WE'RE SEEING IS THE NUMBER OF CIRM DERIVATIONS IS GOING UP. SO THE PROPORTION OF CIRM UTILIZATION, MY SENSE IS, AGAIN, IT'S A LITTLE BIT OF A SENSE BASED ON EYEBALLING DATA, THAT PROPORTION IS GOING UP. THERE'S GOING TO BE SOME STABILITY IN THE H1S OF THE WORLD BECAUSE OF THEIR RECOGNITION AS REFERENCE LINES, BUT THE DIVERSITY IS NOW CHANGING AGAIN.

I DON'T KNOW, UTA OR ELLEN, IF YOU ALL HAVE FURTHER THOUGHTS BECAUSE I KNOW THEY'RE A BIT CLOSER TO THE PROJECTS THEMSELVES.

DR. FEIGAL: ACTUALLY I'M GOING TO HAVE DR. GRIESHAMMER TALK ABOUT SOME OF THE ISSUES IN TERMS OF FORMULATING A NEW BANK THAT WE HAVE. THAT PARTICULAR BANK HAS BECOME AN INITIATIVE TO REALLY CREATE AN INDUCED PLURIPOTENT STEM CELL BANK THAT WILL ALSO INCLUDE HUMAN EMBRYONIC STEM CELL-DERIVED LINES. SO LET ME LET UTA GIVE A LITTLE BIT OF A SUMMARY OF THAT INITIATIVE AND WHY WE'RE DOING THAT.

DR. GRIESHAMMER: ACTUALLY WITH REGARD TO THAT PARTICULAR INITIATIVE, I THINK LATER IN TODAY'S MEETING WE'LL HAVE A DISCUSSION ON THAT. MAYBE I CAN DEFER UNTIL THEN SPEAKING ABOUT THE HUMAN INDUCED PLURIPOTENT STEM CELL INITIATIVE.

JUST TO COMMENT ON BERNIE'S QUESTION, ONE OBSERVATION THAT I HAVE THAT COMES FROM LOOKING AT PROGRESS REPORTS AND WHY PEOPLE ARE GENERATING NEW HUMAN EMBRYONIC STEM CELL LINES COMES ACTUALLY OUT OF RESEARCH PROJECTS INTERESTED IN UNDERSTANDING THE HUMAN EMBRYO. AND IN THE PROCESS OF STUDYING HOW EMBRYONIC STEM CELL LINES COME ABOUT DURING THE ISOLATION, THEY GENERATE NEW HUMAN EMBRYONIC STEM CELL LINES THAT THEN BECOME PART OF THIS COLLECTION. AND I THINK IN SOME CASES PEOPLE THEN DISCOVER THAT THEY MIGHT BE BETTER SUITED FOR SOME OF THE STUDIES THAT OTHER PEOPLE WANT TO USE.

SO ANOTHER MORE PRACTICAL EXAMPLE IS PEOPLE TRYING TO DERIVE NEW HUMAN EMBRYONIC STEM CELL LINES THAT MIGHT BE PARTICULARLY ADAPTABLE TO SCALE-UP FOR CULTURING THERAPEUTIC APPLICATIONS AND LOOKING INTO DERIVING HUMAN EMBRYONIC STEM CELL LINES THAT PHENOTYPICALLY RESEMBLE MORE MOUSE EMBRYONIC STEM CELL LINES THAT ARE CONSIDERED MORE NAIVE IN THEIR DEVELOPMENTAL POTENTIAL. AND SO

THERE'S SORT OF RESEARCH PROJECTS THAT LEAD TO THE GENERATION OF THESE LINES, BUT I THINK HAVE A HIGH POTENTIAL FOR ULTIMATELY COMING UP WITH LINES THAT MIGHT BE MORE SUITABLE FOR THERAPEUTIC SCALE-UP.

DR. BOTKIN: I'M A NONSCIENTIST, SO I WOULDN'T HAVE A GOOD ANSWER, BUT WOULD ENDORSE THE NEED FOR THAT TYPE OF PAPER TO DESCRIBE, I THINK, EXACTLY WHAT BERNIE IS ADVOCATING THERE.

I WOULD SAY FROM MY PERSPECTIVE WITH THE NIH PANEL, ONE OF THE THINGS I'VE BEEN IMPRESSED WITH IS THE NUMBER OF LINES RELATIVELY RECENTLY THAT HAVE COME THROUGH FROM PREIMPLANTATION GENETIC DIAGNOSTIC CONTEXT. AND SO THEY'RE EMBRYOS WITH KNOWN MENDELIAN MUTATIONS. AND I THINK THOSE LINES SEEM TO BE PARTICULARLY INTERESTING, OBVIOUSLY, FOR CERTAIN DISEASE COMMUNITIES. I DON'T HAVE THE UNDERSTANDING TO KNOW EXACTLY HOW THOSE LINES ARE USEFUL IN THAT CONTEXT, BUT I THINK SUCH A PAPER MIGHT DESCRIBE HOW EMBRYOS OF THAT SORT MIGHT BE CRITICALLY USEFUL FOR DIFFERENT DISEASE CONTEXTS.

DR. ROBERT TAYLOR: AND I GUESS ONE OTHER POINT. I WISH I KNEW THE NUMBERS OFF THE TOP OF MY HEAD, BUT THERE HAVE BEEN CALCULATIONS TO TRY TO PREDICT -- AND, JOHN, YOU MIGHT KNOW THIS BETTER THAN I -- FOR HLA MATCHING THAT SORT OF KIND OF

NUMBERS, AN IDEALIZED NUMBER OF HUMAN EMBRYONIC STEM CELLS THAT MIGHT BE REQUIRED TO BE ABLE TO CREATE TISSUES THAT ARE HISTOCOMPATIBLE WITH THE MAJORITY OF HUMANS THAT MIGHT NEED THOSE IN A DISEASE SETTING. SO THERE ARE SOME NUMBERS, I THINK, THAT POSSIBLY COULD BE DERIVED THAT COULD BE USEFUL TO THE PUBLIC TO UNDERSTAND WHY WE MIGHT NEED MORE OF THESE THAN ARE CURRENTLY AVAILABLE.

DR. WAGNER: I GUESS THE ONLY THING TO ADD TO THAT IS THAT I THINK THE TWO MAJOR CATEGORIES YOU BOTH MENTIONED, ONE IS THE GENETIC DISEASE MODELS AND THE OTHER IS FOR POTENTIAL CLINICAL APPLICATION WHICH THEN RELATES TO THE HLA TYPING ASPECT. SO AS WE HAVE DEVELOPED NEW METHODOLOGIES, AND WHATEVER THAT SHOULD BE IN TERMS OF MANUFACTURING A CELL LINE, THAT MIGHT HAVE POTENTIAL CLINICAL USE. CERTAINLY THE OLD CELL LINES WERE NOT OPTIMALLY DERIVED JUST FROM A CLINICAL POINT OF VIEW. THERE'S OTHER ISSUES AS WELL.

SO CERTAINLY I THINK THERE IS STILL A SIGNIFICANT NEED FOR THE DEVELOPMENT OF NEW CELL LINES. BUT THE ONE THING THAT HASN'T BEEN STATED IS WHETHER OR NOT WE KNOW THAT A CELL LINE WILL BE USABLE INDEFINITELY. SO THE FACT THAT YOU HAVE A CELL LINE TODAY THAT MAY BE GENETICALLY GOOD, LET'S

SAY, HOWEVER YOU DEFINE THAT, THROUGH LONG-TERM USE, WHETHER OR NOT THAT STABILITY IN THE GENETIC AREA IS MAINTAINED I'M NOT SURE IS KNOWN AND MAY NOT BE MAINTAINABLE. SO THERE MIGHT BE A SHELF LIFE, SO TO SPEAK, OF A CELL LINE THAT WOULD NECESSITATE CONTINUATION OF DEVELOPMENT OF NEW CELL LINES OVER TIME.

DR. OLSON: I JUST WANT TO MAKE THE POINT -- AND I APPRECIATE WHAT JOHN HAS SAID BECAUSE OBVIOUSLY I THINK THE STABILITY OF LINES IS A QUESTION THAT MANY OF US ARE CONCERNED ABOUT AND THAT WE PUT OUT QUESTIONS FOR. BUT I DO SAY THAT -- I WOULD NOTE THAT ANYBODY WHO INTENDS TO MAKING RESEARCH BANKS, THAT YOU ONLY PASSAGE FOR CERTAIN TIMES. WHEN YOU TALK ABOUT THERAPEUTICS, YOU DO SOMETHING CALLED MAKE A MASTER CELL BANK AND A WORKING CELL BANK, AND YOU SET VERY CAREFUL SPECIFICATIONS ON THE NUMBER OF PASSAGES YOU CAN USE. THAT IS SUPPOSEDLY BASED ON EXPERIMENTAL DATA AS TO THE STABILITY OF THE LINE OVER THE COURSE OF THOSE PASSAGES.

I AGREE THAT YOU HAVE TO BE CAREFUL, AND PARTICULARLY IN RESEARCH USE WHERE PEOPLE, I THINK, LOTS OF TIMES TEND TO NOT BE COGNIZANT OR MAY IN SOME CASES NOT BE COGNIZANT OF THE PASSAGE NUMBER OF

THEIR CELLS. BUT I'D SAY WHEN YOU CERTAINLY START TALKING ABOUT THERAPEUTIC USE, THAT'S ONE OF THE IMPORTANT THINGS FOR CONSIDERATION.

DR. WAGNER: LIKE WE'VE ALREADY BEEN DISCUSSING IN SOME WAYS ARE THE WAY YOU MANUFACTURE A CELL LINE TODAY IS VERY DIFFERENT THAN THE WAY THEY MANUFACTURED H1. YES, PEOPLE ARE NOW LEARNING HOW TO CREATE MASTER CELL BANKS, BUT WE'RE STILL IN A LEARNING PHASE. SO, THEREFORE, AT LEAST IN THE IMMEDIATE FUTURE, THERE'S GOING TO BE THIS CONTINUED NEED FOR DEVELOPMENT OF THE OPTIMAL CELL BANK. AND SO AT LEAST IN THE NEAR FUTURE, THERE IS STILL A SIGNIFICANT NEED.

DR. LOMAX: THANK YOU FOR THOSE COMMENTS. WE WILL BE DISCUSSING CELL BANKING A BIT MORE THIS AFTERNOON.

DR. ROBERT TAYLOR: I KNOW YOU HAVEN'T HAD A CHANCE TO CRUNCH THE DATA, BUT I'M CURIOUS WHETHER YOU CAN GIVE US A LITTLE BIT OF A PREVIEW ABOUT THE APPLICATIONS AND THE KINDS OF GRANTS BECAUSE UTA HAS RAISED A REALLY INTERESTING QUESTION, CERTAINLY INTERESTING TO ME, ABOUT USING THESE TO TRY TO UNDERSTAND EARLY HUMAN EMBRYOLOGY. WHERE DO YOU SORT OF SEE THE BIG -- I WOULD ASSUME SORT OF NEURODEGENERATIVE DISEASES WOULD PROBABLY BE AT THE

TOP, BUT WHERE DO YOU SORT OF SEE THINGS GOING IN THE SCIENTIFIC CATEGORIES THAT YOU STARTED TO BREAK DOWN?

DR. LOMAX: AGAIN, I WOULD DEFER EITHER TO MY SCIENCE COLLEAGUES OR THE DATA. I MUST SAY I DON'T HAVE A CRYSTAL BALL IN THAT AREA, BUT IT'S REALLY A DATA EXERCISE. I THINK DR. FEIGAL COULD OFFER SOME INSIGHT THERE.

DR. FEIGAL: WELL, ALL I WAS GOING TO SAY IS UTA MENTIONED WE ARE GOING TO HAVE A PRESENTATION, I THINK, LATER THIS MORNING ON THE BANK AND THE RATIONALE FOR WHY WE'RE PUTTING IT TOGETHER. MAYBE WE COULD HOLD THAT PART OF THE CONVERSATION AT THAT TIME.

CHAIRMAN LO: SOUNDS LIKE A GOOD PLAN.

DR. WAGNER: I JUST WANT TO MAKE ONE MORE COMMENT, WHICH IS GOING BACK TO WHAT YOU WERE TALKING ABOUT BEFORE IN TERMS OF THE HLA TYPING. THAT IS IS THAT THOSE NUMBERS ARE ALREADY KNOWN. WE'VE LOOKED AT VARIOUS RACIAL BACKGROUNDS, AND WE CAN TELL YOU FOR OTHER PURPOSES, NOT FOR ES CELLS, BUT OTHER PURPOSES CAN GIVE YOU THE TOP 30 HLA HAPLOTYPES BY RACE. AND SO --

DR. ROBERT TAYLOR: I THINK I READ IT WAS SEVERAL HUNDRED OR SOMETHING.

DR. WAGNER: FOR CAUCASIAN. IT DEPENDS ALSO WHAT LEVEL OF MATCH YOU WANT. IF YOU'RE LOOKING FOR ONE ANTIGEN MATCH OUT OF ALL OF THEM, THEN THAT'S A VERY DIFFERENT NUMBER. AND FOR CAUCASIANS OF NORTHERN EUROPEAN DESCENT, THE NUMBER IS MUCH MORE RESTRICTED. AND FOR AFRICAN-AMERICANS, IT WOULD BE MUCH LARGER. SO ALTHOUGH I CAN'T TELL YOU THOSE NUMBERS OFF THE TOP OF MY HEAD, THOSE NUMBERS ARE KNOWN.

SO IF IT'S IMPORTANT FOR CIRM AND FOR A NATIONAL NIH BANK, THEN I THINK WITHIN THE YEAR WE SHOULD THEN ACTUALLY CRUNCH THOSE NUMBERS BECAUSE YOU ARE GOING TO FIND THAT THE NUMBERS ARE ACTUALLY QUITE LARGE.

DR. LOMAX: THANK YOU, EVERYONE, FOR THOSE COMMENTS BECAUSE THAT HELPS SORT OF EXPAND THE DISCUSSION BEYOND WHERE I COULD HAVE TAKEN IT. THANK YOU. THAT'S WHY WE HAVE A COMMITTEE.

CHAIRMAN LO: LET'S TURN IT OVER TO SCOTT TO UPDATE US ON REGULATORY AMENDMENTS. I WANTED TO JUST POINT OUT THAT IN THIS WONDERFUL FOLDER THAT I KEEP LOSING, THE YELLOW DOCUMENT ON THE RIGHT-HAND SIDE IS THE UPDATED VERSION OF THE CIRM REGULATIONS.

MR. TOCHER: THANKS, BERNIE. AND THANKS, GEOFF. GEOFF JUST ASKED ME TO SPEND ABOUT MAYBE A

MINUTE AT THE MOST, I HOPE, JUST TO UPDATE YOU ON NEW REGULATIONS AND ALSO FOR NEWER PEOPLE IN THE ROOM UNFAMILIAR WITH THE PROCESS FOR WHAT HAPPENS WITH THE WORK THAT GOES ON HERE TODAY. THIS IS REALLY SORT OF JUST THE BEGINNING OF THE PROCESS.

THE POLICIES THAT YOU FORMULATE HERE ARE THEN TRANSLATED INTO THE REGULATORY LANGUAGE THAT BERNIE JUST REFERRED TO. AND THIS LANGUAGE MUST UNDERGO AN ADMINISTRATIVE PROCESS THAT IS GOVERNED BY ANOTHER STATE AGENCY. SO THE POLICY CALLS AND ADVICE THAT YOU GIVE THE ICOC THEN UNDERGOES A PUBLIC COMMENT PROCESS. SO THE PUBLIC AT LARGE GETS TO WEIGH IN ON THESE POLICIES AND HELP SHAPE AND REFINE THEM.

AND WITH THE WORK OF THIS GROUP AND BERNIE AND GEOFF THROUGHOUT, THOSE POLICIES ARE FURTHER REFINED UNTIL WE HAVE SETTLED ON A PLACE WHERE WE WANT TO BE. AND THE END RESULT IS THE REGULATORY LANGUAGE THAT YOU HAVE IN FRONT OF YOU. AND THIS HAS THE FULL FORCE AND EFFECT OF ANY OTHER LAW THAT WOULD BE ADOPTED BY THE LEGISLATURE, FOR INSTANCE. SO IT UNDERSCORES THE IMPORTANCE AND THE WEIGHT OF THE WORK THAT YOU DO HERE AND THE ADVICE THAT YOU GIVE THE ICOC.

IN TERMS OF AN UPDATE OF THE REGULATORY

PROCESS, RECENTLY OR LAST YEAR THE WORKING GROUP RECOMMENDED SOME REVISIONS TO A REGULATION THAT GOVERNS OR DEFINES ACCEPTABLY DERIVED RESEARCH MATERIALS, STEM CELL LINES. AND WE ADDED LINES THAT ARE DERIVED UNDER LICENSE FROM THE AUSTRALIAN NATIONAL HEALTH AND MEDICAL RESEARCH COUNCIL. AND THOSE AMENDMENTS SUCCESSFULLY CONCLUDED THE REGULATORY PROCESS AND ARE PART OF THE UPDATE THAT BERNIE JUST REFERRED TO.

CHAIRMAN LO: WHY DON'T WE NEXT ASK ELLEN FEIGAL TO UPDATE US ON A WORKSHOP ADDRESSING PATIENT ADVOCATE PARTICIPATION IN CLINICAL RESEARCH DECISIONS.

DR. FEIGAL: THANK YOU VERY MUCH, AND I'M PLEASED TO TALK WITH YOU TODAY. THE ROLE OF THE PATIENT ADVOCATE, INDIVIDUAL PATIENTS, PATIENT ADVOCACY ORGANIZATIONS, REPRESENTATIVES FROM THEM ARE VERY IMPORTANT TO CIRM. AND SO FROM THE GENESIS OF CIRM, PATIENTS HAVE REALLY HAD A MAJOR ROLE TO PLAY IN THE DEVELOPMENT AND THE CREATION AND THE IMPLEMENTATION OF THE DIFFERENT PROGRAMS THAT WE PUT TOGETHER.

WITH THIS IN MIND, CIRM WAS VERY INTERESTED IN A CONFERENCE THAT THE HASTINGS CENTER WAS PUTTING TOGETHER. AND THE HASTINGS CENTER IS

REALLY A MAJOR THINK TANK POLICY RESEARCH GROUP THAT WAS FOUNDED IN 1969 THAT ENGAGES EXPERTS IN A VARIETY OF DIFFERENT POLICY ISSUES PRIMARILY DEVOTED TO THE LIFE SCIENCES, TO MEDICINE, AND WERE THINKING ABOUT PUTTING TOGETHER A CONFERENCE TALKING ABOUT THE ROLE OF THE PATIENT VOICE IN THE DEVELOPMENT OF INNOVATIVE TECHNOLOGIES. AND THE REASON WHY THIS HAS COME UP IS THERE'S BEEN SORT OF A PENDULUM SWING BACK AND FORTH IN TERMS OF HOW DO YOU GET INNOVATION INTO IMPLEMENTATION AND INTO PRACTICE?

WE HEARD YESTERDAY FROM JEFF SHEEHY ABOUT THE ROLE OF THE PATIENT ADVOCATES DURING THE HIV EPIDEMIC AND HOW PRIOR TO 1987 THERE WERE REALLY NO THERAPIES THAT WERE AVAILABLE TO PATIENTS WITH REALLY DEVASTATING DISEASES. AND IT WAS REALLY THE PATIENT ADVOCATE VOICE THAT REALLY GARNERED ENERGY AND CATALYZED EXPERTS AND REALLY DEVELOPED A FORCE TO REALLY PUT AN URGENCY AND PRESSURE ONTO THE REGULATORY AGENCY TO THINK ABOUT NEW WAYS IN TERMS OF ACTUALLY HELPING CATALYZE THE DEVELOPMENT OF NEW TECHNOLOGIES DEVOTED TOWARDS A PARTICULAR EPIDEMIC FOCUS.

AND IT WAS BECAUSE OF THIS THAT THE REGULATORY AGENCY ACTUALLY THOUGHT ABOUT NEW WAYS TO DO ITS BUSINESS. AND IT LED TO THE CREATION OF WHAT

WAS CALLED ACCELERATED APPROVAL IN 1992 WHERE DRUGS COULD THEN BE REVIEWED AND APPROVED ON THE BASIS OF A VALIDATED BIOMARKER, IN THAT INSTANCE, VIRAL LOAD, AS OPPOSED TO DOING A BODY COUNT, WAITING TILL PEOPLE DIED, WAITING TILL PEOPLE DEVELOPED AN OPPORTUNISTIC INFECTIOUS DISEASE.

SO WITH THAT IN MIND, THE HASTINGS CENTER AND CIRM WAS REALLY INTERESTED, AND THERE REMAINS A TREMENDOUS DEGREE OF MEDICAL CONDITIONS FOR WHICH THERE REALLY IS AN UNMET MEDICAL NEED, WHAT CAN BE DONE TO TRY AND CATALYZE HOW WE APPROACH INNOVATION IN MEDICAL TECHNOLOGIES IN THE REGULATORY PROCESS.

SO WHAT CIRM DID WAS HELP SPONSOR AND ALSO HELPED PROVIDE SOME INSIGHTS INTO THE DESIGN OF THE AGENDA FOR THAT CONFERENCE ON THE ROLE OF THE PUBLIC VOICE IN DEVELOPING NEW MEDICAL TECHNOLOGIES. IT WAS LED BY DR. MICHAEL GUSMANO, A RESEARCH SCHOLAR AT THE HASTINGS CENTER, ALSO AN ASSOCIATE PROFESSOR OF HEALTH POLICY MANAGEMENT AT NEW YORK MEDICAL COLLEGE. AND 20 PARTICIPANTS WERE INVITED TO THIS CONFERENCE. SO IT WAS A VERY SMALL, INTERACTIVE CONFERENCE, AND IT WAS THOUGHT THAT IT WOULD BE ONE OF MULTIPLE FACE-TO-FACE SESSIONS THAT WOULD TAKE PLACE. SO THIS IS NOT THE END OF THE DISCUSSION. I GUESS YOU COULD SAY IT'S REALLY A CONTINUING

DISCUSSION THAT'S GOING TO TAKE PLACE AND EVOLVE.

BUT THESE PARTICIPANTS INCLUDED THE REGULATORY AGENCY. WHAT HAPPENS A LOT OF TIMES IS PEOPLE GET TOGETHER IN A CONFERENCE, AND THE VOICE THAT ISN'T IN THE ROOM IS THE ONE THAT'S THE CAUSE OF ALL THE PROBLEMS. SO WHAT WAS DONE IS ACTUALLY INCLUDE THE MAJOR STAKEHOLDERS IN THAT CONFERENCE. SO IT INCLUDED THE FDA STAFF, WHO IS ACTUALLY AT THIS JUNCTURE VERY INTERESTED IN TRYING TO SEE WHAT COULD THEY DO DIFFERENTLY IN INVOLVING THE PATIENT IN DISCUSSING MEDICAL TECHNOLOGIES. IT ALSO INCLUDED REPRESENTATIVES OF SEVERAL PATIENT GROUPS, INDUSTRY AND HEALTH POLICY SCHOLARS, INCLUDING EXPERTS ON THE REGULATORY PROCESS AND THE ROLE OF PATIENTS IN HEALTH POLICY DECISION-MAKING.

FROM CIRM DR. DUANE ROTH, WHO'S VICE CHAIR OF OUR ICOC, OUR BOARD, AND IS ALSO HEAD OF AN ORGANIZATION CALLED CONNECT, WHICH IS BASED IN SAN DIEGO, AND REALLY TRIES TO HELP ENTREPRENEURS DEVELOP THEIR MEDICAL TECHNOLOGY. AND I ALSO ATTENDED AND PARTICIPATED IN THIS DISCUSSION.

IT WAS A DISCUSSION-ORIENTED AGENDA. THERE WERE BACKGROUND PAPERS AND POLICY ISSUES THAT WERE SENT TO THE PARTICIPANTS IN ADVANCE AND WHICH WE WERE ALL EXPECTED TO READ. AND THEN ACTUALLY AT

THE TIME OF THIS TWO-DAY WORKSHOP, THERE WERE SHORT BRIEFING-TYPE PRESENTATIONS THAT WERE LED BY EXPERTS IN RESEARCH, ETHICAL, LEGAL DISCIPLINES, AND THEY REALLY LED MORE OF AN INTERACTIVE DISCUSSION DURING THIS TIME PERIOD OF THE TWO-DAY CONFERENCE.

I GUESS THIS IS WHAT HAPPENS WHEN YOU GO FROM PC TO MAC.

SO AT ANY RATE, THE MAJOR ISSUE AND THE FOCUS FOR THIS WORKSHOP IS WHAT ROLE SHOULD PATIENTS AND ALSO THE BROADER PUBLIC, THE CONSUMERS, PLAY IN DEVELOPMENT OF NEW MEDICAL TECHNOLOGY. THE PATIENT VOICE IS IMPORTANT. I THINK THAT'S BEEN ACCEPTED ACROSS A MAJOR SWATH OF OUR ESTABLISHMENT. WHAT PEOPLE WERE TRYING TO GRAPPLE WITH IS HOW MUCH INFLUENCE AND HOW MANY SHOULD BE INVOLVED AND AT WHAT POINT IN THE CONTINUUM OF THE DEVELOPMENT OF TECHNOLOGY SHOULD THAT REALLY BE FOCUSED? WHAT'S THE VALUE? ARE CURRENT MECHANISMS FOR PATIENT AND CONSUMER VOICE IN THE FDA PROCESS SUFFICIENT? AND WHAT MORE SHOULD THE AGENCY DO?

SO THIS CONFERENCE WAS VERY MUCH FOCUSED ON THE REGULATORY AGENCY IN THE UNITED STATES, WHICH IS THE MAJOR AGENCY FOR APPROVING, REVIEWING, AND APPROVING NEW TECHNOLOGIES. AND BY TECHNOLOGIES, I'M BEING VERY BROAD. I'M TALKING ABOUT DRUGS,

BIOLOGICS, CELL THERAPIES, DEVICES, A VARIETY OF DIFFERENT PRODUCTS AND THERAPIES THAT COULD BE HELPFUL TO PATIENTS WITH HIGH UNMET MEDICAL NEEDS. AND WHAT MORE SHOULD THE AGENCY DO?

SO THE VALUE OF INCLUDING PATIENTS AND CONSUMERS IN A DELIBERATIVE PROCESS COULD REALLY PROVIDE AN ENHANCED POTENTIAL TO BROADEN THE MEANING OF BENEFITS AND RISKS. JUST LIKE WE SEE AT CIRM, IT WAS REALLY THE OPPORTUNITY TO GO BEYOND THE TECHNICAL AND THE SCIENTIFIC AND TO THINK ABOUT WHAT IMPORTANT VALUES AND BENEFITS WOULD BE IMPORTANT TO THE PATIENT, THE PERSON WHO ACTUALLY HAS THE CONDITION, AND AT WHAT POINT IN THE DEVELOPMENT OF THE DISEASE WOULD THEY BE WILLING TO TAKE A CERTAIN PERCENTAGE OF RISK, AND HOW TO INCLUDE THAT INPUT INTO THE OVERALL REVIEW AND APPROVAL OF THESE TYPES OF TECHNOLOGIES.

BUT WAY BEFORE THE APPROVAL STAGE, HOW CAN YOU INCLUDE THAT INPUT MUCH EARLIER SO THAT WHEN COMPANIES OR ACADEMICS ARE THINKING ABOUT DEVELOPING THERAPIES, HOW CAN THEY TAKE THAT VOICE AND THOSE PERSPECTIVES AND TAKE IT INTO CONSIDERATION AS THEY'RE EVEN TRYING TO DEVELOP THEIR RESEARCH STUDIES OR DEVELOP THEIR CLINICAL STUDIES?

SO IT WAS ALSO TRYING TO PAY INCREASED

ATTENTION TO THE HETEROGENEITY AND THE VALUE OF WHAT WE CALL CONDITIONALITY, THAT WE KNOW ALL PATIENTS DON'T SPEAK WITH THE SAME VOICE. THEY ALSO HAVE DIFFERENT PERSPECTIVES. THEY'RE AT DIFFERENT POINTS IN TIME IN THEIR MEDICAL CONDITION. AND, THEREFORE, THERE MAY BE DIFFERENT RISKS THAT DIFFERENT INDIVIDUALS ARE WILLING TO TAKE BASED UPON WHERE THEY'RE SITTING.

IN ADDITION, WHAT WE WON'T BE TALKING ABOUT TODAY, BUT ALSO HAS TO BE CONSIDERED IS THE ROLE OF THE CONSUMER OR EVEN OF THE PAYER. AND WHAT IS OF VALUE TO THEM? AND IT MAY BE VERY DIFFERENT THAN WHAT'S OF VALUE TO THE PATIENT, AS WE KNOW, AND SO HOW TO TAKE INTO CONSIDERATION WHAT'S GOING ON IN HEALTH ECONOMICS BECAUSE AT END OF THE DAY, WE JUST DON'T WANT TO COMPLETE A SUCCESSFUL RESEARCH EXPERIMENT THAT SOMEBODY CAN PUBLISH OR BE ABLE TO GET THE DATA TO GET ANOTHER GRANT, BUT WE WANT SOMETHING THAT CAN BE UTILIZED BEYOND A CLINICAL TRIAL, ACTUALLY GET INTO CLINICAL PRACTICE. SO WE NEED TO THINK OF THE VALUE TO THE PATIENTS, TO THE PROVIDER, AND HOW TO MAKE SURE WE'RE ALL ON THE SAME PAGE ABOUT MOVING THAT PRODUCT FORWARD SO THAT ACTUALLY IT WILL BE REIMBURSED AND PAID FOR AND PEOPLE CAN PRESCRIBE IT, PEOPLE CAN USE IT.

IT WAS ALSO TO THINK ABOUT HAVING A MORE OPEN AND TRANSPARENT PROCESS THAT CAN REALLY ENHANCE LEGITIMACY AND TRUST IN THE PROCESS. WE DO THIS AT CIRM AS WELL BECAUSE ALL OF OUR PUBLIC MEETINGS -- WELL, WHAT I SHOULD SAY IS ALL OF OUR MEETINGS ARE HELD IN PUBLIC WITH OUR BOARD MEETINGS. AND SO WHAT WE TRY AND DO IS BE VERY TRANSPARENT ABOUT THE TOPICS, ABOUT HOW WE WORK, AND IT'S THOUGHT THAT THESE KIND OF DISCUSSIONS WITH THE AGENCY, IN ORDER TO ENHANCE LEGITIMACY AND TRUST, PROBABLY NEED TO BE HELD IN PUBLIC SETTINGS, THAT THESE CLOSED-DOOR DEAL BREAKING MAY NOT ENGENDER MUCH TRUST. SO THERE WAS A THOUGHT OF HOW TO BE VERY TRANSPARENT ABOUT WHAT THE PROCESS IS AS WELL.

SO SOME OF THE CURRENT AND PROPOSED FDA INITIATIVES ARE THE FOLLOWING. BECAUSE THE FDA WAS PRESENT AT THIS MEETING, THEY WERE THERE FROM THEIR STRATEGIC PLANNING OFFICE, AND THEY WERE TALKING ABOUT THE DIFFERENT WAYS IN WHICH THEY TRY AND ENGAGE THE PATIENTS AND ALSO THE CONSUMER. I THINK MANY OF US MAY BE AWARE OF A PROGRAM THAT THEY HAVE IN PLACE FOR ADVISORY COMMITTEES WHERE THERE'S A SLOT ON AN ADVISORY COMMITTEE. AND AN ADVISORY COMMITTEE IS A PUBLIC MEETING THAT THE FDA HOLDS TO REVIEW THE DATA ON A PARTICULAR PRODUCT TO CONSIDER

WHETHER OR NOT IT SHOULD BE APPROVED FOR COMMERCIALIZATION. AND THERE'S A SLOT ON THAT ADVISORY COMMITTEE THAT'S HELD FOR A PATIENT TO PROVIDE THE, QUOTE, PATIENT PERSPECTIVE, AND THERE'S ALSO A SLOT FOR A CONSUMER, A PUBLIC CONSUMER. AND IT COULD BE SOMEBODY INVOLVED IN POLICY OR OTHER ASPECTS.

WE'RE FAMILIAR WITH THAT. BUT BECAUSE THOSE ADVISORY COMMITTEES ARE FEW AND FAR BETWEEN AND THERE'S A SINGLE SLOT, THERE'S REALLY A VERY SMALL NUMBER OF PATIENTS AND CONSUMERS THAT CAN REALLY PARTICIPATE IN THAT.

THE OTHER PART OF THE ADVISORY COMMITTEE THAT ENGAGES THE PUBLIC IS A SEGMENT CALLED THE PUBLIC COMMENT PERIOD WHERE BASICALLY WHAT HAPPENS IS THERE'S AN OPEN MICROPHONE AT A SET TIME IN THE FULL-DAY CONFERENCE. MEMBERS OF THE PUBLIC, INCLUDING PATIENTS, CAN GET UP AND PROVIDE THREE TO FIVE MINUTES OF THEIR PERSPECTIVE. AND THEY'RE REALLY ANECDOTES, AND IT'S A WAY TO PROVIDE PUBLIC COMMENT, BUT IT'S REALLY NOT A DISCUSSION. IT'S USUALLY THANK YOU VERY MUCH FOR YOUR COMMENTS, AND THEN THEY SIT DOWN, AND THEN THE COMMITTEE GOES BACK TO WORK ON WHAT THEY WERE DOING. SO IT'S A WAY, BUT IT'S NOT A VERY SATISFYING WAY OF REALLY HAVING A

DISCUSSION.

SO WHAT THE FDA IS THINKING OF DOING IS NOT JUST HOW TO EXPAND THE ROLE AND THINK ABOUT PATIENTS IN DIFFERENT PARTS OF THE PRODUCT DEVELOPMENT SPECTRUM, BUT HOW TO INCREASE THE NUMBERS OF PATIENTS AND CONSUMERS THAT CAN BE INVOLVED IN THE DISCUSSION. SO THEY'RE ACTIVELY LOOKING TO HAVE MORE OF A PATIENT REPRESENTATIVE PROGRAM WHERE THEY REALLY TALK WITH ORGANIZATIONS AND REALLY HAVE MORE OF A DIALOGUE WITH PATIENT REPRESENTATIVES ON PARTICULAR TOPICS.

THEY ALSO HAVE CURRENTLY A RESEARCH ADVOCACY PROGRAM, BUT UNLESS THE PATIENT ORGANIZATION HAPPENS TO STUMBLE ACROSS THIS PROGRAM ON A WEBSITE, PROBABLY MOST PATIENT ORGANIZATIONS AREN'T AWARE OF THIS PROGRAM. THEY'RE ALSO TRYING TO ESTABLISH MORE OF AN FDA/PATIENT NETWORK, MORE OF AN EDUCATION AND ADVOCACY TOOL. IN ADDITION, THEY'RE WORKING ON A NEW BENEFIT RISK ASSESSMENT TOOL THAT IS REALLY LOOKING AT PARTICULAR DIFFERENT PARAMETERS OF A PRODUCT THAT WOULD BE IMPORTANT TO TRY AND QUANTITATE AND BALANCE THE BENEFITS AS WELL AS THE RISKS OF A PRODUCT AS IT'S GOING THROUGH AND TRY TO PROVIDE MORE OF AN ANALYTICAL, QUANTITATIVE FRAMEWORK TO MAKE A DECISION.

OFTEN WHAT YOU SEE ABOUT A PRODUCT IS THERE'LL BE SORT OF A PRESENTATION ON THE RISKS, THERE'S A SEPARATE PRESENTATION ON THE EFFICACY, AND THEN PEOPLE GO THROUGH QUITE A BIT OF ANGST TRYING TO WEIGH DO THOSE BENEFITS OUTWEIGH THE SIDE EFFECTS THAT COULD HAPPEN. SO WHAT THIS FRAMEWORK, THIS TOOL, IS TRYING TO DO IS LAY OUT WHAT THOSE DIFFERENT RISKS ARE, THE EFFICACY, THE LEVEL OF UNCERTAINTY AROUND WHETHER THOSE BENEFITS OR RISKS COULD OCCUR, AND THEN THINK ABOUT A WAY OF HOW YOU CAN MITIGATE SOME OF THOSE SIDE EFFECTS AND HOW EFFECTIVE THAT MITIGATION MIGHT BE AND ALSO CONSIDER OTHER ALTERNATIVE THERAPIES THAT PATIENT COULD BE TAKING.

WHAT IT'S TRYING TO DO IS PROVIDE AN ANALYTICAL, QUANTITATIVE TOOL SO THAT YOU CAN ACTUALLY COME UP WITH A MORE STANDARDIZED WAY OF EVALUATING THE BENEFIT RISK EQUATION. WHAT THE AGENCY IS THINKING ABOUT IS HOW TO GET THE PATIENT PERSPECTIVE INTO DEVELOPING THIS TOOL AND USING THIS TOOL AT DIFFERENT ASPECTS OF THE PRODUCT DEVELOPMENT SPECTRUM.

THE OTHER QUESTION THAT CAME TO MIND AND WAS DISCUSSED DURING THIS WORKSHOP WAS THE IMPORTANCE OF REACHING OUT TO A BROADER RANGE OF

VOICES. THE BIG QUESTION IS HOW REPRESENTATIVE ARE THE REPRESENTATIVES? A BIG ISSUE AROSE IS THERE'S MAYBE A FINITE NUMBER OF PATIENT ADVOCATE ORGANIZATIONS WHO GET TO SIT IN ON MEETINGS OR PARTICIPATE. ARE THEY REALLY REPRESENTATIVE OF THE BROADER COMMUNITY OF PATIENTS? DO THEY GO BACK AND TALK TO THEIR ORGANIZATION? DO THEY SOLICIT INPUT? DO THEY TRY TO REPRESENT MORE THAN JUST THEMSELVES, BUT ACTUALLY A MUCH BROADER ORGANIZATION OF COMMUNITY OF PEOPLE WITH THAT CONDITION?

THE OTHER ISSUE THAT CAME UP WAS THE PROBLEM OF DEFERRING TO EXPERTS. YOU MAY HAVE THESE DIFFERENT INDIVIDUALS AROUND THE TABLE, BUT HOW DO YOU MAKE SURE THAT SOME PEOPLE DON'T HAVE A STATUS OF A SECOND-CLASS CITIZEN? HOW DO YOU MAKE SURE THAT THERE'S NOT A CONTINUOUS DEFERRAL TO THE EXPERTS AS OPPOSED TO HAVING A MORE BALANCED DISCUSSION?

IN ADDITION, SOME ADVOCACY RAISE THE ISSUE OF TRYING TO AVOID THE URGENCY NARRATIVE. OFTEN WE MAY GET MORE TESTIMONIALS OF PEOPLE WHO COME IN WITH A VERY EMOTIONAL, VERY TEARFUL, BUT NOT NECESSARILY EVIDENCE-BASED EXPLANATION OF WHAT THE ISSUES ARE. AND IT'S VERY HEART RENDING AND IT'S VERY IMPORTANT TO HEAR; BUT WHEN YOU'RE THINKING OF THE AGENCY AND

THE PUBLIC HEALTH ISSUES THEY HAVE TO DEAL WITH, HOW DO YOU MAKE SURE THAT YOU GET THE EVIDENCE AND THE DATA INTO THAT DISCUSSION IN ADDITION TO THE VERY INDIVIDUALIZED, PERSONALIZED, MORE EMOTIONAL APPEAL OF THE ISSUE?

SO THE MAJOR THEME WAS REALLY TO INCLUDE THE VOICE OF CONSUMERS AND PATIENT AND BALANCE THE NEED FOR MORE VOICES AND THE VALUE OF REGULAR INTERACTION AMONG THESE GROUPS.

SO THE POINT WAS TO THINK ABOUT A WAY TO MOVE BEYOND JUST HAVING PATIENTS BE ENGAGED AT THE REVIEW PROCESS AT THE END OF THE ROAD, SO TO SPEAK. ALL THE STUDIES HAVE ALREADY BEEN DONE, WE'RE NOW COMING FORWARD FROM THE COMPANY OR THE SPONSOR TO PUT A NEW TECHNOLOGY POTENTIALLY INTO THE MARKETPLACE, AND THAT'S WHEN THE PATIENTS ARE INVOLVED. WELL, THAT'S AT THE VERY END OF THE GAME. WHAT IF THE END POINTS WEREN'T DESIGNED RIGHT? WHAT IF PARTICULAR QUALITY OF LIFE PARAMETERS WEREN'T CONSIDERED? WHAT IF A VARIETY OF DIFFERENT RISK ISSUES WEREN'T THOUGHT OF IN THE EQUATION? AND NOW YOU'RE AT THE END. YOU CAN'T REALLY CHANGE IT AT THAT POINT IN TIME. IS THERE SOMETHING MUCH SOONER THAN THAT WHERE YOU COULD INVOLVE PATIENTS AND CONSUMERS?

SO THERE'S A QUESTION OF SHOULD THERE BE SOME SORT OF CITIZENS COUNCIL TO ADDRESS POLICY QUESTIONS? SHOULD THEY SUPPLEMENT EXISTING PROGRAMS WITH ADDITIONAL DELIBERATIVE METHODS? SHOULD THEY DO SURVEYS WITH DELIBERATIVE POLLING, HAVE CITIZEN JURIES, HAVE MORE CONSENSUS CONFERENCE AND TOWN HALL MEETINGS WITH PATIENTS?

THE THEME THAT CAME OUT IS THAT THE AGENCY DOESN'T ASK ENOUGH OF THE PATIENTS OR OF THE CONSUMERS, THAT ACTUALLY WE SHOULD BE ASKING MORE. I KNOW AT CIRM WE ASK A LOT OF OUR PATIENT ADVOCATES. WE ENGAGE THEM IN ALL OF OUR BOARD MEETINGS, IN OUR SUBCOMMITTEE MEETINGS, AND IN A VARIETY OF DIFFERENT AREAS. BUT IT REALLY INVOLVES PROBABLY A VARIETY OF DIFFERENT AREAS, NOT JUST AN ADVISORY MEETING. BUT IN ORDER FOR THEIR ROLE TO BE CREDIBLE, THERE NEEDS TO BE TRAINING. THAT IT SHOULD FOCUS ON THE PROCESS OF DELIBERATION IN ADDITION TO THE CONTENT OF WHAT THEY'RE GOING TO TALK ABOUT. SO REALLY SOME TRAINING IN HOW TO HAVE A VERY VALUABLE DELIBERATIVE PROCESS.

I DON'T MEAN TO SAY THE TRAINING SHOULD ONLY BE LIMITED TO PATIENTS. IT SHOULD BE EXPANDED TO SCIENTISTS AND TO CLINICIANS AS WELL. AND THAT REGULAR INTERACTION IS VALUABLE, AND THAT GENUINE

DELIBERATION REALLY REQUIRES A BIDIRECTIONAL CONVERSATION BETWEEN SCIENTISTS AND ACTIVISTS, THAT IT REQUIRES ENGAGEMENT FROM THE OUTSET IN THE FRAMING OF THE ISSUE AS WELL AS ITS IMPLEMENTATION, THAT REQUIRES ONGOING COLLABORATION BETWEEN MEETINGS, THAT THERE SHOULD BE CLEAR EXPECTATION ON ALL SIDES, AND THAT THERE SHOULD BE EQUAL PARTICIPATION SO THAT ADVOCATES DO NOT FEEL AS THOUGH THEY ARE SECOND IN RANK.

I KNOW DURING OUR REVIEW PROCESS FOR SCIENTIFIC PRESENTATIONS, WE HAVE SIX OR SEVEN DIFFERENT PATIENT ADVOCATES THAT SIT ON WHAT WE CALL OUR GRANTS REVIEW GROUP. SO WE HAVE SCIENTISTS AND EXPERTS IN THE FIELD AND WE HAVE OUR PATIENT ADVOCATES. AND THEN WE HAVE A CERTAIN PART OF THE REVIEW SESSION THAT WE CALL PROGRAMMATIC WHERE WE HAVE THE PATIENT ADVOCATES LEAD THAT SESSION. BUT IT'S A DELIBERATIVE DISCUSSION AND INTERACTION THAT TAKES PLACE. AND I THINK PEOPLE HAVE FOUND THAT TO BE A VERY VALUABLE PART OF THE PROCESS.

SO SOME OF THE VERY PRELIMINARY RECOMMENDATIONS FROM THIS CONFERENCE ARE THE FOLLOWING. ONE IS THAT THERE SHOULD BE A GREATER OUTREACH TO IDENTIFY A BROADER RANGE OF STAKEHOLDERS, THAT THE FDA SHOULD ADOPT AN ACTIVE

RATHER THAN A PASSIVE APPROACH, THAT THEY SHOULD BE REACHING OUT TO GROUPS THAT NOT ONLY HAVE WORKED WITH THE FDA IN THE PAST, BUT POSTING INFORMATION ON THE WEBSITE ABOUT THE OPPORTUNITIES WHERE PATIENTS COULD INTERACT, AND THAT THE FDA SHOULD MORE ACTIVELY WORK WITH PROFESSIONAL ASSOCIATIONS, UNIVERSITIES, INDUSTRY, AND ADVOCACY GROUPS TO IDENTIFY A BROADER RANGE OF PARTICIPANTS.

I KNOW WE AT CIRM ARE TRYING TO DO THAT AS WELL. WE'RE VERY APPRECIATIVE OF THE PATIENTS AND THE ORGANIZATIONS THAT WORK WITH US NOW, BUT WE KNOW WE NEED TO DO MORE IN TERMS OF REACHING OUT TO A BROADER COMMUNITY OF PATIENT ADVOCATES.

WE WANT THE FDA TO DEVELOP NEW MECHANISMS FOR PUBLIC INPUT, TO MOVE BEYOND THE ADVISORY AND REVIEW COMMITTEES, THAT THESE MECHANISMS ARE AND REMAIN IMPORTANT, BUT THEY DON'T REFLECT THE RANGE OF DECISIONS IN WHICH PUBLIC INPUT COULD BE RELEVANT. RIGHT NOW IN THE ADVISORY COMMITTEE THERE'S VERY RIGOROUS CONFLICT OF INTEREST REQUIREMENTS FOR PARTICIPATION ON ADVISORY AND REVIEW COMMITTEES THAT REALLY RESTRICT THE NUMBER OF PARTICIPANTS WHO CAN ENGAGE WITH THE FDA. SO THERE NEEDS TO BE A BROADER VENUE OF MECHANISMS WHERE INTERACTION COULD TAKE PLACE.

IN ADDITION, IT WAS RECOMMENDED THAT THE FDA REALLY ENCOURAGE REPRESENTATIVES TO REPORT BACK TO THE GROUPS THAT THEY REPRESENT AND ENCOURAGE THEM TO SEEK INPUT FROM THOSE GROUPS.

THE OTHER RECOMMENDATION WAS THAT THE FDA SHOULD PROVIDE TRAINING ON THE PROCESS OF DELIBERATION, AND THAT THIS TRAINING SHOULD BE OFFERED TO SCIENTIFIC EXPERTS AS WELL AS TO MEMBERS OF THE PUBLIC, THE PATIENTS, AND CONSUMER ADVOCATES.

THERE WAS GREAT ENTHUSIASM FOR UTILIZING THIS NEW BENEFIT RISK ASSESSMENT TOOL TO SOLICIT PERSPECTIVES FROM A BROADER SET OF STAKEHOLDERS, THAT THIS TOOL COULD REALLY ENCOURAGE MORALE RAISING AND SHOULD NOT BE LIMITED TO THE REVIEW PROCESS, AND THAT IF THE FDA DID PROVIDE SUFFICIENT TRAINING AND TECHNICAL INFORMATION, THIS TOOL COULD REALLY EMPOWER PUBLIC REPRESENTATIVES TO ADDRESS A RANGE OF IMPORTANT QUESTIONS.

AND I RECENTLY PUT THE LEADER OF THIS CONFERENCE IN CONTACT WITH THE EUROPEAN MEDICINE'S AGENCY BECAUSE THEY HAVE BEEN USING A BENEFIT RISK TOOL FOR SEVERAL YEARS, AND THINKING ABOUT MAYBE SHARING EXPERIENCES AND LESSONS LEARNED FROM THE EUROPEAN WITH THE U.S. SO THAT PERHAPS THEY COULD TRY AND HARMONIZE SOME OF THESE ISSUES TOGETHER.

AND THEN ONCE THESE THINGS ARE PUT IN PLACE, TO REALLY DEVELOP EVALUATIONS OF EACH PROCESS THAT ARE DESIGNED TO ENCOURAGE PUBLIC PARTICIPATION AND ASSESS TO WHAT EXTENT THESE PROCESSES ARE FAIR, FLEXIBLE, AND TRANSPARENT.

SO THAT'S A VERY BRIEF DIGEST OF A TWO-DAY CONFERENCE IN WHICH THERE WERE A LOT OF VERY INTERESTING, PROVOCATIVE ISSUES THAT WERE RAISED IN WHICH I THINK SOME OF THE MAJOR STAKEHOLDERS WERE PRESENT. SO IT WAS A VERY CONSTRUCTIVE, I THINK, PRODUCTIVE MEETING. I THINK IT IS GOING TO RESULT IN SOME FUTURE DISCUSSIONS AS WELL. WE'D CERTAINLY BE INTERESTED IN SOME OF YOUR THOUGHTS AND PERSPECTIVES ON THIS PROCESS AND PERHAPS HOW YOU OR CIRM MIGHT BE FURTHER ENGAGED IN IT. I THINK IT IS GOING TO LEAD FROM THIS TYPE OF DISCUSSION PERHAPS IN SOME CHANGES IN WHICH THE PATIENT VOICE, THE PUBLIC VOICE COULD HAVE MORE OF A TRANSPARENT INPUT INTO SOME OF THESE REGULATORY PROCESSES.

CHAIRMAN LO: QUESTIONS? COMMENTS? I WAS ASKING FOR QUESTIONS AND COMMENTS.

DR. PRIETO: I JUST WONDERED HOW MUCH OF A BARRIER WAS FELT THAT THE CONFLICT OF INTEREST ISSUES WERE FOR PATIENT ADVOCATES. I HAVEN'T SEEN THAT AS A MAJOR STUMBLING BLOCK AT LEAST ON THE ICOC

FOR THOSE OF US IN THE ADVOCACY COMMUNITY. JUST WONDERED IF YOU COULD FLESH OUT THAT DISCUSSION A LITTLE MORE.

DR. FEIGAL: IT WAS BROUGHT UP AS AN ISSUE. I ACTUALLY THINK IT'S A BROAD ISSUE ACROSS THE SCIENTIFIC, CLINICAL, TECHNICAL EXPERTS AS WELL. BUT IT DOES RAISE AN ISSUE. FOR EXAMPLE, YOU KNOW, IF THERE'S ANY KIND OF -- FOR EXAMPLE, SOME PATIENT ORGANIZATIONS RECEIVE FUNDING FROM PHARMACEUTICAL AGENCIES OR FROM COMPANIES OR DIFFERENT. IF THERE'S EVEN A PERCEPTION, IT'S NOT EVEN AN ACTUAL CONFLICT OF INTEREST, BUT EVEN IF THERE'S A PERCEPTION OF CONFLICT OF INTEREST, THERE'S A CONCERN WHETHER OR NOT THAT COULD INFLUENCE THAT PERSON'S OPINION AND PERSPECTIVES ON THE TABLE.

I DO AGREE IT'S PROBABLY MORE OF AN ISSUE FOR THE SCIENTISTS AND CLINICIANS AND SOME OF THE TECHNICAL EXPERTS THAN FOR SOME OF THE PATIENT ORGANIZATIONS, BUT IT IS AN ISSUE THAT ARISES. IT'S ALSO A VERY TIME-INTENSE EFFORT THAT TAKES PLACE WITH THESE ADVISORY COMMITTEES, AND ONLY A RELATIVELY FEW NUMBERS CAN REALLY PARTICIPATE. THERE'S REALLY ONE SLOT FOR THAT TYPE OF INPUT.

SO IT WAS RAISED AS AN ISSUE. HOW MUCH OF AN ISSUE IT IS I REALLY DON'T HAVE THAT INSIGHT TO

TELL YOU.

DR. ROBERTS: THIS MAY BE A DEFINITIONAL QUESTION OR MAYBE IT GOES MORE SUBSTANTIVELY TO YOUR POINTS. MOST OF THE TIME YOU'RE TALKING ABOUT PATIENTS, BUT SOMETIMES YOU ALSO BROUGHT IN CONSUMERS. AND AT ONE POINT YOU SAID CONSUMERS AND PATIENTS. SO THAT WOULD SUGGEST THEY'RE TWO DIFFERENT GROUPS. I WONDERED IF YOU JUST DISTINGUISH BETWEEN CONSUMERS AND PATIENTS.

AND THEN I WONDERED IF THERE WAS ANY DISCUSSION ABOUT WHEN THEIR INTERESTS MIGHT CONFLICT AND HOW THAT WOULD BE RESOLVED IN THE GREATER PARTICIPATION OF CONSUMERS AND PATIENTS AND THE BROADER PUBLIC.

DR. FEIGAL: WE ACTUALLY USED -- THE PUBLIC IS THE BROAD UMBRELLA.

DR. ROBERTS: THAT'S EVERYBODY.

DR. FEIGAL: AND THERE'S PATIENTS AND THERE'S PATIENT ADVOCACY ORGANIZATIONS. AND THERE ARE CONSUMERS WHO MAYBE AT SOME POINT IN TIME MAY BE PATIENTS, MAY NOT BE PATIENTS NOW. SO I THINK ACTUALLY ALL OF THE ABOVE IS WHAT WE'RE TALKING ABOUT. GENERALLY THE PATIENT SLOT ON AN ADVISORY COMMITTEE IS LIMITED TO SOMEBODY WITH A DISEASE AND HAS A NEAR-TERM ISSUE WITH THE DISEASE. THEY COULD

ALSO REPRESENT THEMSELVES. THEY COULD BE A PATIENT.

GENERALLY FOR ADVISORY COMMITTEES, THEY HAVE A BROADER INFLUENCE. THEY'RE PART OF AN ORGANIZATION, SO THEY REPRESENT A GROUP. SO BY PATIENTS, IT'S SOMEBODY WITH A CONDITION.

A CONSUMER MAY BE A PATIENT NOW, MAY BE A PATIENT LATER, IT MAY BE A WRITER, IT MAY BE SOMEBODY INVOLVED IN PUBLIC POLICY, MAYBE A RELATIVE, A CARETAKER, BUT THEY'RE NOT AT THIS POINT IN TIME PRESUMABLY THE PATIENT, BUT THEY'RE INCREDIBLY ENGAGED AND INVOLVED AND INTERESTED IN THE ISSUE, AND ABSOLUTELY THEY CAN'T ALL BE PAINTED WITH THE SAME BRUSH. THEY MAY HAVE -- PART OF THE ISSUE THAT AROSE FROM SOME CAMPS IS THE AGENCY, THE PENDULUM HAS SWUNG TO THE POINT THEY'RE VERY RISK AVERSE. SO ANYTHING THAT'S INNOVATIVE IS GOING TO BE VIEWED MORE SKEPTICALLY.

WE TALKED ABOUT STEM CELL RESEARCH. TALK ABOUT INNOVATION, TALK ABOUT LEVELS OF UNCERTAINTY, TALK ABOUT WE DON'T KNOW WHAT SOME OF THE ISSUES ARE THAT COULD ARISE. THE POINT IS WITH INNOVATION UNCERTAINTY IS INHERENT, SO HOW COULD YOU QUANTITATE HOW MUCH UNCERTAINTY YOU'RE WILLING TO TAKE? SO THE VIEWS OF SOMEBODY WHO ACTUALLY HAS THE DISEASE, THE CONCERNS OF SOMEBODY WHO'S ACTUALLY INTERESTED IN

THE BROADER PUBLIC HEALTH POLICY, THEY DON'T WANT TO HARM PEOPLE. SO HOW DO YOU BALANCE THOSE ISSUES AS YOU'RE MOVING FORWARD?

ONE THING THAT WAS BROUGHT UP IS THIS ISSUE OF CONDITIONALITY. IN THE UNITED STATES WE TEND TO HAVE AN ON-OFF SWITCH. A DRUG IS EITHER APPROVED OR IT'S NOT. IN EUROPE THERE MAY BE A CONDITIONAL APPROVAL WHERE IT GOES INTO A CERTAIN SUBSET OF THE POPULATION, AND THEN PERHAPS IN ANOTHER LENGTH OF TIME IT MIGHT BE BROADENED. SO THE THOUGHT WAS MADE CAN WE HAVE MORE THAN AN ON-OFF SWITCH? CAN WE HAVE MORE OF A CONDITIONAL TYPE OF PROCESS PUT IN PLACE?

DR. ROBERT TAYLOR: SO JUST TO CLARIFY ACTUALLY, DOROTHY, PARTLY IN RESPONSE TO YOUR QUESTION, ONE OF THE CONSUMERS, AS ELLEN MENTIONED, IS THE PAYER. AND THAT'S A PARTICULAR CONSUMER WHO MIGHT BE CONFLICTED WITH A PATIENT IN TERMS OF THE OUTCOME. I THINK THAT'S ONE OF THE THINGS THAT WE SHOULD KIND OF NOT -- I THINK THAT NEEDS TO BE STATED MAYBE OUTRIGHT.

THE QUESTION THAT I WAS GOING TO RAISE IS THAT THE OVERRIDING PHILOSOPHY OF THE FDA CURRENTLY HAS BEEN VERY MUCH, I THINK, SORT OF SHROUDED IN TRADE SECRECY AND IS REALLY A BLACK BOX. SO FOR

THIS KIND OF TRANSPARENCY TO HAPPEN, IT'S GOING TO HAVE TO COME FROM ABOVE THE FDA RATHER THAN FROM BELOW, IT SEEMS TO ME. DO YOU SEE THAT HAPPENING? IS THERE REALLY AN INTEREST IN HAVING THAT HAPPEN? BECAUSE I THINK REALLY THE SORT OF CONFLICT OF INTEREST PROTECTION OF THE PRODUCT SORT OF FROM AN ECONOMICS POINT OF VIEW IS, IN MY VIEW, ONE OF THE SORT OF STRONG FEATURES OF WHAT THE FDA DOES. UNLESS THAT WERE TO REALLY CHANGE, I DON'T SEE HOW THESE THINGS ARE GOING TO HAPPEN.

DR. FEIGAL: I DON'T SEE -- TO BE VERY BLUNT, TRADE SECRETS AREN'T GOING TO BE MADE PUBLIC. PROPRIETARY INFORMATION ISN'T GOING TO BE MADE PUBLIC. I DON'T SEE TRANSPARENCY IN TERMS OF SHARING A SPONSOR'S INNER WORKINGS ABOUT HOW THEY DEVELOP SOMETHING BECAUSE THEN YOU ACTUALLY UNDERMINE THE WHOLE BUSINESS. AT THE END OF THE DAY, THEY HAVE TO HAVE SOME SORT OF PROTECTIONS OF HOW TO MOVE FORWARD.

WHAT I WAS TALKING ABOUT IS TRANSPARENCY OF THE PROCESS OF HOW DECISIONS GET MADE, AND COULD THERE BE MORE TRANSPARENCY IN HOW YOU GET DELIBERATIVE INPUT. I'M NOT SUGGESTING, AND I DON'T THINK ANYBODY WOULD EVER HAVE A PROCESS WHERE ALL THE COMPANY'S DATA AND INFORMATION IS OUT THERE.

WHAT THE FDA DOES DO IS THEY DO POST THE BRIEFING DOCUMENTS BEFORE ADVISORY COMMITTEE MEETINGS. AND IN EUROPE THEY DO POST THE SUMMARY BASIS OF APPROVAL AND THE SUMMARY BASIS OF DISAPPROVAL. THE UNITED STATES ONLY POSTS SUMMARY BASIS OF APPROVALS. THEY ACTUALLY DON'T SHARE INFORMATION WHEN SOMETHING IS NOT APPROVED UNLESS IT'S THE TOPIC OF AN ADVISORY COMMITTEE. OFTENTIMES ADVISORY COMMITTEES ARE THE ONLY PUBLIC WAY YOU GET TO HEAR, IF SOMETHING'S REJECTED, WHY IT WAS REJECTED. BUT IF THERE'S NOT AN ADVISORY COMMITTEE, THERE WILL NOT BE A PUBLIC POSTING OF THE DATA THAT WENT INTO THAT DECISION.

IN EUROPE, HOWEVER, THEY DO HAVE A SUMMARY BASIS OF WHY THEY MIGHT REJECT AN APPLICATION.

CHAIRMAN LO: I WANT TO TRY AND MOVE US ALONG. JEFF, YOU HAD A COMMENT OR QUESTION HERE.

DR. BOTKIN: QUICK COMMENT AND A CIRM-RELATED QUESTION. SO THIS IS SO INTERESTING AND I THINK ADDRESSES SUCH A LONG-STANDING AND IMPORTANT PROBLEM. I'VE CERTAINLY SEEN COMMITTEES I'VE BEEN ON, EVERYTHING FROM THE SORT OF MUTE TOKENISM OF THE PUBLIC REPRESENTATIVE TO THE TEARFUL URGENCY THAT, IN FACT, HAS A SIGNIFICANT INFLUENCE ON HOW COMMITTEES THINK ABOUT THESE THINGS.

ONE THING I PARTICULARLY LIKE TOO IS JUST

THE NOTION THAT THERE'S A SENSE OF EQUIVALENCY OF PEOPLE WHO SIT AROUND THE TABLE IN THAT OFTENTIMES IT'S THE PUBLIC OR PATIENT REPRESENTATIVE WHO'S SUPPOSED TO REPRESENT SOME OTHER GROUP, BUT YET I, SITTING HERE AS A BIOETHICIST, I'M NOT SUPPOSED TO REPRESENT THE BIOETHICS COMMUNITY. OR IF I AM, SOMEBODY SHOULD TELL ME THAT. SO I THINK OFTENTIMES THE SCIENTISTS AND OTHER EXPERTS AREN'T SEEN AS REPRESENTATIVE OF A LARGER COMMUNITY WHEN, IN FACT, THEY MAY WELL BE. AND SO I THINK SORT OF PUTTING THAT OUT ON THE TABLE A LITTLE BIT MORE TO UNDERSTAND WHAT ROLES ARE AROUND THE TABLE.

SO SPECIFIC CIRM QUESTION WOULD BE, AS WE THINK ABOUT PATIENT REPRESENTATIVES, SEEING A NUMBER OF DIFFERENT COMMUNITIES THAT ARE REPRESENTED IN THAT FASHION, ARE THERE REPRESENTATIVES OUT THERE? ARE THE EMBRYO DONOR PATIENT COMMUNITY, IS THAT VOICE PART OF THE CIRM PROCESS?

DR. FEIGAL: THE EMBRYO -- I DON'T KNOW IF GEOFF WANTS TO COMMENT ON THAT, BUT WE THINK CERTAINLY, IN TERMS OF OUR STANDARDS, HAVE THOUGHT ABOUT THE PROTECTIONS AND THE VOICE OF WHAT WOULD BE IMPORTANT TO THE DONOR. AND MAYBE GEOFF WOULD WANT TO COMMENT ON THAT.

DR. LOMAX: IT'S A LITTLE BIT INDIRECT,

BUT I KNOW WE HAVE COLLEAGUES FROM INSTITUTIONS, I DON'T WANT TO NECESSARILY DEMAND THAT THEY COMMENT, BUT PERHAPS THEY HAVE A COMMENT. BUT WHAT WE'VE LEARNED FROM EMBRYO DONATION HAS LARGELY BEEN SORT OF OUTREACH TO THE INSTITUTIONS THAT HAVE DERIVED LINES AND REALLY A KIND OF INFORMAL HOW'S IT GOING. AND THE HOW'S IT GOING THAT I'VE HEARD IS THAT WHEN PEOPLE UNDERSTAND THE NATURE OF THE DONATION AND THE INTENT OF THE RESEARCHERS, AND THEY REALLY DO APPRECIATE GETTING A SENSE OF HOW THEIR MATERIALS ARE GOING TO BE USED. THEY'RE VERY EXCITED. IT'S REALLY BEEN FROM THE STANDPOINT OF PUTTING FEELERS OUT THERE TO ASK THE QUESTION ARE WE MISSING ANYTHING? WHAT I'M HEARING BACK IS NO. IN FACT, PEOPLE REALLY APPRECIATE THE OPPORTUNITY TO HAVE THAT OPTION, PARTICULARLY WITH SOMETHING LIKE AN EMBRYO FOR WHICH THEY'VE MADE AN IMPORTANT BOTH FINANCIAL AND SORT OF SOCIAL INVESTMENT, AND HAVING THAT PARTICULAR OPTION AVAILABLE TO THAT PARTICULAR PERSON IS THE SORT OF HIGHEST VALUE OPTION, IF YOU WILL, AS OPPOSED TO THE OTHER ALTERNATIVES. AND THE FACT THAT CALIFORNIA HAS CREATED THAT OPPORTUNITY FOR THEM IS, AGAIN, VIEWED AND VALUED.

I SEE DENISE'S HEAD. I'M REFLECTING BACK ON A CONVERSATION THAT WE HAD. SO, AGAIN, IF YOU

HAVE SOME COMMENTS, PLEASE FILL IN THE BLANKS FOR ME.

DR. BERNSTEIN: I THINK THAT YOU SAID IT ALL. ONE AREA I WOULD SAY WITH EMBRYO DONATION IS THAT --

DR. FEIGAL: I KNOW OUR TRANSCRIBER IS GOING TO WANT YOU TO USE THE MIKE.

DR. BERNSTEIN: I KEEP THINKING THAT IT'S CARRYING TO IT. I THINK IT WAS BOB NACHTIGALL THAT DID A PAPER ON EMBRYO DONATION. ONE OF THE THINGS THAT HE LOOKED AT WAS SEPARATING THE TYPES OF RESEARCH THAT WERE DONE WITH EMBRYOS. SO IT'S IMPORTANT TO SEPARATE THAT OUT. SOME PEOPLE ARE KIND OF GUNG HO ON THE STEM CELL RESEARCH. THEY WANT TO BE PART OF IT, NOT JUST SCIENTIFICALLY, BUT POLITICALLY. AND THERE'S SOME PEOPLE THAT SAY YOU CAN DO WHATEVER YOU WANT WITH MY EMBRYOS, BUT I DON'T WANT CELLS PROPAGATED, AND I DON'T WANT THEM OUT THERE FOR -- MY CELLS OUT THERE AND MY DNA OUT THERE FOR ETERNITY.

SO AS LONG AS THEY HAVE CHOICES, I THINK IT'S REALLY IMPORTANT, AND NOT JUST THE CHOICE OF DONATION, BUT DONATION TO ANOTHER COUPLE IF THEY'D LIKE, OR JUST DISCARDING THEM. IT'S JUST REALLY IMPORTANT. AND CALIFORNIA, STATE OF CALIFORNIA

GIVES PEOPLE LOTS OF CHOICES. SO I THINK GENERALLY PEOPLE ARE HAPPY WITH THE CHOICES.

DR. WAGNER: ONE IS A QUESTION, WHICH IS WHAT ARE YOU ASKING OF THIS COMMITTEE TO SAY OR DO?

DR. FEIGAL: I THINK IT WAS, ONE, PROVIDE INFORMATION SO YOU'RE AWARE OF WHAT'S HAPPENING. TWO, ARE THERE PARTICULAR -- SINCE WE HAVE A SEAT AT THE TABLE, IS THERE PARTICULAR ETHICAL RESEARCH IMPERATIVE OR CONSIDERATIONS WE SHOULD BRING INTO THE DISCUSSION THAT PERHAPS IS NOT YET PART OF THE DISCUSSION? AND, THREE, ANYTHING ELSE YOU THINK COULD BE KEY OR RELEVANT OR WHAT YOU SEE HERE THAT MAYBE MIGHT BE SOMETHING THAT MIGHT BE EXPORTABLE TO HOW WE DO BUSINESS. THOSE ARE JUST SOME THOUGHTS OF WHAT THIS BOARD COULD DO.

DR. WAGNER: I JUST WANTED TO MAKE SURE THAT WE RESPONDED IN A WAY THAT MET WHAT YOUR HOPE WAS. I GUESS MY COMMENT, FIRST OFF, I THINK THAT THIS IS EXTREMELY IMPORTANT. IT'S SO COMPLICATED. YOU'VE TOUCHED ON MANY DIFFERENT TOPICS. AND AFTER A WHILE IT BECAME OVERWHELMING BECAUSE THERE ARE SO MANY DIFFERENT ISSUES TO REALLY DIVE DEEPER INTO.

ONE THING, THOUGH, THAT MAKES IT EVEN MORE COMPLEX, WHICH I'M SURE THAT YOU DISCUSSED, BUT I MISSED IT HERE, WAS REALLY THE TYPES OF

DELIBERATIONS YOU HAVE WITH THE FDA VARIES WITH WHAT KIND OF TRIAL IT IS. YOU WILL NOT HAVE A PUBLIC COMMENT PERIOD FOR A PHASE I TRIAL MOST FREQUENTLY, YET THAT'S THE HIGHEST RISK TRIAL. YOU KNOW, I THINK THAT IN TERMS OF WHAT I'VE LEARNED MOST FROM CIRM, BEING INVOLVED FOR WHATEVER NUMBER OF YEARS, IS REALLY HOW TO CONSIDER BEST UTILIZING THE POWER OF THE PUBLIC. AND THE REASON WHY THAT HAPPENS, I THINK HERE, AND THIS IS JUST OFF THE TOP AND PEOPLE COULD BEAT IT DOWN, IS IN PART BECAUSE OF THE PUBLICITY AROUND THIS TOPIC IN CALIFORNIA, THE PUBLIC'S OBVIOUS COMMITMENT TO IT THROUGH THE PROPOSITION, BUT ALSO BECAUSE THE FUNDING LEVEL IS A BIT DIFFERENT.

WHEN THEY THINK OUTSIDE THIS AREA, IT IS REALLY DIFFICULT FOR THE AVERAGE INVESTIGATOR TO EVEN BEGIN TO IMPLEMENT SOMETHING THAT YOU ARE BRINGING UP, ALTHOUGH VERY IMPORTANT, IN PART BECAUSE OF THE FACT THAT -- ON YOUR LIST HERE YOU DIDN'T MENTION NIH. FOR THE MAJORITY OF THE WORLD, OUR ABILITY TO DO SUCH RESEARCH IS DEPENDENT UPON THE NIH. AND THE NIH FUNDING IS AT A VERY DIFFERENT LEVEL, SUCH THAT YOU WOULD LIKE TO HAVE THIS INFORMATION BEFOREHAND. AND, IN FACT, THEY SHOULD WANT THIS INFORMATION BEFOREHAND BECAUSE, AS YOU

STATED FROM THE VERY BEGINNING, WITHOUT THE PUBLIC'S INPUT, IT MAY INFLUENCE -- THE RESULT OF THAT DISCUSSION, SHOULD IT HAVE OCCURRED, MIGHT INFLUENCE NOT ONLY THE DESIGN OF THE TRIAL THAT IS TO BE UNDERTAKEN, BUT COULD INFLUENCE THE FUNDING OF THAT BY THE FUNDING AGENCY, WHETHER IT BE CIRM OR THE NIH OR WHOEVER IT IS.

IN ANY EVENT, I THINK IT'S EXTRAORDINARILY IMPORTANT, I THINK IT'S EXTRAORDINARILY COMPLEX, I THINK THAT WE NEED TO FOCUS ON WHAT STAGE OF THE RESEARCH WE'RE TALKING ABOUT. AND WHEN IT COMES DOWN TO EVERYTHING THAT CIRM IS DOING NOW, IT PROBABLY SHOULD BE FOCUSED MORE ON PHASE I RATHER THAN THE PHASE III-IV, AND FIGURE OUT HOW YOU CAN BEST DO THAT BECAUSE I THINK IT COULD SET THE STAGE FOR THE REST OF THE UNITED STATES.

DR. FEIGAL: I DO WANT TO ADD WE DID HAVE NIH REPRESENTATIVES. NIH HAS ACTUALLY REALLY LED IN BRINGING IN PATIENTS AND PATIENT ADVOCACY ORGANIZATIONS. THE NIH DIRECTOR HAS A DIRECTOR'S CONSUMER ALLIANCE GROUP, THE NCI DIRECTOR HAS A PATIENT ADVOCACY ORGANIZATION GROUP THAT IT WORKS WITH. THE REVIEW COMMITTEES OF ALL OF THE NIH GROUPS HAVE SOME KIND OF A PATIENT PERSPECTIVE PART OF IT. USUALLY IT DEPENDS ON THEIR AREA OF

EXPERTISE. IT MAY BE FOR CLINICALLY APPLICABLE ORGANIZATION GRANTS, LOOKING AT THE INFORMED CONSENTS. IT MAY BE DEPENDING IF THEY HAVE A DIFFERENT AREA OF EXPERTISE INVOLVED IN THAT WAY. ALL OF THE DATA SAFETY MONITORING, WHICH SETS THE POLICY FOR THE LARGE TRIALS, HAVE TO HAVE A PATIENT REPRESENTATIVE FOR NIH-FUNDED CLINICAL TRIALS.

SO THERE'S A VARIETY OF WAYS, I AGREE. NIH HAS REALLY TRIED TO INCLUDE THEM. HOW THAT IMPACTS ON WHICH APPLICATIONS ARE CHOSEN FOR FUNDING, THAT VALUE OF INFLUENCE MAY BE DIFFERENT OR NOT AS GREAT AS ONE WOULD LIKE, BUT THEY DO QUITE A BIT IN TERMS OF TRYING. I AGREE AT CIRM THAT WAS ONE THING WE WERE TRYING TO BRING OUT AT THIS CONFERENCE IS DON'T WAIT TILL THE END. THE PACKAGE IS ALREADY PUT TOGETHER. NOW YOU'RE COMING AND ASKING FOR THE PATIENT VOICE. IT NEEDS TO BE REALLY WHEN WE'RE DOING THE RESEARCH THAT THE PATIENT INPUT AND VOICE NEEDS TO COME IN.

I KNOW AT CIRM WE'RE TRYING TO DO THAT THROUGH THE DIFFERENT SESSIONS THAT WE HAVE. AND WE'RE ASKING THE FDA IS THERE SOME PART OF THE PROCESS EARLIER ON WHEN THE SPONSOR -- AT THE PRE-IND STAGE, BEFORE THEY GO INTO FIRST IN HUMAN, IS THERE A WAY TO GET SOME KIND OF PATIENT

PERSPECTIVE AND INPUT?

SOMETIMES THEY WILL PUT TOGETHER ADVISORY COMMITTEES ON A TOPIC. SOME PATIENT ADVOCATE ORGANIZATIONS ORGANIZE THEIR OWN CONFERENCES TO TALK ABOUT SPECIFIC ISSUES FOR EARLY CLINICAL TRIALS. FRIENDS OF CANCER RESEARCH, WHO WAS PRESENT AT THIS MEETING, DOES A LOT TO ACTUALLY PUT OUT WORKSHOPS AND ORGANIZE THEM ON SPECIFIC TOPICS. SO I AGREE WITH YOU. PROBABLY WHERE WE CAN PLAY A ROLE IS MORE IN THE EARLIER STAGE.

DR. WAGNER: FOR EXAMPLE, YOU HAVE AN EXTRAORDINARY EXAMPLE OF THE USE OF HUMAN EMBRYONIC STEM CELLS FOR THE TREATMENT OF SPINAL CORD INJURY, AND YOU HAVE ANOTHER ONE FOR BATTEN'S DISEASE WHERE THERE ARE EXAMPLES WHERE THE TRIALS ENDED PREMATURELY. WHAT I DON'T KNOW IS WHETHER OR NOT, COULD THERE HAVE BEEN SOMETHING DONE IN A DIFFERENT WAY THAT WOULD HAVE MINIMIZED THAT RISK? COULD WE HAVE KNOWN SOMETHING IN ADVANCE PERHAPS BY BRINGING IN THESE PATIENT ADVOCACY GROUPS THAT SOMEHOW COULD HAVE BETTER ENSURED A MORE RAPID PROCESS THAT MIGHT BE LESS COSTLY?

I BRING THAT UP BECAUSE OF THEIR HIGH PROFILE. AGAIN, THERE'S A GREAT DEAL OF INVESTMENT MADE INTO THESE PROJECTS THAT THEN ABRUPTLY ENDED IN

PART BECAUSE OF ACCRUAL, IN PART BECAUSE OF THE LENGTH OF TIME IT TOOK TO MOVE THEM TO CLINICAL IMPLEMENTATION, AND ALL THAT HAS A MAJOR IMPACT.

DR. FEIGAL: THANK YOU.

CHAIRMAN LO: I'M LOOKING AT THE AGENDA AND THE TIME HERE. I'D LIKE TO SUGGEST WE SORT OF MOVE ON. THIS IS SORT OF THE FIRST MEETING IN AN ONGOING PROJECT, AND THE HASTINGS CENTER IS LIKELY TO WRITE THIS UP WITH A FORMAL SET OF RECOMMENDATIONS. SO WE'LL LOOK FORWARD TO HEARING MORE UPDATES FOR SUBSEQUENT MEETINGS.

I THINK FOR OUR WORKING GROUP THIS IS SOMETHING I THINK WE'LL DEFINITELY KEEP OUR EYES CLOSELY ON. IF IT TURNS OUT TO BE AN ISSUE, IT'S A VERY COMPLICATED AND IMPORTANT ISSUE, IF WE WANT TO DEAL WITH IT FURTHER, WE CAN COME BACK TO IT AT THE END OF THE MEETING AND DECIDE TO WHAT EXTENT WE REALLY WANT TO PURSUE THIS AS AN ISSUE REALLY TARGETED TO CIRM AS OPPOSED TO THIS BROADER INITIATIVE THAT CIRM IS PARTIALLY SUPPORTING AS WELL AS PARTICIPATING IN AT THE HASTINGS CENTER.

BUT WE DO HAVE A NUMBER OF POLICY ISSUES WITH REGARD TO RECOMMENDATIONS FOR MODIFYING THE REGULATIONS THAT I'D LIKE TO WORK ON. DO YOU FOLKS -- I WOULD SUGGEST -- IT'S 10:30 NOW. WE'VE

BEEN GOING AT FOR ABOUT AN HOUR AND A HALF. I WOULD VOTE FOR SORT OF PUSHING AHEAD TO SORT OF HEAR FROM SCOTT AND GEOFF ON THE PROPOSED AMENDMENTS.

HAVING SAID THAT, I'M ALWAYS ACCUSED OF SORT OF NEGLECTING THE CALLS OF NATURE. SO IF PEOPLE REALLY WANT A BREAK, WE CAN DO THAT NOW. I CAN'T STOP YOU OBVIOUSLY FROM VISITING THE FACILITIES WHICH ARE THATAWAY AND TO THE LEFT.

GEOFF, YOU AND SCOTT WANT TO GET US STARTED.

DR. LOMAX: I WANTED TO REMIND EVERYONE FOR THIS SEGMENT WE'VE GOT COPIES OF THE MATERIALS. ALL THE MATERIALS ARE COPIED FOR MEMBERS OF THE PUBLIC. AND WE DID SEND AROUND SOME ADVANCE COMMENTS AND COPIES OF THOSE COMMENTS. THEY'RE AVAILABLE AS WELL. SO AS A REMINDER, THAT AS WE MOVE THROUGH THESE ITEMS, THERE ARE COMMENTS ASSOCIATED WITH THEM, AND YOU MAY WANT TO REFER TO THOSE. I WILL TRY TO PARAPHRASE SOME OF THEM IN THIS PRESENTATION, BUT I'M ALWAYS AWARE OF THE PERILS OF PARAPHRASING. SO WE DID INCLUDE THE FULL TEXT OF THE COMMENTS AS WELL TO ENSURE THAT WE'RE NOT SORT OF MISREADING OR MISREPRESENTING THOSE COMMENTS IN ANY WAY.

WITH THAT SAID, THERE ARE THREE SECTIONS

OF THE REGULATIONS THAT WE ARE PROPOSING AMENDING. I'D LIKE TO COVER THEM. 160 IS A DISCRETE ITEM, AND THEN THERE'S A SERIES OF PROPOSED AMENDMENTS IN THE 170 SECTION AND COVER THAT AS A BLOCK. AND THEN THE 180S, I WOULD SUGGEST, REALLY ACTUALLY JUST KIND OF FALLS OUT. IF WE MOVE FORWARD ON 170, THE 180 IS A BIT TECHNICAL. SO THE BULK OF THE DISCUSSION IS IN THIS 170 SECTION, BUT I'LL START ON SECTION 160, WHICH DEALS WITH THE --

CHAIRMAN LO: I'D JUST REMIND PEOPLE THAT WE HAVE A COPY OF GEOFF'S SLIDES IN YOUR BRIEFING BOOK. IT LOOKS LIKE THIS.

DR. LOMAX: SO THE FIRST PROPOSAL DEALS WITH THE COMPOSITION OF THE OVERSIGHT COMMITTEES. AS YOU MAY BE AWARE, WE GAVE SORT OF A BROAD SORT OF GUIDANCE FOR HOW THESE COMMITTEES WOULD BE CONSTITUTED, AND THIS WAS TO ALLOW INSTITUTIONS TO SORT OF POPULATE THEIR COMMITTEES WITH EXPERTISE APPROPRIATE TO THE TYPES OF RESEARCH THEY WERE DOING. BUT IN ADDITION, WE INCLUDED PROVISIONS WHERE THERE WOULD BE AN OUTSIDE MEMBER AND A PATIENT ADVOCATE.

DURING THE DELIBERATIONS, THERE WAS A SENSE THAT THE NONSCIENTIST PUBLIC MEMBER SHOULD NOT RECEIVE ANY TYPE OF COMPENSATION, ANY COMPENSATION

OF ANY KIND FOR PARTICIPATING IN THE COMMITTEE WORK. THE RATIONALE BEING THAT THIS MAY BE SORT OF COERCIVE OR SOMEHOW INFLUENCE THEIR JUDGMENT ON THE COMMITTEE.

SINCE THIS AMENDMENT HAS BEEN IN PLAY, WE'VE HEARD FROM A NUMBER OF INSTITUTIONS THAT ONE OF THE DIFFICULTIES THIS DOES CREATE FOR INSTITUTIONS IS THAT INSTITUTIONS HAVE A VARIETY OF COMMITTEES THAT INVOLVE SORT OF OUTSIDE OR IMPARTIAL MEMBERS. AND TYPICALLY INSTITUTIONS, THEIR PREFERENCE IS TO FORM A COMMITTEE AND THEN EVERYONE ON THE COMMITTEE WHO'S NOT AFFILIATED WITH THE INSTITUTION, THEY LIKE TO HAVE A PER DIEM OR SOME SORT OF MODEST SORT OF ACKNOWLEDGEMENT OF THEIR PARTICIPATION, AND THAT THAT'S SORT OF UNIFORM ACROSS IRB'S, ANIMAL REVIEW COMMITTEES, FOR EXAMPLE. AND, AGAIN, THE PREFERENCE FROM AN ADMINISTRATIVE PERSPECTIVE IS WE'D LIKE TO HAVE A UNIFORM POLICY WE CAN APPLY TO EVERYONE. AND THAT THIS POLICY IS A BIT UNUSUAL IN THAT THERE'S SORT OF ONE PERSON WHO GETS EXCEPTIONAL TREATMENT IS THE SORT OF OUTSIDE VOLUNTEER PERSON WHO'S TRYING TO HELP THE STEM CELL PROGRAM.

ONE OF THE OTHER THINGS WE'VE BEEN ABLE TO DO AS CIRM IS WE'VE INTERACTED WITH A NUMBER OF

THESE MEMBERS, AND THEY'RE SORT OF VERY ADAMANT ABOUT THEIR ROLE, AND WE'RE ALWAYS RAISING TOUGH ISSUES, AND A $50 PER DIEM IS NOT GOING TO CHANGE MY APPROACH TO THIS. SO WHAT WE'VE SORT OF SUGGESTED IN THE SPIRIT OF PROVIDING FLEXIBILITY IS TO REALLY JUST STRIKE THE LANGUAGE PROHIBITING REMUNERATION OF THE NONSCIENTIST PUBLIC MEMBER AND JUST, AGAIN, AFFORD INSTITUTIONS THE FLEXIBILITY TO APPLY THEIR POLICIES BROADLY.

SO THAT'S THE PROPOSAL BEFORE YOU ALL, AND WE'RE ASKING YOU TO CONSIDER THAT TODAY.

CHAIRMAN LO: GEOFF, IF I MAY JUST MAKE A CLARIFYING COMMENT. SO THIS BASICALLY JUST REMOVES THE PROHIBITION, LEAVING IT UP TO THE INSTITUTION TO DECIDE WHETHER OR NOT THEY WANT TO PROVIDE COMPENSATION. SO IT'S NOT REQUIRING THEM TO COMPENSATE PEOPLE. IT'S NOT REQUIRING THEM TO TREAT SCRO MEMBERS LIKE IRB MEMBERS OR ANIMAL. JUST LEAVING THEM THE OPTION TO DO WHAT THEY SEE FIT WITHOUT THE PROHIBITION.

DR. LOMAX: CORRECT. IN REGULATORY PARLANCE, WE WOULD REMAIN SILENT ON THE ISSUE. SO IT'S REALLY, AGAIN, DEFERRING TO THE JUDGMENT OF THE INSTITUTION OF HOW THEY WOULD LIKE TO ADMINISTER THESE COMMITTEES.

CHAIRMAN LO: COMMENTS, THOUGHTS ON THIS? PAT TAYLOR IS AN OLD NEW MEMBER. HE'S THE EXPERIENCED NEW MEMBER, BUT WASN'T HERE THIS MORNING. SO I JUST WANTED TO RECOGNIZE HIM.

DR. PAT TAYLOR: I ACTUALLY GOT LOCKED OUT OF MY ROOM WHICH CAUSED ME TO BE LATE.

IT STRIKES ME AS A VERY GOOD AMENDMENT. INSTITUTIONS DO HAVE THEIR OWN PRACTICES AND CULTURES. AND IN THE INTEREST OF NOT PROMOTING SOMETHING THAT'S EXCEPTIONAL JUST FOR SCRO'S, IT SEEMS WISE TO REMOVE THIS PROHIBITION.

IN ADDITION, IT'S TRULY HARD TO RECRUIT PEOPLE OFTEN. SO IT SEEMS IMPORTANT TO GIVE INSTITUTIONS THE FLEXIBILITY TO ACTUALLY OPERATE ACCORDING TO THEIR OWN NEEDS. THANKS.

CHAIRMAN LO: OTHER COMMENTS? THOUGHTS?

DR. PRIETO: I JUST WOULD LIKE TO ALSO STRONGLY SUPPORT THIS. THINKING BACK TO SOME OF THE DISCUSSIONS WE HAD EARLY ON IN THE DAYS OF THE STANDARDS WORKING GROUP ABOUT THIS AND AVOIDING CONFLICTS AND SUCH, BUT HAVING HAD THE EXPERIENCE NOW FOR SEVERAL YEARS WORKING WITH CIRM, SEEING WHAT A BURDEN IT IS FOR PATIENT ADVOCATES WHO OFTEN ARE GIVING UP THEIR DAY JOB ON WHICH MOST OF US DEPEND AND THAT INCOME IN ORDER TO PARTICIPATE IN SOMETHING

WHERE I THINK WE MAKE AN IMPORTANT CONTRIBUTION TO DEVELOPING POLICY AND IMPLEMENTING IT, I THINK THIS HELPS TO MAKE IT POSSIBLE. AND SO I HOPE THAT MOST INSTITUTIONS WILL TAKE THAT IN MIND AND ALLOW THAT REIMBURSEMENT.

CHAIRMAN LO: ANY OTHER COMMENTS?

DR. LOCKHART: I THINK ALSO IN KEEPING WITH THE IDEA OF NOT TREATING PATIENT ADVOCATES OR PUBLIC MEMBERS AS SECOND CLASS CITIZENS, IT WOULD ALSO SPEAK TO THE ISSUE OF FAIRNESS, THAT THEY NOT BE HELD OUT AS A GROUP WHO IS PARTICULARLY VULNERABLE TO COERCION AND WE'RE NOT ABLE TO RECEIVE A PER DIEM. I THINK IT WOULD REALLY HELP WITH THAT KIND OF FAIRNESS, EVEN PLAYING FIELD THAT SEEMS IMPORTANT.

DR. LOMAX: CAN I JUST POINT OUT, BY THE WAY, WE HAD A BOWLING ALLEY BUILT BELOW US AT CIRM, AND WE HAD DRILLING LIKE THIS GOING ON FOR SIX MONTHS. I FEEL LIKE SOMEBODY HAS GOT MY NUMBER. I JUST HAD TO POINT THAT OUT. I'M REALIZING THESE SYNAPSES ARE FIRING THAT ARE PUTTING ME INTO THIS VERY ODD PLACE.

DO YOU WANT TO ASK FOR PUBLIC COMMENT IN EACH OF THE SECTIONS? I KNOW WE HAVE A NUMBER OF INSTITUTIONAL MEMBERS HERE.

CHAIRMAN LO: ANY CONCERNS AMONG THE SWG? SO FAR WE'VE HEARD SUPPORTIVE COMMENTS WITH REGARD TO THE AMENDMENT. ANY CONCERNS THAT ANY MEMBERS WANT TO RAISE? OKAY. THEN I WANT TO OPEN IT UP TO THE PUBLIC. ARE THERE ANY MEMBERS OF THE PUBLIC WHO WOULD LIKE TO COMMENT ON THIS? AND WOULD YOU COME ALL THE WAY FORWARD, TRY AND LEAN INTO THAT MICROPHONE, AND GIVE YOUR NAME IF YOU WANT TO SPEAK.

SEEING NONE, LET'S -- GEOFF, SINCE WE'RE NOT A QUORUM, SHOULD WE VOTE ON A SENSE OF THE COMMITTEE?

DR. LOMAX: I DON'T THINK WE NEED A VOTE. I WILL DEFER TO SCOTT. I THINK BASED ON THE RECORD --

CHAIRMAN LO: INFORMAL. HOW DO YOU WANT ME TO ACTUALLY DO THAT?

MR. TOCHER: YOU CAN GET THE COMMENTS YOU'VE RECEIVED.

CHAIRMAN LO: SO THE COMMENTS I'VE RECEIVED ARE ALL SUPPORTIVE OF THIS CHANGE WITH NO COMMENTS EXPRESSING CONCERNS OR OPPOSITION. SO I WOULD SUGGEST THAT THE SENSE OF THIS MEETING, AND A LOT OF NODS GOING AROUND THE TABLE, IS THAT WE WOULD RECOMMEND -- THE SENSE OF THE MEETING IS THAT IT WOULD BE A GOOD IDEA FOR THE ICOC TO ADOPT THIS

PROPOSED CHANGE.

WE DON'T HAVE A QUORUM, SO IT WON'T COUNT ANYWAY IF WE HAVE A MOTION AND SECOND.

DR. PRIETO: I THINK WE'RE ALL IN AGREEMENT.

CHAIRMAN LO: IT SOUNDS LIKE WE'RE IN AGREEMENT.

GEOFF, YOU WANT TO MOVE US ON TO 100070 AND THE THREE PART.

DR. LOMAX: YES. SO I THOUGHT I'D TRY TO ENCAPSULATE THE NEXT SET OF PROPOSED AMENDMENTS BECAUSE IT GETS A BIT DETAILED. SO I THOUGHT I'D MAYBE FIRST BACK IT UP WITH A LITTLE BIT OF A CONCEPTUAL OVERVIEW HERE, WHICH IS, FIRST OF ALL, THE PRIME DIRECTIVE FOR THE OVERSIGHT COMMITTEES WERE REALLY TO ADDRESS GAPS IN THE EXISTING REGULATORY FRAMEWORK. AND THE REAL DIRECTIVE FROM THE NATIONAL ACADEMIES WAS GAMETE AND EMBRYO WORK AND ANIMAL WORK.

AS A REMINDER, OUR REGULATIONS CONTINUE TO REQUIRE FULL COMMITTEE REVIEW OF PROTOCOLS THAT INVOLVE ANY TYPE OF EMBRYO, GAMETE, OR PLURIPOTENT TRANSPLANTATION TO ANIMAL WORK. IN ADDITION, THERE'S SOME OTHER CONDITIONS AROUND NEURAL TRANSPLANTATION TO ANIMALS.

SO I THINK WE COVERED THE SCOPE. I DON'T THINK. WE DO COVER THE SCOPE OF RECOMMENDATIONS FROM THE NATIONAL ACADEMIES; BUT IN ADDITION, WE STARTED WITH A FAIRLY CONSERVATIVE POSTURE WHERE WE ALSO HAD ADDITIONAL REVIEW AND/OR NOTIFICATION REQUIREMENTS FOR OTHER PLURIPOTENT STEM CELL WORK AND PARTICULAR REPROGRAMMING AND IPS WORK EARLY IN THE GAME. AND I THINK IT REFLECTS THE FACT THAT WE'VE ALWAYS TAKEN A RELATIVELY CONSERVATIVE POSTURE.

WE'RE SO CONSERVATIVE, IN FACT, THAT IN SOME AREAS WE REQUIRE MORE THAN WOULD OTHERWISE BE REQUIRED BY THE NIH WITH REGARD TO IPS WORK. AND, AGAIN, OVER TIME AND SORT OF THE TRACKING AND ALL THE VARIOUS INITIATIVES WE HAVE WHERE WE GO OUT AND BOTH DO ON-SITE EVALUATIONS OF GRANTEES AND REVIEW THEIR PROGRESS, WE'RE NOT SEEING A SET OF SORT OF DIFFICULT OR ETHICAL CONCERNS ARISING OUT OF MAINSTREAM IPS RESEARCH.

AND SO I THINK THE SORT OF CONCEPTUAL THOUGHT HERE IS IS IT REALLY TIME TO THINK ABOUT HAVING -- IF YOU'VE GOT A CIRM GRANT OR AN NIH GRANT INVOLVING IPS RESEARCH, THE REQUIREMENTS ARE BASICALLY THE SAME. THAT'S KIND OF CONCEPTUALLY WHERE WE ARE PROPOSING TO MOVE THE REGULATIONS.

I THINK THE OTHER PART THAT I'D REALLY LIKE TO EMPHASIZE FROM MY ROLE AS THE INDIVIDUAL WHO DOES ACTUALLY CHASE PEOPLE DOWN AND ASK A LOT OF QUESTIONS ABOUT THEIR REVIEW AND THEIR OVERSIGHT PROGRAM, INCLUDING, AGAIN, GOING ON SITE AND REALLY LOOKING AT WHAT'S GOING ON ON THE GROUND, IS THAT WHEN WE'RE SORT OF GOING OUT AND DEMANDING THAT PEOPLE KEEP RECORDS AND HAVE MEETINGS, WE REALLY WANT -- AND REVIEW THINGS, THAT WE REALLY WANT TO MAKE SURE THAT THEY'RE FOCUSING ON THE IMPORTANT STUFF AND THAT WE ALWAYS SPEND A LOT OF TIME MAKING SURE THAT THOSE BASES ARE COVERED.

SO I HAD A RECENT SITE VISIT, FOR EXAMPLE, AND WE WERE VERY MUCH DIGGING INTO MAKING SURE THAT ALL THE ANIMAL WORK WAS CAREFULLY DOCUMENTED, THE REVIEWS WERE THERE, THE APPROVALS WERE DOCUMENTED, MINUTES FROM THE MEETING, ETC., ETC. NOW, THAT'S VERY TIME-CONSUMING. AND WHAT WE WANT TO DO IS REALLY RESERVE OUR ADMINISTRATIVE CAPACITY TOWARDS MAKING SURE THOSE THINGS ARE THERE, BUT WE HAVE RECENTLY BEEN SPENDING A LOT OF TIME TRACKING DOWN BASICALLY WHAT WE CALL NOTIFICATION REQUIREMENTS, WHICH IS IS THE FILE COMPLETE, THAT SOMEONE TOLD SOMEBODY THEY WERE GOING TO DO SOME REPROGRAMMING WORK WITH A SOMATIC STEM CELL LINE. AND THAT TYPE

OF ACTIVITY, I THINK, CONSUMES BANDWIDTH, AND IT'S BANDWIDTH THAT'S BETTER UTILIZED FOCUSING ON, AGAIN, THE GAPS, IF YOU WILL.

SO PART OF WHY WE'RE PROPOSING THIS IS TO OPTIMIZE, I THINK, OUR ADMINISTRATIVE PROGRAM SO THAT WE'RE REALLY LOOKING WHERE WE NEED TO BE LOOKING TO BE DOING OUR JOB. SO THAT'S THE SORT OF ADMINISTRATIVE CAPACITY POINT.

WITH THAT SORT OF KIND OF FRAMING, I'LL GET INTO THIS TABLE WHICH REALLY TRIES TO SORT OF COMPARE AND CONTRAST WHERE WE ARE AND WHERE WE WOULD PROPOSE WE GO TO.

SO THE FIRST LINE IS, AGAIN, JUST A REMINDER THAT SOMETHING LIKE A DERIVATION OF A HUMAN EMBRYONIC STEM CELL LINE, WE WOULD CONTINUE TO REQUIRE FULL REVIEW OF THAT TYPE OF WORK.

THE OTHER AREA, AGAIN, WHERE WE THINK IT'S IMPORTANT TO HAVE SOME TYPE OF NOTIFICATION, BUT WHAT WE'RE PROPOSING IS A BIT MORE FLEXIBILITY IS THE AREA OF NEW IPSC DERIVATION WITH IDENTIFIABLE CELLS OR HUMAN SUBJECTS RESEARCH WHERE YOU HAVE IPSC DERIVATION. AND, AGAIN, THIS WOULD STILL BE A BIT MORE THAN THE NIH REQUIRES, BUT WE THINK IT'S IMPORTANT. I'LL EXPLAIN WHY.

SO THE STANDARD WE CURRENTLY HAVE IS THE

NOTIFICATION OF THE SCRO COMMITTEE. ONE OF THE PROBLEMS WE DO HAVE IS WE ARE, AS OUR GRANTEE PORTFOLIO EXPANDS, THERE ARE INSTITUTIONS THAT DON'T HAVE EASY ACCESS TO A SCRO COMMITTEE, AND THAT COULD BE A ROADBLOCK. SO WHAT WE'VE DONE OVER THE YEARS IS WE'VE INCORPORATED A SECOND PATHWAY FOR SOME OF THESE REGULATORY CHECKPOINTS. AND THAT IS, THEY CAN DESIGNATE A RESPONSIBLE INSTITUTION OFFICIAL. THAT WOULD BE SOMEONE WHOSE -- IT HAS TO BE SOMEONE WHO HAS DECISION AUTHORITY. TYPICALLY IT'S IN THE OFFICE OF GENERAL COUNSEL. BUT A HIGH LEVEL OFFICIAL WHO CAN CERTIFY BACK TO US THAT SOMETHING HAS HAPPENED.

AND, AGAIN, THAT'S SOMETHING THAT WE'RE USING EMBRYONIC STEM CELL LINES THAT ARE REGISTERED. IT'S A VERY CLEAR-CUT DETERMINATION AS OPPOSED TO WHERE YOU NEED A COMMITTEE LIKE YOU'RE DOING A VERY INTRIGUING ANIMAL STUDY. YOU STILL NEED THE OVERSIGHT COMMITTEE FOR THAT BECAUSE THAT'S MORE OF A DELIBERATIVE SITUATION WHERE YOU NEED TO THINK ABOUT WHAT YOU ARE DOING AS OPPOSED TO, NO, THE STEM CELL LINE OF CHOICE MEETS THE REGULATORY REQUIREMENT AND I'M CERTIFYING THAT. SO WE'RE ALLOWING THESE CERTIFICATIONS AT CERTAIN POINTS.

WHAT WE'RE PROPOSING IS THAT IF YOU'RE

DOING NEW IPSC DERIVATION WITH IDENTIFIABLE CELLS, WE INCLUDE THE INSTITUTIONAL OFFICIAL OPTION. AND THE POINT THERE IS -- THE POINT OF THE REQUIREMENT IS TO SAY WHEN YOU'RE DERIVING IPS LINES, ONE OF THE THINGS THAT WE CARE ABOUT DEEPLY IS THE QUALITY OF CONSENT. AND WE'D LIKE TO HAVE SOMEBODY, EITHER A COMMITTEE OR AN INDIVIDUAL, WHO'S INTIMATE WITH THE CIRM REQUIREMENTS AND CAN REALLY THINK IN THE CONTEXT OF THIS PROTOCOL, GIVEN THEY'RE IDENTIFIABLE AND WE MAY HAVE ACCESS TO THE PRIMARY DONOR, IS THERE ANYTHING ELSE WE MIGHT WANT TO THINK ABOUT IN TERMS OF THE CONSENT TO MAKE SURE THAT THE ULTIMATE PRODUCT, THE IPS LINE, WILL BE OPTIMALLY USEFUL OR COMPLIANT WITH CIRM STANDARDS.

AGAIN, IF IT'S HUMAN SUBJECTS RESEARCH, IT STILL HAS TO GO TO AN IRB FOR APPROVAL. SO WHAT THAT INDIVIDUAL OR THE COMMITTEE WOULD BE ABLE TO DO IS SORT OF INTERACT WITH THE IRB TO SORT OF THINK ABOUT ARE THERE OPPORTUNITIES HERE TO ENHANCE CONSENT IF SOMEONE HAS DETERMINED THAT'S A GOOD THING TO DO?

SO, AGAIN, THE NATURE OF THE CHANGE IS TO REALLY EXPAND THE EXISTING STANDARD TO ALLOW GREATER FLEXIBILITY WITHIN THE ORGANIZATION SO THAT IN EVERY CASE YOU WOULDN'T NECESSARILY NEED A SCRO TO DO IPS

WORK WITH IDENTIFIABLE CELLS.

THE OTHER THING I'D POINT OUT IS THIS IS A PRETTY LIMITED EXAMPLE WHEN YOU'D ENCOUNTER THIS SITUATION. IN FACT, YOU'RE PROBABLY GOING TO ENCOUNTER IT IN CLINICAL PROTOCOLS WHERE YOU'RE PROPOSING TO ACTUALLY USE AUTOLOGOUS CELLS AND TRANSPLANT THEM INTO AN INDIVIDUAL. SO IN ALL LIKELIHOOD, IN REALITY YOU'RE STILL GOING TO BE IN A SITUATION WHERE YOU'RE GOING TO NEED A SCRO COMMITTEE FOR THIS PARTICULAR CIRCUMSTANCE. BUT IN THE LIMITED CASE WHERE YOU'RE DOING WORK WITH IDENTIFIABLE CELLS, BUT YOU'RE NOT DOING ANY HUMAN TRANSPLANTATION WORK, AGAIN, IT PROVIDES MORE OPTIONS.

THAT'S SORT OF ITEM 1, AND THAT'S SORT OF, AGAIN, THE PROPOSAL THERE. SO I'LL PAUSE THERE. ARE THERE ANY QUESTIONS OR THOUGHTS AT THAT STAGE?

CHAIRMAN LO: GEOFF, ARE YOU GIVING US SORT OF THE OVERVIEW OF ALL THE PROPOSED CHANGES, AND THEN YOU'RE GOING TO DEAL WITH THEM ONE BY ONE IN MORE DETAIL? DO YOU WANT US TO FINISH THIS OVERVIEW?

DR. LOMAX: LET ME DO THAT. THAT'S FINE. THE TABLE IS SO MUCH EASIER TO OPERATE ON, BUT WHY DON'T I DO THAT, THEN I CAN GO TO THE SLIDE AND WE

CAN COME BACK TO THE TABLE IF WE WANT.

OKAY. SO THAT'S, AGAIN -- AND THE OTHER THING TO KEEP IN MIND HERE IS THAT THIS IS FOR NEW DERIVATION. AND, AGAIN, WE THINK IT'S IMPORTANT FOR THE ACTUAL DERIVATION OF LINES, AGAIN, TO BE PAYING ATTENTION TO CONSENT AND ALL THE DETAILS.

SO THE MAJOR THRUST OF THE NEXT REQUIREMENTS DEAL WITH ACTUALLY THE USE OF DERIVED IPSC'S. SO NOW YOU'RE NOT ACTUALLY CREATING THEM, BUT YOU'RE GETTING THEM FROM SOMEPLACE ELSE AND YOU'RE USING THEM IN RESEARCH. AGAIN, IN THE PREVIOUS -- THE CURRENT STANDARDS, IF YOU'RE USING IDENTIFIABLE IPSC, YOU WOULD NOTIFY THE SCRO, AN INSTITUTIONAL OFFICIAL. AND IN THIS CASE WE CURRENTLY REQUIRE THE NOTIFICATION, BUT WE'RE PROPOSING THAT THERE BE EITHER NO NOTIFICATION OF A SCRO REQUIRED OR, AGAIN, INCLUDE -- SORRY. LET ME JUST PAUSE AND LOOK AT THIS FOR A MOMENT.

LET ME MOVE ON TO THE NEXT ONE BECAUSE I BELIEVE I ACTUALLY HAVE TO LOOK AT THE STANDARD. IT'S MISLEADING HERE. I THINK THE CURRENT STANDARD REQUIRES NOTIFICATION OF A SCRO. WHAT WE'RE SAYING IS NOTIFICATION OF A SCRO OR AN INSTITUTIONAL OFFICIAL. IT SAYS NOTIFICATION OF THE SCRO AS AN OPTION. LET ME GO BACK AND LOOK AT THAT. LET ME

JUST MOVE TO THE ACTUAL SLIDE ITSELF.

GIVE ME A MOMENT TO GET MY BRAIN SET HERE. SO THIS IS REALLY THE GIST OF THE RECOMMENDATION, THAT THERE WOULD BE -- SO I'VE DISTINGUISHED BETWEEN DERIVATION AND USE. AND WHAT WE'RE SAYING IS THERE WOULD BE NO NOTIFICATION REQUIREMENT FOR THE USE OF INDUCED PLURIPOTENT CELLS EITHER TO THE SCRO COMMITTEE OR AN INSTITUTIONAL OFFICIAL. AND, AGAIN, THE IDEA HERE IS AT CIRM, IF WE INDICATE TO THE GRANTEE THEY MUST MAKE A NOTIFICATION, THAT NECESSITATES SORT OF AN EXCHANGE BETWEEN CIRM AND THE GRANTEE DOCUMENTING THAT NOTIFICATION. AND THAT'S ACTUALLY A LOT OF WORK NOW THAT IPSC'S ARE REALLY THE MAINSTAY OF A LOT OF THE GRANTS WE'RE FUNDING.

SO WE'RE PROPOSING ELIMINATING THE NOTIFICATION REQUIREMENT, BUT TO KEEP IN MIND THAT CIRM STILL HAS REQUIREMENTS THAT THE MATERIALS YOU USE IN RESEARCH, THERE'S A GENERAL REQUIREMENT THAT THE MATERIALS THAT MEET CERTAIN STANDARDS, EITHER THE GRANTEE CAN DOCUMENT THAT THEY HAVE BEEN OBTAINED WITH PROPER CONSENT, THERE'S NOT BEEN PAYMENTS FOR CELLS, OR IN THE CASE OF ANONYMIZED CELLS, IF THEY'RE DEIDENTIFIED, WHICH WE'LL GET TO. SO THERE'S STILL REQUIREMENTS THAT THE MATERIALS

HAVE BEEN OBTAINED WITH CONSENT AND MEET SORT OF BASIC STANDARDS FOR GOOD PROCUREMENT OF MATERIALS. BUT WHAT WE'RE TRYING TO GET OUT OF THE PROCESS ARE ALL THE LITTLE NOTES GOING BACKWARDS AND FORWARDS ABOUT WHO WAS NOTIFIED WHEN AND THAT TYPE OF INTERACTION. SO THAT'S THE PROPOSAL HERE.

AND, AGAIN, THE COMMENTS WERE MOST NUMEROUS IN TERMS OF THIS AREA. AGAIN, OUR GRANTEES MADE A NUMBER OF COMMENTS. LET ME JUST GO BACK AND LOOK AT THESE COMMENTS.

AGAIN, POINTING OUT THAT WE'VE GOT THE IRB. THE IRB'S ARE ALWAYS GOING TO BE SORT OF A CHECKPOINT WHEN WE'RE USING IDENTIFIABLE MATERIALS. AND THIS WAS A POINT I WAS TRYING TO MAKE EARLIER. AGAIN, IN MOST CASES WE DON'T HAVE A LOT OF WORK INVOLVING IDENTIFIABLE CELLS. SO IT'S NOT -- IT WOULD BE IN A SORT OF CLINICAL CONTEXT WHERE YOU WOULD HAVE ALL THE REVIEWS ANYWAY.

AGAIN, IS THAT CLEAR? I DON'T KNOW IF I SORT OF EXPLAINED THAT AS CLEARLY AS I COULD HAVE.

CHAIRMAN LO: LET ME TRY AND CLARIFY AND THEN ASK A QUESTION. SO ORIGINALLY WHEN IPSC DERIVATION USE WAS FIRST BEING PROPOSED, WE TOOK A CONSERVATIVE ROUTE AND SAID WE WILL ERR ON THE SIDE OF MAKING SURE THAT THERE ARE NO ISSUES IN

DERIVATION OR USE. AS WE GAIN MORE EXPERIENCE, THE QUESTION IS DO WE NEED SCRO INVOLVEMENT AS MUCH AS WE HAVE HAD SINCE THE BEGINNING. SINCE THERE IS AN IRB THAT IS GOING TO LOOK AT ALL WORK WITH IDENTIFIABLE TISSUES, IS THERE SOMETHING SPECIFIC ABOUT AN IPS CELL THAT WOULD MAKE US WANT TO SINGLE THAT OUT FOR ADDITIONAL REVIEW BY A SPECIALLY CONSTITUTED COMMITTEE?

AND SO I THINK THAT'S THE BACKGROUND. WE'RE NOT SORT OF SAYING ANYTHING GOES. WE STILL HAVE THINGS IN PLACE IN TERMS OF IRB REVIEW AS WELL AS ADDITIONAL REQUIREMENTS, THAT LAST BULLET AT THE BOTTOM, FOR USE THAT REQUIRE TRANSPLANTATION INTO NONHUMAN ANIMALS WHICH WOULD NOT NECESSARILY BE COVERED BY THE IRB.

GEOFF, LET ME ASK YOU A QUESTION. SO THE SCIENCE, AGAIN, HAS PROGRESSED, AND NOW PEOPLE ARE TAKING SOMATIC CELLS AND DIRECTLY REPROGRAMMING THEM WITHOUT GOING THROUGH A PLURIPOTENT IPS STAGE. AND ONE OF THE CONCERNS WE HAD RAISED WAS CERTAIN USES OF DERIVATIVES OF PLURIPOTENT CELLS, INCLUDING TRANSPLANTATION OF NEURAL PRECURSOR CELLS, INTO THE BRAINS OF THE NONHUMAN ANIMALS AND ALSO THE DERIVATION OF GAMETES FROM PLURIPOTENT CELLS, WE SINGLED THOSE TWO OUT AS NEEDING SPECIAL

CONSIDERATION.

NOW THAT WE'RE ABLE TO DIRECTLY REPROGRAM SOMATIC CELL NEURAL PRECURSOR CELLS, THE POSSIBILITY IS THERE THAT THIS MAY OCCUR FOR GAMETE PRECURSOR CELLS AS A GRANT TO FUND THIS, BUT ALSO PERHAPS GAMETES. HOW DOES THAT DIRECT USE OF DIRECT REPROGRAMMING OF IDENTIFIABLE SOMATIC CELLS FOR THOSE PURPOSES, HOW DOES THAT FIT IN WITH THESE NEW RECOMMENDATIONS TO REVISE THE REGULATIONS?

DR. LOMAX: WELL, AGAIN, NONE OF THAT HAS CHANGED WHEN I REFERRED TO SORT OF THE GAPS, IF YOU WILL, IN THE IOM. SO WHAT IT IS IS WHEN THE PROTOCOL PROPOSES TO MOVE INTO CERTAIN SENSITIVE USES, THAT NECESSITATES A FULL SCRO REVIEW. IT REQUIRES SOME SORT OF DELIBERATIVE PROCESS. AND THAT WOULD INCLUDE THE NEURAL WORK WITH ANIMALS. SO EVEN IF THE CELL IS NOT PLURIPOTENT, NEUROLOGICAL PRECURSORS GOING INTO THE BRAINS OF ANIMALS, ANY GAMETE WORK, AND WE'VE FRAMED IT TO CAPTURE ALL THE VARIOUS CONTINGENCIES, SO IT'S RESEARCH INVOLVING THE CREATION OR USE OF HUMAN GAMETES. SO IT CAPTURES -- IT WOULD CAPTURE THE REPROGRAMMING EXAMPLE. SO ALL THAT WORK, NONE OF THAT WORK IS CHANGING.

YOU MIGHT VIEW THIS IN TERMS OF JUST

DEVELOPING THE FEEDSTOCKS, THE PLURIPOTENT FEEDSTOCKS FROM SOMATIC CELLS OR SORT OF USING THOSE IN USES OTHER THAN THE ONES YOU DESCRIBE, THAT WE'RE TRYING TO SORT OF, AGAIN, REDUCE THE ADMINISTRATIVE FLOWS AROUND THOSE TYPES OF EXPERIMENTS, BUT NOT CHANGING THE ONES THAT YOU ALL INDICATED HAD TO BE REVIEWED.

DR. ROBERTS: SO IS IT CLEAR, THEN, IN THE WAY THAT THE STANDARDS ARE STRUCTURED THAT THIS PROVISION WOULD NOT APPLY TO THE TRANSPLANTATION AND GAMETE USES THAT BERNIE JUST MENTIONED?

DR. LOMAX: CORRECT. SO ACTUALLY IN THE YELLOW DOCUMENT, YOU WILL SEE IN SECTION 170, A AND B COVER EMBRYO WORK. SO THEY'RE COVERED IN COMPLETELY SEPARATE SECTIONS AS CLEAR CATEGORIES OF WORK THAT DEMAND FULL REVIEW. WE'RE NOW IN SECTION C. THEY SORT OF MOVE IN A SOMEWHAT STEPWISE MANNER DOWN THAT SCALE, WITH C BEING MORE THE DEVELOPMENT OF INDUCED PLURIPOTENT LINES.

DR. ROBERTS: AND THERE'S NO NEED IN C TO BE CLEAR THAT THIS DOES NOT APPLY TO THE USES IN THE PRIOR SECTIONS?

DR. LOMAX: NO. OUR GRANTEES ARE WELL AWARE OF THAT.

DR. ROBERTS: I GUESS I WOULD FEEL MORE

COMFORTABLE ABOUT THIS IF YOU CAN EXPLAIN HOW WE KNOW THAT THE ONLY DIFFERENCE WILL BE SORT OF THIS ADMINISTRATIVE NOTIFICATION. THE ONLY DIFFERENCE IN NOT REQUIRING NOTIFICATION AND THE SPECIAL SCRO REVIEW WILL BE JUST THE ELIMINATION OF THESE SORT OF ADMINISTRATIVE HASSLES THAT HAVE TAKEN TOO MUCH TIME WITHOUT ANY REAL ETHICAL SUBSTANCE TO THEM.

DR. LOMAX: SURE. AGAIN, WE DO A NUMBER OF THINGS WITHIN THE GROUP. SO THE TYPICAL EXAMPLE, A PROPOSAL COMES IN, IT'S REVIEWED BY A SCIENCE OFFICER AS A FIRST SCAN TO MAKE SURE, AGAIN, THERE'S NOTHING IN THERE THAT WOULD NECESSITATE SOME KIND OF DOCUMENTATION, AND THAT'S OUR PREGRANT AWARD REVIEW. IN ADDITION, WE CONTINUE AT A SAMPLE LEVEL TO GO THROUGH AND WE'RE LOOKING AT AN INSTITUTION-BY-INSTITUTION BASIS OF THE PORTFOLIO. THAT'S WHAT I DO IN TERMS OF THE COMPLIANCE PROGRAM, WHICH I'VE DESCRIBED PREVIOUSLY.

SO WHAT WE DO HAVE IS A SERIES OF INDIVIDUALS CHECKING PROTOCOLS AND EVALUATING THEM AGAINST THESE REQUIREMENTS BOTH IN-HOUSE AND GOING BACK TO THEIR INSTITUTIONS. SO I DON'T KNOW IF THAT KIND OF GIVES YOU THE LEVEL OF COMFORT.

DR. ROBERTS: I GUESS WHAT I MEAN IS THAT I THINK THE ARGUMENT IS THAT THIS SHOULD BE CHANGED

BECAUSE THERE'S ENOUGH ETHICAL REVIEW DONE BY THE IRB ANYWAY AND BY THE OTHER STANDARDS FOR ACCEPTABLE RESEARCH MATERIALS. IN OTHER WORDS, I GUESS I'M JUST WONDERING IF THERE'S SOMETHING THAT'S NOT -- SOME TYPE OF REVIEW THAT'S NOT ACHIEVED BY THE IRB REVIEW AND THE OTHER STANDARDS THAT WOULD BE ACHIEVED IF THERE WAS NOTIFICATION. DO YOU SEE WHAT I'M SAYING? TO BE ENSURED THAT WE'RE NOW NOT GOING TO MISS SOMETHING BECAUSE OF DOING AWAY WITH THE NOTIFICATION REQUIREMENT.

DR. LOMAX: I'LL MAKE A QUICK COMMENT, AND THEN IT LOOKS LIKE THE COMMITTEE MEMBERS. ONE OF THE SITUATIONS THAT EXISTS NOW IS A LOT OF INSTITUTIONS HAVE MOVED TO A COMBINED IRB-SCRO MODEL, BUT THAT'S NOT A HUNDRED PERCENT. SO ONE OF THE REALITIES WE'RE DOING WITH THIS, IN A LOT OF CASES, IF IT COMES TO THE IRB, THERE'S SORT OF THE STEM CELL PERSPECTIVE IN THAT DISCUSSION AUTOMATICALLY, BUT THAT'S NOT A HUNDRED PERCENT.

AGAIN, THE BIGGER DILEMMA WE FACE IS WHEN THERE'S NOT THE SCRO CAPACITY. THERE'S AN ESTABLISHED IRB, AND WHAT DOES THE INSTITUTION DO? TYPICALLY WHAT THEY'LL DO IS -- I CAN'T SAY IT HAPPENS IN ALL THE CASES, BUT THEY'LL CONTACT ME. WE UNDERSTAND THERE'S THIS REQUIREMENT. SO, AGAIN,

THERE'S THIS -- FROM THE SORT OF VANTAGE POINT THAT I HAVE, A LOT OF THAT GETS COVERED BY ESTABLISHED INSTITUTIONS. SOME OF THE NEWER FOLKS ARE ENGAGED AND MAKING SURE THAT THOSE THINGS ARE COVERED, BUT I CAN'T SAY WITH ABSOLUTE HUNDRED PERCENT CERTAINTY IN EVERY CASE WE GET THAT. THAT'S, I THINK, THE CHALLENGE WE HAVE IN REGULATIONS IS HOW MUCH ASSURANCE DO WE NEED AND HOW DO WE DO THAT.

DR. ROBERTS: I'D LOVE TO HEAR MORE DISCUSSION ABOUT THAT AND PEOPLE'S VIEWS ON THAT.

CHAIRMAN LO: I WANT TO GET PAT TAYLOR ON THIS. I DO WANT TO SAY THAT AS A NONLAWYER TRYING TO READ THROUGH REGULATIONS, I ALWAYS HAVE TO GO BACK AND LOOK UP COVERED STEM CELL LINES. SO 100070 (C) AND (D) REALLY HAVE TO DO WITH THE CREATION OR USE OF A COVERED STEM CELL LINE. AND A COVERED STEM CELL LINE, BY OUR DEFINITION, IS A PLURIPOTENT STEM CELL LINE.

SO MY CONCERN IS THAT IF SOMEONE SAYS I'M NOT GOING TO CREATE A PLURIPOTENT STEM CELL LINE, I'M JUST GOING TO TAKE A SOMATIC CELL AND TURN IT INTO A GAMETE PRECURSOR OR TRY AND TURN IT INTO A GAMETE, AGAIN, THIS IS MY NAIVE READING.

DR. ROBERTS: I'M A LAWYER. I SHOULD BE ABLE TO READ IT.

CHAIRMAN LO: IT SEEMS LIKE IT DOESN'T -- THERE'S NOTHING IN THIS 100070 SECTION THAT APPLIES TO THAT DIRECT REPROGRAMMING TO GAMETE PRECURSORS OR GAMETES; WHEREAS, I THINK OUR INTUITION WOULD BE WE'D WANT SOME OVERSIGHT. NOW, IF IT'S IDENTIFIABLE, IT GOES BEFORE AN IRB. BUT IF IT'S NOT IDENTIFIABLE, WHICH IS YOUR NEXT SECTION, THE D SECTION, THAT'S NOT HUMAN SUBJECTS RESEARCH, SO IT'S OUTSIDE THE PURVIEW OF THE IRB.

SO I JUST WANTED TO SET THAT UP FOR YOU, DOROTHY, AND FOR PAT IN PARTICULAR BECAUSE I KNOW, PAT, YOU DO THIS DAY IN AND DAY OUT.

DR. PAT TAYLOR: I THINK THIS DOES REALLY SET IT OUT VERY NICELY. THERE ARE ALWAYS TWO BASES FOR SCRO REVIEW. ONE, OF COURSE, WAS THE PROVENANCE OF EMBRYONIC STEM CELLS. AND THE OTHER WAS PECULIAR USES, AS YOU POINT OUT, BERNIE, HAVE EVOLVED OVER TIME. SO IF I UNDERSTAND THIS CORRECTLY, THE THOUGHT IS THAT, LOOK, IN THE CASE OF IPS CELLS, WHICH IS THE SAME DERIVATION ISSUES, WE'RE OBVIOUSLY NOT GOING TO REQUIRE A SCRO REVIEW. BUT THE GENERAL PRINCIPLE SEEMS TO BE THAT USES THAT WOULD OTHERWISE REQUIRE SPECIALIZED REVIEW OUGHT PERHAPS TO CONFORM, BUT I THINK THAT'S KIND OF A MOVING TARGET.

SO INSTITUTIONS ARE OF MANY MINDS ON

WHETHER IT'S, FOR EXAMPLE, DEIDENTIFIED CELLS OUGHT TO BE -- USES TO CREATE ORGANS, FOR EXAMPLE, OUGHT TO BE SUBMITTED TO SPECIALIZED REVIEW. I THINK YOU'RE RIGHT, BERNIE, THOUGH, THAT THE PARTICULAR SECTIONS ARE SOMEWHAT DATED. PLURIPOTENCY IS OBVIOUSLY A BIG PROBLEM WITH GAMETES, EMBRYOID BODIES. THERE'S A MOVING TARGET.

A SIMPLE STANDARD MIGHT JUST BE TO SAY THAT THE CIRCUMSTANCES WHERE THERE'S SCRO REVIEW FOR EMBRYONIC STEM CELL USES OUGHT TO MATCH IPS USES AS THEY EVOLVE.

DR. LOMAX: THAT WAS A LITTLE BIT OF OUR STARTING POINT WHEN WE STARTED WITH DERIVATION, AND WE'RE NOW TRYING TO SORT OF MOVE THAT TO THE DOWNSTREAM USES.

DENISE, CAN I JUST CALL YOU OUT HERE? I WOULD LIKE TO ADDRESS BERNIE'S POINT HERE. I KNOW WE'VE DONE A LOT OF OUTREACH. I THINK IT'S EXCEPTIONALLY CLEAR TO THOSE IN THE SORT OF OVERSIGHT WORLD THAT ANY APPLICATION OF MATERIALS -- ANY PROTOCOL INTENDING TO DERIVE OR OTHERWISE DEVELOP GAMETES WOULD BE SUBJECT TO SCRO REVIEW. I'M JUST CURIOUS --

CHAIRMAN LO: BEFORE YOU GO THERE, GEOFF. PAT, I THINK YOU'RE RIGHT. IT'S A MOVING TARGET AND

WE NEED TO KEEP UP WITH THE CHANGING SCIENCE. OUR PROBLEM IS THAT AS A REGULATORY BODY WE HAVE TO GIVE PEOPLE CLEAR NOTICE OF WHAT'S ON THE RIGHT SIDE OF THE BRIGHT LINE AND WHAT'S ON THE OTHER SIDE.

DR. PAT TAYLOR: YOU'RE ABSOLUTELY RIGHT, BERNIE.

CHAIRMAN LO: I DON'T KNOW IF WE ACTUALLY HAVE TO PROVIDE THE SPECIFIC THESE ARE THE TYPES OF THINGS THAT YOU NEED SOME SORT OF SPECIAL REVIEW AND YOU CAN BE FLEXIBLE.

I GUESS MY OTHER QUESTION IS THAT I WOULD AGAIN DEFER TO THOSE OF YOU WHO ARE MUCH MORE EXPERIENCED WITH REGULATORY ISSUES. BUT IT STRIKES ME WE HAVE TO MAKE SURE THAT THE CLEAR LANGUAGE OF OUR REGULATIONS IS WHAT WE WANT IT TO BE. AND TO SAY THAT WHILE PEOPLE UNDERSTAND IT TO INCLUDE THIS AND THAT IS, I THINK, NOT QUITE THE SAME AS MAKING SURE THAT THE LANGUAGE IN THE REGULATIONS ITSELF MAKES IT CLEAR THAT ON CERTAIN THINGS WE GIVE FLEXIBILITY, ON CERTAIN THINGS WE WANT SPECIAL REVIEW. WE MAY CHOOSE TO SAY YOU CAN DECIDE WHAT KIND OF REVIEW, MAYBE DECIDE YOUR IRB IS FINE.

SO, AGAIN, THESE ARE ISSUES WHERE I REALLY WANT TO DEFER TO THE EXPERTISE OF THOSE OF YOU WHO REALLY THOUGHT LONG AND HARD ABOUT THESE ISSUES. I

JUST WANTED TO SET THAT UP BEFORE BECAUSE IT'S A DIFFERENT QUESTION THAN WHAT WE'RE ASKING DENISE AS SOMEONE WHO'S REALLY, AND I'LL VOUCH FOR HER, SHE'S TERRIFIC. SHE REALLY UNDERSTANDS THIS, KNOWS WHAT PEOPLE IN SCRO'S ARE THINKING.

DR. PAT TAYLOR: SO HISTORICALLY THE NAS GAVE US THE GIFT, OF COURSE, OF A COUPLE SPECIFIC USES. AND SINCE MOST OF THE FOCUS OF THE NAS STANDARDS WAS ON PROVENANCE, IT SEEMS A MINOR THING. BUT THEN RAPIDLY THERE GOT TO BE INTERESTING CHANGES.

SO WHEN UNIVERSITIES AND HOSPITALS STARTED THINKING ABOUT MAYBE MAKING THE LONGER CHANGES, PEOPLE STARTED TO SAY, WAIT, WHAT'S HAPPENING HERE? THERE'S THIS SCRO AND IT'S GOING TO BE REVIEWING ALL KINDS OF BASIC SCIENCE RESEARCH THAT'S GOING ON IN ALL KINDS OF INTERESTING AREAS. IT LOOKS LIKE AN IMPOSSIBLE TASK FOR ESCRO'S AND EVEN WITHIN INSTITUTIONS UNDEFINABLE.

SO I THINK THERE IS NO CLEAR STANDARD EVEN WITHIN INSTITUTIONS. A SCRO MIGHT NOT EVEN BE THE RIGHT BODY TO DO IT. NORMALLY IT WOULD BE AN IRB BECAUSE A LOT OF THESE ARE BASIC SCIENCE FUNCTIONS BECAUSE THEY'RE JUST NOT IRB FUNCTIONS. I THINK ONE OUGHT TO BE WARY OF INCLUDING A BIG, LONG LIST

BECAUSE INSTITUTIONS WILL FIND THEIR ADMINISTRATION'S REAR END.

DR. BOTKIN: I HAD A QUESTION THAT I WANTED TO THROW IN. WHAT DO WE MEAN BY NOTIFICATION, OR WHAT DOES THIS POLICY MEAN BY NOTIFICATION? IN OTHER CONTEXT, IRB'S, FOR EXAMPLE, THEY HAVE TO APPROVE THINGS THAT ARE EXEMPT FROM THE IRB BECAUSE YOU WANT TO MAKE SURE IT FITS WITHIN THE CATEGORY THAT YOU ARE MAKING SURE IT FITS IN. MAYBE THERE'S ENOUGH OVERSIGHT BY THE FUNDER HERE TO SAY WE KNOW WHAT CATEGORIES WE'RE TALKING ABOUT. A LOT OF TIMES, IF THE INVESTIGATOR IS MAKING THE CALL ABOUT WHICH CATEGORY IT'S IN, THEY MAY BE WRONG.

SO DOES NOTIFICATION SIMPLY MEAN INCLUDING ON A DATABASE, OR IS THERE SOME IMPLICATION THAT THE INSTITUTION IS SAYING, YES, WE AGREE. IT'S IN THIS CATEGORY. GO FORWARD.

DR. LOMAX: AGAIN, THIS WILL VARY ON AN INSTITUTION-BY-INSTITUTION BASIS, BUT TYPICALLY THE MODEL THAT WE LIKE TO SEE AND WHAT WE DO SEE IS IT'S A COMMUNICATION TO THE COMMITTEE FROM THE INVESTIGATOR SAYING I HAVE A CIRM-FUNDED PROTOCOL WHERE WE WILL BE UTILIZING SOMATIC CELLS TO CREATE IPS CELLS, AND THEY ARE IDENTIFIABLE UNDER COMMON RULE. AGAIN, THE INTENT THERE IT'S A NOTIFICATION,

IT'S A MESSAGE TO THE OVERSIGHT COMMITTEE, SO IT GIVES THEM THE OPPORTUNITY TO SAY, OKAY, SAY, THEIR MATERIALS ARE COMING FROM AN INTERNAL BANK WITHIN THE INSTITUTION. HEY, THEY'RE GOING TO BE DEVELOPING MATERIALS WITH A CIRM GRANT. THE BANK'S COMING UP IN THE FUTURE, WHICH YOU WILL HEAR ABOUT THIS AFTERNOON. WE KNOW WHAT'S REALLY IMPORTANT IS THAT THE CONSENT PROTOCOL IS OF A CERTAIN LEVEL THAT THEY WILL HAVE OPTIMAL UTILITY FOR BANKING AND RESEARCH PURPOSES BASED ON THE CIRM REQUIREMENTS. SO REALLY IT'S A MESSAGE TO GET PEOPLE TO THINK ABOUT CONSENT.

AGAIN, THE CONCEPT HERE IS THAT WE STILL WANT THE MESSAGE, BUT YOU DON'T NECESSARILY -- THE SCRO DOESN'T NECESSARILY NEED TO BE THE MESSENGER. THE IRB COULD STILL THINK ABOUT THAT IN THE INSTITUTION IF, SAY, AN OFFICIAL WHO'S INTIMATE WITH OUR CONSENT REQUIREMENTS GETS THAT NOTIFICATION, THEY COULD GO TO THE IRB AND SAY WHAT'S REALLY IMPORTANT HERE FROM A CIRM PERSPECTIVE IS THE CONSENT. AND IF WE HAVE AN OPPORTUNITY TO THINK ABOUT THAT IN THIS REVIEW, THAT'S WHAT WE NEED TO DO.

DOES THAT MAKE SENSE? IT'S THE CONNECTION BETWEEN THE MATERIALS, OUR CONSENT REQUIREMENTS, AND

COMING OUT WITH AN IPS CELL AT THE OTHER END THAT IS ROBUST FOR RESEARCH PURPOSES. THAT'S THE INTENT OF THE POLICY.

DR. LOCKHART: IF I COULD JUST ADD SOMETHING KIND OF RELATED. AS WE'RE LOOKING AT THIS, I'M THINKING MOSTLY ABOUT KIND OF BURDEN, ADMINISTRATIVE BURDEN, VERSUS BENEFIT. SO WOULD WE BE LOSING ANYTHING BY LOSS OF NOTIFICATION? PARTICULARLY, DO YOU THINK THERE'S A BENEFIT TO THE SCRO IN KNOWING THAT SOME OF THESE CELL LINES, SOME OF THESE IDENTIFIABLE CELL LINES ARE IN USE? I'M ALSO THINKING ABOUT INSTITUTIONAL COORDINATION. SO NOW IF THAT NOTIFICATION IS GOING TO THE IRB, AND INSTITUTIONS WHERE THOSE ARE SEPARATE PROCESSES IN IRB AND A SCRO, IS ANYTHING LOST BY THE SCRO POSSIBLY NOT BEING AWARE THAT THESE LINES ARE IN USE IF THEY LACK THE NOTIFICATION?

AND AS WELL, WOULD A PROGRAM BASICALLY AT CIRM BE LOSING ANYTHING IF THIS NOTIFICATION IS LOST IN TERMS OF TRACKING, MONITORING THOSE KINDS OF THINGS?

DR. LOMAX: MY SENSE FROM TALKING TO OUR GRANTEES IS NO BECAUSE THOSE INSTITUTIONS THAT HAVE -- NOW, AGAIN, WE'RE TALKING ABOUT IDENTIFIABLE CELLS AND DERIVING. THOSE INSTITUTIONS ARE STILL

GOING TO GO TO THEIR SCRO FOR CIRM WORK. THEY'VE ESTABLISHED THOSE. WHAT IT'S DOING IF FOR THOSE INSTITUTIONS THAT ARE NEVER GOING TO HAVE A SCRO, THIS GIVES THEM ANOTHER AVENUE TO KIND OF INTERACT WITH THE IRB. IT'S THE INSTITUTIONAL OFFICIAL.

SO IN TERMS OF YOUR QUESTION, I WOULD EMPHATICALLY SAY NO BECAUSE I DON'T THINK IT'S GOING TO CHANGE THINGS FOR OUR EXISTING GRANTEES THAT HAVE THIS INFRASTRUCTURE IN PLACE. ALL WE'RE DOING IS ADDING ANOTHER PATHWAY FOR GRANTEES THAT MAY NEVER HAVE A SCRO.

THE OTHER PROBLEM WE'VE RUN INTO IS THAT THERE WAS AT A TIME THE ABILITY TO GO OUT TO A THIRD-PARTY OVERSIGHT COMMITTEE IN CALIFORNIA AND GET THOSE SERVICES. THAT OPTION NO LONGER EXISTS. AGAIN, WE'RE HITTING A BOTTLENECK AT THE SCRO COMMITTEE ACCESS POINT, AND THAT IS ACTUALLY BECOMING A REAL PROBLEM FOR THE RESEARCH COMMUNITY.

DR. PRIETO: WITH SOME OF THESE, THE THIRD, FOURTH, AND THE LAST ONE, I'M A LITTLE JUST UNCOMFORTABLE WITH THE GENERAL IDEA OF OFFERING NO NOTIFICATION OF ANYONE AS AN OPTION JUST ON PRINCIPLE. I WONDER HOW MUCH OF A BURDEN IS IT TO NOTIFY AN INSTITUTIONAL OFFICIAL THAT YOU'RE DOING SOMETHING? IS THAT A SIGNIFICANT BURDEN FOR THE

RESEARCHERS?

DR. LOMAX: CONCEPTUALLY TO SAY THE COMMUNICATION IS BURDENSOME, PEOPLE VARY. IT CAN BE FAIRLY SIMPLE. IT COULD BE AS EASY AS A SHORT E-MAIL, AND THAT DOESN'T SOUND TERRIBLY BURDENSOME. PART OF THE CHALLENGE IS AT OUR END. WE'RE VERY COMMITTED TO THE FACT THAT IF WE HAVE A REQUIREMENT IN PLACE, WE NEED TO THEN MAKE A POSITIVE VERIFICATION THAT THAT REQUIREMENT HAS BEEN MET BECAUSE IT'S PART OF OUR STANDARDS. WE TAKE THEM VERY SERIOUSLY. SO ESPECIALLY WHEN WE GET DOWN INTO SORT OF THE DEIDENTIFIED MATERIALS, THAT'S A LOT OF -- THERE'S A LOT OF WORK GOING ON IN THAT AREA.

AND I GUESS MY QUESTION WOULD BE IS THERE -- WE'VE TO DATE REALLY NOT SEEN ANY PROBLEMS FROM A KIND OF OVERSIGHT OR ETHICS PERSPECTIVE, BUT WE DO SPEND A LOT OF TIME GOING BACK AND VERIFYING NOTIFICATION. SO IT IS ADMINISTRATIVELY A LOT OF WORK. AND IF THE VIEW IS THAT THAT'S TIME WELL SPENT, THEN WE KEEP DOING THAT WORK.

I THINK IT'S THE IMPLEMENTATION SIDE THAT BECOMES QUITE CHALLENGING HERE.

DR. PRIETO: WOULD THERE BE A WAY OF REDUCING THAT ADMINISTRATIVE BURDEN AT OUR END AND AT THE REPORTING END JUST BY REQUIRING THAT THE

INSTITUTION CERTIFY, MAKE A STATEMENT THAT THEY HAVE DONE WHAT WE EXPECT THEM TO DO? I THINK TO PUT A LEVEL OF RESPONSIBILITY THERE. JUST THE FACT THAT THERE HAVE NOT BEEN PROBLEMS DOESN'T SAY TO ME THAT THERE WILL NOT BE ETHICAL PROBLEMS.

DR. LOMAX: AGAIN, IF MY COLLEAGUES HAVE VIEWS HERE. THE WAY WE'VE ALWAYS PROCEEDED IN THE CONTEXT OF EVALUATING GRANT AWARDS THROUGH THE LENS OF ALL OUR POLICIES, MEDICAL, ETHICAL, AND SCIENTIFIC, IS ON A GRANT-BY-GRANT BASIS EXCEPT FOR CERTAIN, SAY, BROADER STATEMENTS THAT APPLY TO THE INSTITUTION. BECAUSE ALL THESE REQUIREMENTS ARE EVALUATED ON A PROTOCOL-BY-PROTOCOL, GRANT-BY-GRANT BASIS, I'M NOT SURE -- I'M NOT TERRIBLY COMFORTABLE WITH THE IDEA THAT THERE WOULD BE SOME KIND OF BLANKET THAT WOULD SORT OF CHANGE THAT. AGAIN, WE DO STILL SPEND A LOT OF TIME LOOKING AT INDIVIDUAL AWARDS FOR ALL THESE DETAILS, AND I THINK THAT'S AN IMPORTANT PART OF OUR JOB. I'M JUST NOT SURE HOW TO OPERATIONALIZE SOMETHING THAT WOULD BE SORT OF BROADER IF THAT WAS YOUR POINT THERE.

DR. PRIETO: I DON'T KNOW THAT IT WOULD HAVE TO BE EVEN NECESSARILY SEPARATE FROM THAT PROCESS, BUT PERHAPS AS PART OF THAT IT WOULD BE EXPECTED THAT GRANTEES CERTIFY THAT THEY HAVE

NOTIFIED THEIR INSTITUTIONAL OFFICIAL THAT THEY ARE DOING X, IN THIS CASE USING THESE CELL LINES, AND THAT THEY MEET THE STANDARDS.

DR. LOMAX: AGAIN, THE WAY WE'VE TYPICALLY DONE THAT IS ACTUALLY GET VERIFICATION, SEE THE NOTIFICATION. SO LET ME TAKE THAT BACK TO STAFF AND SEE IF THERE'S ALTERNATIVE WAYS OF MAKING THAT DETERMINATION. AT THE MOMENT IT'S NOT OCCURRING TO ME HOW EXACTLY WE'D DO THAT.

CHAIRMAN LO: LET ME MAKE A SUGGESTION THAT TRIES TO BRING TOGETHER A LOT OF THE THOUGHTS I'VE BEEN HEARING. SO I WANT TO SORT OF TIE TOGETHER WHAT A NUMBER OF YOU HAVE BEEN SAYING.

SO, PAT, YOU REALLY UNDERLINED THE IMPORTANCE OF LOOKING FOR SENSITIVE USES OF STEM CELLS THAT WOULD REQUIRE A GREATER LEVEL OF SCRUTINY THAN JUST BASIC SCIENCE MANIPULATION IN THE LABORATORY TO LOOK AT RECEPTORS AND GENE EXPRESSION AND THINGS. AND, NICOLE, YOU POINTED OUT THERE'S REALLY A BALANCE THAT WE NEED TO SORT OF TAKE INTO ACCOUNT OF THE BENEFITS OF WHATEVER REGULATIONS WE HAVE VERSUS THEIR BURDENS.

IT STRIKES ME THAT ONE OF THE THINGS WE HAVE TRIED TO DO IN THE PAST IS TO SAY LET'S LOOK AT THE THINGS THAT WE ARE CONCERNED MIGHT HAVE AN

UNACCEPTABLE RISK OF PROBLEMS AND TO REALLY FOCUS OUR SCRUTINY OR OVERSIGHT ON THAT, AND THEN TO SORT OF START TO LET GO OF THINGS WHERE THE EXPERIENCE HAS SHOWN THAT THE RESEARCH IS REALLY NOT SENSITIVE, NOT CONTROVERSIAL, DOESN'T RAISE ISSUES THAT AREN'T CLEARLY COVERED, AND TO NOT THEN REQUIRE REGULATIONS WHICH, AS GEOFF POINTED OUT, DO IMPOSE SOME LEVEL OF ADMINISTRATIVE BURDEN WHICH WE COULD TRY AND MINIMIZE. BUT IN POINT OF FACT, ALL OF US FROM INSTITUTIONS KNOW THAT IF A REGULATION'S IN PLACE, IT TENDS TO SAY LET'S MAKE SURE WE DOCUMENT IT AND CHECK IT AND THINGS.

SO I GUESS I'M SORT OF TRYING TO POSE THE QUESTION OF WHETHER WE CAN -- AGAIN, THIS IS ONE OF THE CRITICISMS THAT THE COMMON RULE FACES, THAT YOU DOCUMENT SO MANY THINGS LIKE WE RENEWED OUR RESEARCH PROTOCOL EVEN THOUGH WE'RE JUST IN THE WRITING UP THE DATA PHASE AND WE'RE NOT INTERACTING WITH SUBJECTS AT ALL, AND IT'S ALL DEIDENTIFIED DATA AT THIS POINT, YOU STILL HAVE TO RENEW IT AND DOCUMENT YOU RENEWED IT AND STUFF. SO I'M JUST TRYING TO STRUGGLE WITH CAN WE MAKE SURE THAT WE'RE CLEAR ON THAT THERE IS SOME ACCEPTABLE REVIEW OF THINGS THAT WE THINK ARE SENSITIVE OR OF CONCERN, COUPLE THAT WITH SORT OF SAYING AND THERE ARE ALL THESE OTHER

THINGS WHICH HAVE FALLEN UNDER THE AMBIT OF NOTIFICATION THAT MAYBE NOW WE DON'T THINK, WITH MORE EXPERIENCE, WE NEED TO.

I GUESS THE QUESTION I ORIGINALLY POSED, GEOFF, AND, SCOTT, I GUESS YOU'VE BEEN INVOLVED, IS IS IT REALLY CLEAR FROM WHAT WE'VE DRAFTED THAT SOME OF THE THINGS THAT WE'RE CONCERNED ABOUT STILL REQUIRE SOME SORT OF OVERSIGHT THAT WE'RE COMFORTABLE WITH? I THINK THAT'S THE BALANCE.

THEN IF THAT'S CLEAR, I THINK NOTIFICATION OF ALL THESE BASIC SCIENCE DEIDENTIFIED IN VITRO ONLY, NOT DERIVING ANYTHING THAT'S A PRECURSOR TO A GAMETE. AND, PAT, YOU COMPLICATED IT, OF COURSE, BY SAYING, WELL, SUPPOSE YOU DERIVE AN ORGAN. YOU'RE NOT JUST DOING LIVER CELLS. YOU'RE ACTUALLY PUTTING ON SCAFFOLDING AND DERIVING AN ORGAN FOR TRANSPLANTATION, OR A HEART WHICH HAS EVEN MORE SYMBOLIC VALUE IN THE CULTURE.

DR. PAT TAYLOR: THOSE, OF COURSE, DO NOT TRADITIONALLY REQUIRE SPECIAL REVIEW.

CHAIRMAN LO: IT'S JUST A HUNK OF DEIDENTIFIED TISSUE THAT WE'RE MANIPULATING IN A LAB. WHEN IT GOES INTO AN ANIMAL, THE IACUC DEALS WITH ANIMAL SAFETY AS THEIR AMBIT. THAT WAS ONE OF THE REASONS NAS THOUGHT ABOUT, WELL, COULD A SCRO

THINK MORE BROADLY ABOUT THESE ISSUES THAT HAVE TO DO WITH ALLEGED VIOLATIONS OF BOUNDARIES BETWEEN HUMANS AND ANIMALS AND SYMBOLIC TRANSGRESSIONS. IT LEADS US INTO A MURKY AREA, BUT AT LEAST TO THE EXTENT THAT WE KNOW THERE ARE THINGS THAT ARE REALLY GOING TO RAISE SENSITIVITIES, ARE WE COMFORTABLE WE'VE HANDLED THEM APPROPRIATELY?

AND, AGAIN, FOR THOSE OF US WHO AREN'T USED TO WRITING REGULATIONS AND INTERPRETING THEM, I JUST ALWAYS LIKE TO LOOK FOR LOOPHOLES, THAT IF I CAN SORT OF SAY I READ THIS AND IT DOESN'T APPEAR TO ME THIS NEEDS TO GO TO ANYBODY'S REVIEW, LET'S JUST GO SAIL ON AND DO IT.

DR. WAGNER: I THINK BASED ON JUST THE VERY LAST COMMENTS YOU MADE, TO ME I WOULD STILL FEEL COMPELLED TO HAVE A HIGHER LEVEL OVERSIGHT OF IDENTIFIABLE IPS CELLS. THE FIELD IS MOVING SO RAPIDLY, AS YOU'VE ALSO POINTED OUT, I THINK IT'S BEYOND WHAT MOST IRB'S ARE CAPABLE OF MONITORING. AND ITS IMPACT ON THE CONSENT FORM IS ALSO EVOLVING AS NEW TECHNOLOGIES, NEW METHODOLOGIES EVOLVE.

FOR THE VERY REASON WHY A SCRO IS DEVELOPED FOR ES CELL DERIVATIONS, WHICH NO ONE IS CONTESTING, IT SOUNDS LIKE, THAT THAT CONTINUE, WE'RE DOING THAT IN A WAY BECAUSE WE'RE TRYING TO

ENSURE OR ASSURE SOCIETY THAT THESE CELLS WHICH HAVE TREMENDOUS POTENTIAL, AND IT'S NOT JUST WHERE THEY'RE DERIVED FROM, BUT IT'S HOW THESE CELLS ARE BEING TESTED AND UTILIZED AND THE CONSENT PROCESSES OF WHAT YOU COULD DO WITH THOSE CELLS, I THINK NEEDS TO BE VERIFIED. AND I JUST THINK IT'S PREMATURE THAT YOU LEAVE IT TO AN IRB AT THIS PARTICULAR POINT, PARTICULARLY IF IT'S AN IDENTIFIABLE CELL LINE.

IT'S ALSO THE GENETIC TESTING THAT'S DONE, BUT, OF COURSE, AN IRB COULD EVALUATE THAT ASPECT OF THINGS, BUT IT IS A PRETTY COMPLEX SET OF ISSUES THAT ARE FAIRLY UNIQUE TO IPS, I THINK. SO I THINK MY FEELING STILL IS I'VE NOT HEARD ANYTHING THAT MAKES ME FEEL SECURE IN THE DERIVATION OF IDENTIFIABLE FROM THE SOMATIC CELL THAT IT SHOULD BE REMOVED FROM A SCRO.

I THINK THAT, ALSO, I WOULD LIKE TO ALSO POINT OUT -- MAYBE WE SHOULD GET AWAY FROM THE TERM "IPS." MAYBE IT JUST NEEDS TO BE A REPROGRAMMED CELL RATHER THAN JUST SAYING IPS SO THERE'S NOT A LOOPHOLE THAT PEOPLE FEEL LIKE YOU CAN, WELL, THIS IS NOT REALLY IPS, THEREFORE, WE DON'T NEED TO NOTIFY ANYONE.

I WANT TO GET BACK TO ALSO THE USE OF

IDENTIFIABLE CELLS AS WELL AND THE DERIVATION OF DEIDENTIFIED CELLS BECAUSE IT'S NOT QUITE SO STRAIGHTFORWARD, I THINK, AS PEOPLE MIGHT THINK. WHEN WE TALK ABOUT DEIDENTIFICATION, AS A PERSON WHO TAKES CARE OF PATIENTS WITH GENETIC DISEASES, I GET THE TISSUE, I KNOW THE PATIENT. I CAN ASSIGN IT A NUMBER, BUT I STILL KNOW EVEN THOUGH, QUOTE, IT'S DEIDENTIFIED. SO IT'S NOT SO EASY TO SAY WHAT IS DEIDENTIFIED BECAUSE I CAN TELL BY THE MUTATION. I CAN TELL BY THE DATE IT WAS COLLECTED. SO DEIDENTIFIED HAS A DIFFERENT -- IS NOT QUITE SO EASY IN THIS PARTICULAR SETTING.

DR. LOMAX: BERNIE, COULD I JUST ADD THE CLARIFICATION BECAUSE THE SLIDE WAS INCORRECT BEFORE AND I'VE NOW CORRECTED IT. ACTUALLY WE DID HEAR SOME COMMENTS IN THE ADVANCE COMMENTS ALONG THE LINES WHAT YOU WERE SAYING. THE ISSUE WAS IDENTIFIABLE INDUCED PLURIPOTENT CELLS CURRENTLY REQUIRE NOTIFICATION OF THE SCRO. AND THEN WE DID A TWO-PART OPTION, EITHER NOTIFICATION OR TO INCLUDE THE INSTITUTIONAL OFFICIAL AS AN OPTION BECAUSE WE DID HEAR COMMENTS CONSISTENT WITH WHAT YOU WERE SAYING, THAT WE DO SEE SOME VALUE ON THE IDENTIFIABLE CELLS OF NOT JUST RELYING ON THE IRB. SO IT CAME ABOUT 50-50.

SO WE SORT OF THOUGHT, WELL, OKAY, LET'S JUST PUT BOTH OPTIONS ON THE TABLE, NO NOTIFICATION OR CONTINUE NOTIFICATION, BUT EXPAND IT TO, AGAIN, ALLOW THAT OPTION. I MUST SAY THE RESPONSIBLE INSTITUTIONAL OFFICIAL OPTION IS ONE WHERE, AGAIN, IT TENDS TO BE A VERY SMALL COMPANY, BUT THERE'S SOMEONE WHOSE JOB IT IS TO REALLY BE ON THE SORT OF COMPLIANCE SIDE OF THINGS. AND THE EXPERIENCES I'VE HAD WITH THOSE PEOPLE IS THEY'RE VERY ENGAGED IN TERMS OF THE REQUIREMENTS AND ARE TRYING TO IMPLEMENT THE REGULATIONS AS THEY'RE INTENDED. SO THESE ARE VERY RIGOROUS.

DR. WAGNER: AT LEAST IF YOU GO BY WHAT YOUR PROPOSAL IS, NO. 1, NO ONE IS TALKING ABOUT. NO. 2, PERSONALLY I WOULDN'T LEAVE IT TO AN INSTITUTIONAL OFFICIAL FOR THAT SPECIFIC. I WOULD STILL HAVE NOTIFICATION OF A SCRO BECAUSE THE FACT THAT THERE'S SO MANY DIFFERENT THINGS THAT ARE EVOLVING IN THAT, THAT YOU NEED SOMEONE -- IT'S COMPLICATED TO BE LEFT TO ONE INDIVIDUAL. HAVING BEEN ON THE IRB, NOT ON A SCRO SPECIFICALLY, IT OFTENTIMES REQUIRES DISCUSSION BECAUSE THE FIELD IS CHANGING SO RAPIDLY. SO MAYBE FIVE YEARS FROM NOW THAT MIGHT BE DIFFERENT.

DR. LOMAX: THAT CAME OUT. AND, AGAIN,

THERE MAY BE RESEARCHERS FOR WHICH IT'S VERY DIFFICULT TO ACCESS THE SCRO, AND THEY'RE IN A VERY DIFFICULT SITUATION, AND THAT'S SORT OF THE CHALLENGE THAT WE'RE BRINGING TO YOU.

DR. PAT TAYLOR: BERNIE, I DO THINK THAT YOUR FORMULATION OF LOOKING AT WHAT EXPERIENCE HAS TAUGHT IS VERY HELPFUL. SO I DO WANT TO SPEAK IN FAVOR OF THE IDEA OF ELIMINATING MOST NOTIFICATIONS OF IPS USES. AND THE REASON FOR THAT IS TWOFOLD. ONE IS THAT IPS CELLS ARE USED IN THE CONTEXT OF EXPERIMENTAL PURPOSES THAT OFTEN HISTORICALLY WOULD HAVE BEEN FULFILLED USING CONVENTIONAL CELLS. SO THERE'S NOTHING SPECIAL, IN A SENSE, ABOUT THEIR PLURIPOTENCY THAT IS RELATED TO THE RISKS CREATED OR THE REQUIRED REVIEW. OF COURSE, YOU'RE NOT PROHIBITING THAT KIND OF REVIEW. IT'S JUST AS FAR AS CIRM IS CONCERNED WITH ITS PARTICULAR STEM CELL INTERESTS, THERE'S NO REQUIREMENT THAT MOST OF THOSE KINDS OF EXPERIMENTS GET SCRO REVIEW. THERE SHOULDN'T BE SCRO REVIEW BECAUSE, AGAIN, THEY'RE SORT OF CONVENTIONAL USES RAISING NO PARTICULAR RISKS.

AND THERE'S ALSO NOTHING IN THE QUALIFICATIONS OF A SCRO THAT PARTICULARLY QUALIFIES THEM TO DECIDE WHETHER OR NOT CREATION OF A LIVER

SCAFFOLD FROM IPS CELLS VERSUS SOMETHING ELSE IS APPROPRIATE. THERE'S REALLY NOTHING ABOUT A SCRO THAT MAKES IT SUITABLE FOR THAT. THAT'S ONE THING.

I THINK IF WE LOOK AT AREAS THAT HAVE ACTUALLY CAUSED SOME TROUBLE, AND YOU WANT TO BE MODEST, I THINK THERE ACTUALLY IS A FAIRLY DEFINABLE LIST. USE OF IPS CELLS TO CREATE EMBRYOS, TO CREATE GAMETES, TO MAKE GERM LINE MODIFICATIONS, NEURAL MODIFICATIONS, CHIMERAS, IT'S A FAIRLY RATIONAL LIST OF THE REALITIES OF OTHER PLACES WHERE IT IS REQUIRED AND SCRO'S ARE QUALIFIED TO PROVIDE IT.

SO YOU COULD MAKE THAT MINIMAL CORE. I SUPPOSE ONE MIGHT ASK INSTITUTIONS HOW THEY'RE ACTUALLY ADDRESSING NOVEL RISKS JUST TO SEE WHAT THEY'RE DOING. BUT THAT KIND OF CORE, WHICH IS PRETTY DEFINABLE BY ANALOGY TO THE REGULATIONS, AND STILL GIVES YOU THE BULK OF YOUR PROPOSAL, WHICH IS TO ELIMINATE ALL THIS, TO BE HONEST, FAIRLY SENSELESS NOTIFICATIONS.

CHAIRMAN LO: YOU RAISED AN INTERESTING POINT I JUST WANT TO UNDERLINE, WHICH IS THERE MAY BE THINGS THAT WOULD CALL FOR SOME DELIBERATION, AS JOHN MENTIONED, BUT THE SCRO MAY NOT BE UNIQUELY QUALIFIED TO DO THAT; WHEREAS, THERE ARE OTHER ISSUES WHERE WE THINK THE SCRO, AS WE'VE

CONCEPTUALIZED IT, REALLY IS AN APPROPRIATE BODY FOR THAT REVIEW.

DR. PAT TAYLOR: I THINK HIS POINT IS VERY INSIGHTFUL. IT'S JUST THAT INSTITUTIONS HAVEN'T CAUGHT UP WITH HIS POINT.

DR. LOCKHART: SO I THINK TO KIND OF GET TO BERNIE'S QUESTION, I'M THINKING OF THIS IN TWO DIFFERENT WAYS. I THINK THERE ARE SENSITIVE USES, WHICH PAT IS POINTING OUT. BUT THEN ALSO WHEN I LOOK AT SOMETHING LIKE CATEGORY 4 THAT'S LISTED THERE, IS THERE A RISK, AS GEOFF WAS POINTING OUT, ABOUT INVESTIGATORS BASICALLY GETTING IT WRONG? SO ARE THERE INSTANCES OR CASES WHERE WE'D BE WORRIED ABOUT AN INVESTIGATOR DECIDING THIS IS DEIDENTIFIED. I DON'T NEED TO NOTIFY ANYBODY. I'M GOING TO GO AHEAD AND MAKE A NEW LINE, AND THEY DON'T REALLY UNDERSTAND WHAT DEIDENTIFIED MEANS MAYBE. ARE THERE OTHER KINDS OF THINGS WE WANT TO WORRY ABOUT, BOTH SENSITIVE USES, AND THEN OTHER WHAT DO WE WANT TO LEAVE IN THE HANDS OF INVESTIGATORS?

IF WE DO MAKE THAT DECISION THAT NOTIFICATION IS NOT REQUIRED, THEN DO WE NEED TO PROVIDE GUIDANCE TO THE ACTUAL PI WHO'SE MAKING THOSE CALLS SO THAT THEY MAKE THAT INTERPRETATION CORRECTLY?

SECONDLY, IF THIS IS PRIMARILY AN ADMINISTRATIVE BURDEN PROBLEM, THEN IF IT'S DECIDED NOTIFICATION IS NEEDED IN SOME INSTANCES, ARE THERE OTHER APPROACHES WE CAN TAKE TO STREAMLINE SOME OF THIS TO MAKE IT EASIER BOTH FOR INSTITUTIONS AS WELL AS FOR CIRM TO KIND OF TAKE CARE OF IT ON THE OTHER SIDE SO THAT IT'S EASIER, WE GET WHATEVER BENEFIT, THERE'S THE NOTIFICATION, WHILE MAKING IT EASIER, ESPECIALLY SINCE THIS HAS BEEN GOING ON FOR A WHILE, THERE'S PROBABLY SOME BRIGHT IDEAS ABOUT HOW THAT COULD HAPPEN.

DR. WAGNER: JUST TO ADDRESS THE SECOND POINT IS REALLY YOU HAVE THE IRB'S, YOU HAVE THE FEDERALWIDE ASSURANCES THAT THEY HAVE FOR DHHS SO THAT BASICALLY THEY DON'T HAVE TO GO TO DHHS TO GET APPROVAL FOR EVERYTHING THEY DO. IT'S AN ASSURANCE THAT THEY'RE FOLLOWING A CERTAIN POLICY. SO I THINK THERE'S SOMETHING THAT YOU COULD DO LIKE THAT THAT PREVENTS CIRM -- ELIMINATES THE NEED FOR CIRM TO SPECIFICALLY VERIFY EVERY SINGLE APPLICATION.

DR. LOCKHART: OR MAYBE IF INSTITUTIONS ARE ALREADY SUBMITTING PROGRESS REPORTS, MAYBE WHEN THEY SUBMIT THEIR PROGRESS REPORT, THEY INCLUDE THOSE KINDS OF THINGS. THEY INCLUDE THEIR CORRESPONDENCE FROM THE YEAR OR THEIR VERIFICATIONS,

OR THERE'S A CHECKLIST THEY'RE REQUIRED TO FILL OUT OR SOMETHING SO GEOFF IS STILL GETTING INFORMATION HE NEEDS, BUT MAYBE NOT HAVING TO DO IT IN REAL TIME.

DR. LOMAX: WE DO THAT AT THE PROGRESS REPORT PHASE. WE'RE ALWAYS DOING THOSE EVALUATIONS, BUT IT STILL IS A LOT OF -- AS A LOT OF YOU MAY BE AWARE, RESEARCH MOVES DOWN A CERTAIN PATHWAY, THERE'S A PROTOCOL CHANGE, THERE'S A PROTOCOL CHANGE FOR A VERY GOOD REASON CONSISTENT WITH WHAT THEY'RE BEING FUNDED TO DO. OOPS, THERE WAS A NOTIFICATION THERE. I THINK FOR THE MOST PART, TAKING THE SPIRIT OF YOUR COMMENT, WE'RE DOING THAT.

AND, AGAIN, THIS IS OUR SORT OF ONE PROPOSAL ABOUT HOW WE CAN BE DOING THAT FROM A MORE EFFICIENT PERSPECTIVE. AND, AGAIN, THAT'S THE PURPOSE OF THIS CONVERSATION. WE WILL CONTINUE TO THINK ABOUT THIS SORT OF SENSE OF ARE THERE OTHER MECHANISMS TO GET -- WHAT I'M HEARING IS SORT OF THAT EXTRA LOOK OR THAT EXTRA -- THAT'S WHAT I GET. I THINK WE'RE GOING TO SEE WHERE THIS CONVERSATION ENDS UP.

SO THE POINT IS WE ARE DOING THAT BOTH IN THE PROGRESS REPORTS AND WE DO NEED TO HAVE A SET OF THINGS IN PLACE PRIOR TO FUNDING. THAT ABSOLUTELY

HAS TO BE THERE, AND THAT'S WHERE WE SPEND A LOT OF TIME ON THOSE PROTOCOLS.

CHAIRMAN LO: JOHN, SCOTT ACTUALLY HAD A VERY, I THOUGHT, VERY USEFUL PROCEDURAL POINT ABOUT SORT OF WE DON'T NEED TO SOLVE THESE PROBLEMS TODAY BECAUSE THIS IS ONE STEP IN A PROCESS. SCOTT, WHY DON'T YOU WALK US THROUGH THAT A LITTLE BIT.

MR. TOCHER: I THINK THE POINT THAT I WAS JUST MAKING TO BERNIE IS THAT ON SOME OF THESE ISSUES WHERE IT SOUNDS LIKE THERE ARE VERY GOOD POINTS THAT ARE BEING AIRED ON SOME OF THESE AMENDMENTS, THAT IT'S NOT NECESSARILY NECESSARY THAT WE COME TO A FINAL CONCLUSION OR RECOMMENDATION TODAY, BUT THAT WE MAYBE ADVISE THAT THIS IS SOMETHING TO THE BOARD THAT IS WORTH INVESTIGATING FURTHER THROUGH THE PUBLIC COMMENT PROCESS ESPECIALLY. AND SO WE COULD GO FORWARD WITH, AS GEOFF HAS IDENTIFIED, FOR INSTANCE, IN THE THIRD ROW, THAT WE COULD INCLUDE SOME OF THIS AS OPTIONAL LANGUAGE FOR THE PURPOSE OF SOLICITING INPUT FROM THE REGULATED COMMUNITY, AND THEN COME BACK WITH SORT OF THE RESULT OF THAT AND RECOMMENDATIONS BASED ON WHAT WE'VE HEARD AND SORT OF WHAT WOULD BE THE BEST RECOMMENDATION FOR MOVING FORWARD.

CHAIRMAN LO: JOHN WAGNER AND OTHERS.

DR. WAGNER: I GUESS THE ISSUE OF THE DEIDENTIFIED CELLS, IF IT'S TRULY DEIDENTIFIED, THEN PERSONALLY I DON'T HAVE ANY PROBLEMS WITH THAT. BUT I WAS JUST TRYING TO MAKE THE POINT THAT WHAT INVESTIGATORS ARE DOING NOW, AT LEAST THERE'S EXAMPLES OF INVESTIGATORS WHAT THEY'RE DOING NOW, IS THAT THEY'RE NOT TRULY DEIDENTIFIED EVEN THOUGH THEY MAY BE ASSIGNED A NUMBER OR A CODE OR WHATEVER THAT IS. AND WE JUST HAVE TO FIGURE A WAY OF ENSURING DEIDENTIFICATION OR EXPLAINING WHAT THAT MEANS BECAUSE OF THE FACT THAT THIS ALSO HAS AN IMPACT, I THINK, UPON A TOPIC FOR LATER TODAY WHERE YOU'RE GOING TO BE TALKING ABOUT CREATING AN IPS BANK. IF THEY DON'T FULFILL CERTAIN CONSENT REQUIREMENTS, THEY MAY GET EXCLUDED FROM THE BANK, OR YOU MAY FIND THAT THERE IS SOME ETHICAL ISSUE THAT DEVELOPS BECAUSE OF INADEQUATE CONSENTING BECAUSE THESE PATIENTS WERE NEVER REALLY DEIDENTIFIED TO BEGIN WITH OR WHATEVER.

THE FACT IS THAT I'M CONCERNED IT'S GOING TO HAVE MORE RAMIFICATIONS THAN YOU MIGHT THINK. AND WE'LL GET INTO THAT LATER.

DR. ROBERT TAYLOR: I GUESS I WAS GOING TO SAY TO ME THIS ISSUE REALLY REQUIRES A HELL OF A LOT MORE WORK. I THINK IT'S REALLY, REALLY VERY, VERY

COMPLICATED. AND SO FOR ONE, THE SENSE THAT I GET AND KIND OF SORT OF A BROADER PHILOSOPHICAL THING, AND MAYBE I'M MISINTERPRETING THIS, GEOFF, BUT WHEN YOU SORT OF INTRODUCED THIS, YOU TALKED A LITTLE BIT ABOUT THE NIH REQUIREMENTS VERSUS OUR REQUIREMENTS. AND TO BE HONEST, I'VE ALWAYS FELT THAT WE SHOULD HAVE A HIGHER STANDARD IN PART BECAUSE IT'S REALLY THE APPLICATION OF THESE CELLS. AND I THINK THIS DISCUSSION ABOUT DOES PLURIPOTENCY ACTUALLY MEAN ANYTHING ANYMORE, I THINK IT KIND OF DOESN'T WITH REPROGRAMMING.

SO IT'S REALLY THE APPLICATION OF THE CELLS THAT WE'RE TALKING ABOUT RATHER THAN HOW THEY'RE DERIVED, I THINK, IS REALLY THE BIGGEST ISSUE.

AND BECAUSE -- WHEN I VOTED FOR PROP 71, I THOUGHT THAT THERE WAS REALLY AN APPLIED SCIENCE TO THIS. I THINK IT WAS THE EXPECTATION OF THE TAXPAYERS THAT THIS REALLY IS GOING TO LEAD TO APPLICATION, NOT JUST WE CAN DO THE SAME KINDS OF EXPERIMENTS THAT WE USED TO DO IN FORCING FIBROBLASTS NOW WITH AN IPS LINE, BUT THERE'S REALLY INTENDED TO BE AN APPLICATION. I THINK REALLY A LOT OF THESE ISSUES, I'M UNCOMFORTABLE REMOVING THE SCRO FROM LOTS OF THIS OVERSIGHT BECAUSE I THINK THAT

IT'S REALLY THAT ULTIMATE PRECLINICAL CLINICAL APPLICATION THAT'S REALLY WHAT WE'RE HERE FOR. AND THAT, I BELIEVE, REQUIRES A DIFFERENT LEVEL OF ATTENTION THAN THE NIH TYPICALLY AFFORDS FOR THE KINDS OF THINGS THAT WE'RE DOING ON A MORE PURE SCIENCE LEVEL. SO I DON'T KNOW. I DON'T KNOW. I THINK THIS IS COMPLICATED.

CHAIRMAN LO: SO, AGAIN, LET ME JUST SORT OF POINT OUT THAT WHEN IT ACTUALLY INVOLVES INJECTING CELLS THAT ARE COVERED CELLS OR I WOULD SUGGEST ALSO DIRECTLY REPROGRAMMING CELLS, COVERED STEM CELL LINES OR DIRECTLY REPROGRAMMING CELLS, INTO ANIMALS AND NONHUMAN ANIMALS AND HUMANS, CERTAINLY WITH HUMANS, THERE'S A WHOLE LOT OF OVERSIGHT THAT COMES INTO PLAY. AND FOR NONHUMAN ANIMALS, WE'VE SORT OF TRIED TO SAY THERE'S CERTAIN TYPES OF THAT KIND OF RESEARCH INVOLVING INJECTIONS INTO THE CNS, NO INJECTIONS OF HUMAN CELLS INTO BLASTOCYSTS. SO WE'VE, AGAIN, TRIED TO FOLLOW WHAT PAT WAS SUGGESTING, THAT WE LOOK AT END USES OF CELLS THAT ARE SENSITIVE AND TO SORT OF FOCUS ON THAT.

I WANT TO THROW IN ONE MORE COMPLICATION WHICH HAS TO DO WITH THE DEIDENTIFIED CELLS, REPROGRAMMED OR COVERED STEM CELL LINES. TAKING

ACCOUNT OF JOHN'S POINTS ABOUT HOW TAKING OVERT IDENTIFIERS OFF MAY NOT MAKE THEM TRULY IDENTIFIABLE, AT LEAST TO THE PEOPLE WHO ARE INVOLVED AS CLINICIAN INVESTIGATOR, SORT OF IDENTIFYING THE PATIENT AND THE DISEASE AND OBTAINING MATERIALS, ARE THERE SOME USES, END USES OF REPROGRAMMED CELLS THAT EVEN IF THE CELLS ARE DEIDENTIFIED, THE ORIGINAL DONOR MAY HAVE AN INTEREST IN THOSE USES?

SO I GUESS ONE CLEAR THING WOULD BE IF YOU TOOK TRULY DEIDENTIFIED SOMATIC CELLS AND SOMEHOW COULD REPROGRAM THEM INTO GAMETES, AND THEN IN THE LAB USE THOSE GAMETES FOR IVF EXPERIMENTS. AS PROOF OF PRINCIPLE, THEY REALLY ARE GAMETES. THEY FUNCTION LIKE GAMETES. THEY DON'T JUST LOOK LIKE GAMETES. I CAN IMAGINE A LOT OF PEOPLE SAY, WAIT A MINUTE, JUST BECAUSE THEY'RE DEIDENTIFIED.

SO DO WE AGREE WITH THAT, THAT JUST DEIDENTIFICATION DOESN'T TAKE SOME VERY SENSITIVE USES OFF THE TABLE IN TERMS OF SPECIAL OVERSIGHT? AND THEN WHAT IS THAT SET OF HIGHLY SENSITIVE USES? I THINK GIVEN THE POLITICS OF THE COUNTRY, I THINK THE REPRODUCTIVE ISSUES CERTAINLY WOULD PROBABLY FALL INTO THAT, BUT ARE THERE OTHERS?

PAT, YOU RAISED REALLY INTERESTING

QUESTIONS ABOUT CELLULAR TRANSPLANTATION WHERE IT'S AN ORGAN ALL OF WHOSE CELLS COME FROM ME AS OPPOSED TO JUST INJECTING SOME CELLS. I DON'T KNOW THAT WE KNOW THE ANSWER TO THAT BECAUSE THIS IS ALL SO NEW AND THE SCIENCE IS JUST EVOLVING.

DR. PAT TAYLOR: I AGREE WITH YOU. THE DISTINCTION BETWEEN DEIDENTIFICATION AND NOT RESTED ON A SINGLE LINE IN A FEDERAL BIOETHICS REVIEW SAYING THAT REALLY THE ONLY INTEREST OF AN INDIVIDUAL WHEN IT CAME TO CERTAIN KINDS OF RESEARCH WAS PRIVACY. AND, OF COURSE, THERE ARE MANY OTHER INTERESTS THAT PEOPLE HAVE, SUCH AS, AS YOU POINTED OUT IN ARTICLES AND ELSEWHERE, THE PARTICULAR ATTACHMENT THEY HAVE TO PARTICULAR USES OF PARTS OF THEIR BODY, AND A BELIEF IN A SENSE THAT THEY OUGHT TO BE ABLE TO PRESCRIBE CERTAIN USES THEY WOULD OBJECT TO AND HAVE TROUBLE MAKING A DONATION.

SO IT'S SO ARCHAIC THE DISTINCTION BETWEEN DEIDENTIFICATION AND NOT PARTLY FOR THE REASON THAT NOTHING IS -- CERTAINLY DEIDENTIFIED, OF COURSE, BUT PROBABLY BECAUSE IT PROBABLY REALLY NEVER CAPTURED THE FULL RANGE OF HUMAN INTEREST ANYWAY. CERTAINLY THE POTENTIAL OF DIFFICULT USES.

SO ALSO IT'S A BIT ODD TO THINK THAT WHETHER OR NOT AN EXPERIMENT REQUIRES REVIEW FROM A

SOCIAL PERSPECTIVE OUGHT TO TURN ON WHETHER OR NOT THE INDIVIDUAL'S IDENTIFIED. CERTAINLY THE NATURE OF THE EXPERIMENT OUGHT TO BE WHAT DRIVES WHETHER OR NOT IT OUGHT TO BE REVIEWED, NOT THE HAPPENSTANCE THAT AN INDIVIDUAL IS IDENTIFIED OR NOT. ALL THAT RELATES TO IS A FUNCTION OF IRB'S TO PROTECT THE INTEREST OF THE INDIVIDUAL AS NARROWLY ENCAPSULATED.

DR. ROBERTS: IT SEEMS AS IF, THEN, THE CATEGORIES THAT WE'RE CONCERNED ABOUT ARE EXPANDING THE MORE WE DISCUSS THEM. SO FIRST THERE WAS THE -- SO THERE'S THIS ADMINISTRATIVE BURDEN. THERE'S A COUPLE SENSITIVE AREAS WHERE WE MIGHT NEED NOTIFICATION OF SCRO COMMITTEES. THEN I THINK, PAT, YOU SUGGESTED SOME MORE BEYOND THE TRANSPLANTATION TO NONHUMAN ANIMALS AND THE CREATION OF GAMETES. THERE MIGHT BE EVEN MORE THAN THAT. AND THEN NOW THE DISTINCTION BETWEEN DEIDENTIFIED AND IDENTIFIED IS BREAKING DOWN.

SO IT JUST GETS MORE AND MORE CONCERNING ABOUT TAKING AWAY THE REQUIREMENT OF NOTIFICATION OR AT LEAST, LET'S SAY, I THINK IT'S HARDER THAN IT INITIALLY LOOKED TO FIGURE OUT WHERE WE WOULD BE COMFORTABLE DRAWING SOME LINE WHERE WE WOULD BE COMFORTABLE WITH ELIMINATING NOTIFICATION. AT LEAST I'M FEELING THAT WAY. I THINK THIS REQUIRES A LOT

MORE DISCUSSION, BUT ALSO EVEN JUST QUESTIONING WHETHER WE CAN DRAW THAT LINE BECAUSE EVEN IN SAYING MAYBE WE CAN COME UP WITH FIVE SENSITIVE USES WHERE WE WANT IT, THEN MY QUESTION IS WHAT IF TOMORROW A RESEARCHER COMES UP WITH ANOTHER USE WE HADN'T THOUGHT ABOUT?

NOW THEY HAVE BEEN -- THEY DON'T HAVE TO NOTIFY BECAUSE IF IT'S NOT LISTED AMONG THOSE SENSITIVE USES, THEY WOULD FALL UNDER THE CATEGORY OF NO NOTIFICATION REQUIRED. THAT'S SOMETHING THAT WE HAVE TO THINK ABOUT, I THINK. THAT'S NOT SAYING THAT WE COULDN'T COME UP WITH A LIST, BUT JUST THAT WE HAVE TO ANTICIPATE THAT THERE MAY BE ADDITIONAL USES.

MR. SWEEDLER: MY NAME IS IAN SWEEDLER. LIKE SCOTT, I'M A LAWYER AT CIRM. AND I JUST WANTED TO OFFER A COUPLE OF THOUGHTS FROM THINGS THAT OCCURRED TO ME FROM THE SIDELINES. ONE IS TO FOLLOW UP A BIT ON WHAT SCOTT SAID ABOUT THE RULEMAKING PROCESS. SOMEWHERE DOWN THE LINE WE'RE GOING TO HAVE TO CERTIFY TO THE OFFICE OF ADMINISTRATIVE LAW THAT WE DID CONSIDER LESS BURDENSOME ALTERNATIVES TO ANY RECOMMENDATION THAT WE ADOPT, AND THAT THERE'S A REASON FOR GOING WITH THE MORE BURDENSOME ONE.

IN AREAS WHERE I HEAR GENERALIZED

STATEMENTS OF CONCERN, IT WOULD BE ESPECIALLY HELPFUL FOR US IN THE RECORD THAT WE'LL BE USING DOWN THE ROAD TO HEAR EXAMPLES OF REALLY THE SPECIFIC CONCERNS THAT YOU THINK ARE ADDRESSED BY REQUIRING NOTIFICATION AS OPPOSED TO NOT OR APPROVAL AS OPPOSED TO NOT.

AND THEN JUST ANOTHER THOUGHT THAT OCCURRED TO ME. IT SEEMS LIKE THERE ARE THIS SET OF CONCERNS THAT GOES TO WHETHER SOMETHING IS DERIVED FROM AN EMBRYONIC SOURCE OR NOT. THERE'S A SET OF CONCERNS ASSOCIATED WITH WORKING ON SOMETHING DERIVED FROM A SOMATIC SOURCE. THERE'S A SET OF CONCERNS ABOUT IDENTIFIED AND DEIDENTIFIED, AND A SET OF CONCERNS ABOUT POTENTIAL USES. AND IT SEEMS LIKE THOSE CONCERNS SORT OF -- THERE ARE MULTIPLE AXES HERE, BUT WHERE THEY APPLY, THEY APPLY.

AND MAYBE JUST SORT OF BREAKING IT DOWN THAT WAY SO THAT THEY COULD BE DEALT WITH CONSISTENTLY. SO, FOR EXAMPLE, I DON'T KNOW WHY YOU WOULD HAVE A REQUIREMENT FOR USE OF DEIDENTIFIED IPSC'S OTHER THAN BASED ON POTENTIAL USES THAT YOU WOULDN'T HAVE FOR ANY USE OF DEIDENTIFIED SOMATIC CELLS. AND THEN IF IT'S NOT A CONCERN THAT IS SPECIFIC TO STEM CELL RESEARCH, THEN THERE'S ALWAYS A QUESTION OF WHETHER WE SHOULD BE TRYING TO REMAKE

THAT PART OF IT BECAUSE WE DO TRY TO STAY FOCUSED ON THE THINGS THAT ARE OUR FOCUS. SO THOSE ARE JUST SOME COMMENTS FROM THE SIDELINES.

CHAIRMAN LO: THIS, TO BE SURE, DOROTHY, HAS GOTTEN COMPLICATED. IT'S A COMPLICATED SET OF ISSUES. LET ME JUST MAKE ANOTHER SUGGESTION ON WHY THIS IS DIFFICULT. I THINK WE'RE ASSESSING THE RISK OF RESEARCH THAT IS SO SENSITIVE THAT IT REALLY REQUIRES SCRUTINY. AND RISK HAS TWO DIMENSIONS, RIGHT, PROBABILITY AND MAGNITUDE. SO IN TERMS OF PROBABILITY, THE VAST MAJORITY OF IPS OR DIRECT REPROGRAMMING RESEARCH REALLY IS NOT CONTROVERSIAL. IT'S STUDYING THE BASIC SCIENCE OF REPROGRAMMING.

AND SO IS THE CONCERN THAT ALL THOSE PROTOCOLS IF WE -- SO THAT'S A CONCERN, HOW MANY PROTOCOLS WE'RE DOING. BUT THERE ARE A FEW PROTOCOLS THAT REALLY DO RAISE SOME DOOZIES OF ETHICAL ISSUES.

SO WHEN I WAS AT UCSF CHAIRING A COMMITTEE, THE ONE PROTOCOL, THE KINDS OF PROTOCOLS WE GOT, THIS WAS ABOUT SIX MONTHS TO A YEAR AGO, REALLY HAD TO DO WITH TRYING TO DERIVE GAMETES FROM PLURIPOTENT CELLS OR ACTUALLY LATER DIRECT REPROGRAMMING. SO THE QUESTION IS ALWAYS HOW CAREFULLY DO YOU SIFT THROUGH THE VAST MAJORITY OF

UNSENSITIVE, NONSENSITIVE PROTOCOLS TO IDENTIFY THE COUPLE THAT REALLY ARE SENSITIVE? THEN WHERE DO YOU SEND THEM FOR REVIEW?

AND THEN BOTH PAT AND DOROTHY, I THINK, WERE POINTING OUT THE DILEMMA THAT IF WE HAVE A SPECIFIED LIST OF COME TO US IF YOU'RE DOING A, B, AND C, AND SOMEONE ELSE SAYS I'M NOT DOING A, B, AND C. I'M DOING E.

DR. ROBERTS: IT'S WORSE.

CHAIRMAN LO: SO PART OF IT IS TRYING TO REGULATE IN WAYS THAT DOES MORE GOOD THAN HARM. I THINK AT SOME POINT THE FRUSTRATION IS THAT IF YOU'RE TRYING TO REGULATE EVERYTHING TO AVOID AN ERROR OF THE TYPE THAT WE LET SOMETHING THROUGH WITHOUT LOOKING AT IT, THEN YOU RUN THE RISK OF BURDENING A LOT OF THINGS. ON THE OTHER HAND, IF YOU SAY AT SOME POINT WE EXPECT THAT RESEARCHER TO STEP UP AND SAY THIS ISN'T COVERED IN A, B, AND C, BUT I'M JUST WONDERING IF GUYS REALLY ARE COMFORTABLE WITH MY JUST SAYING I DON'T EVEN HAVE TO NOTIFY YOU OF THIS. I JUST NOTIFIED YOU BY CALLING YOU.

AND I THINK SOME OF THE MOST INTERESTING INTERACTIONS WE HAVE ARE WHEN PEOPLE SAY I JUST HAVE A -- SOMETIMES IT'S JUST, OH, I HEARD THAT SOME

RESEARCHERS ARE TRYING TO DO THIS. WOULD THAT EVER HAVE TO COME TO YOUR COMMITTEE? MY FIRST RESPONSE IS IS IT YOU OR YOUR FELLOW OR YOUR BOSS WHO'S DOING THIS RESEARCH? IT'S NOT SOME PEOPLE.

SO I GUESS THAT'S THE OTHER THING. THERE'S A COST TO OVERREGULATING WHEN MOST OF THE THINGS THAT YOU'RE DEALING WITH ARE NOT THAT SENSITIVE.

DR. LOMAX: BERNIE, CAN I COMMENT JUST ON THAT ONE POINT, PLEASE, BECAUSE I THINK I REALLY THINK THE FRAMEWORK WE HAVE HAS BEEN INCREDIBLY ROBUST AND EFFECTIVE. I JUST WANT TO ADVOCATE FOR IT FOR A MOMENT. JUST TO REMIND YOU OF THOSE GUIDEPOSTS OR THE AXIS OF WHICH WE HAVE DECISION POINTS. SO WE DISTINGUISHED QUITE CLEARLY BETWEEN IN VIVO AND IN VITRO RESEARCH, AND ALL THIS IS ABOUT IN VITRO. ONCE YOU GO IN VIVO AND THEN THAT SORT OF HORIZONTAL AXIS, IF YOU WILL, IS BETWEEN SOMATIC AND THEN YOU MOVE TO GAMETE OR EMBRYO. IT'S A FAIRLY SIMPLE, BUT INCREDIBLY ROBUST FRAMEWORK THAT I WILL SAY TO DATE I THINK HAS BEEN VERY EFFECTIVE.

SO JUST TO POINT OUT WHAT WE HAVE IS PRETTY GOOD. I KNOW THIS IS A GREAT CONVERSATION, BUT WE'RE NOW IN ONE LITTLE QUADRANT OF THAT AND REALLY STRUGGLING OVER SOME DETAILS. THAT'S

TERRIFIC. THAT'S WHY WE'RE HERE. I DO WANT TO EMPHASIZE I THINK THAT FRAMEWORK HAS BEEN VERY SUCCESSFUL BOTH IN TERMS OF GETTING THE RIGHT STUFF UNDER THE MICROSCOPE THAT WE WANT AND BEING ABLE TO EDUCATE INSTITUTIONS ABOUT WHAT WE'RE LOOKING FOR.

CHAIRMAN LO: THE EDUCATION. AGAIN, IT'S THE VERY LOW PROBABILITY OF HIGH SALIENCE OR VALENCE OF THE EVENT THAT'S VERY, VERY HARD TO REGULATE, BUT THERE ARE OTHER THINGS THAT SORT OF CAN SLIP THROUGH THE CRACKS. ANIMAL RESEARCH -- INJECTION OF HUMAN STEM CELLS INTO NONHUMAN ANNALS THAT DON'T GO INTO THE BRAIN CAN RAISE SENSITIVITIES. I WOULD JUST WONDER IF I HAD DEVELOPED A SCAFFOLD FOR A HEART AND HAD A HEART THAT WAS MADE OF HUMAN CELLS AND THE SCAFFOLDING WAS SUCH THAT IT LOOKED LIKE A HUMAN BEING HEART, I SAID I'M GOING TO AS PROOF OF PRINCIPLE PUT IT INTO A NONHUMAN ANIMAL BEFORE IT GOES INTO A HUMAN, TECHNICALLY -- AND THEY'RE DEIDENTIFIED CELLS, I'M NOT SURE THAT I NEED TO TALK TO ANYBODY OTHER THAN THE IACUC PEOPLE ABOUT THE WELFARE OF ANIMALS ABOUT THAT. I'M NOT SAYING THAT THE SCRO IS THE BEST OR THE ONLY BODY TO VIEW THAT, BUT I JUST THINK THAT, BOY, WHEN THAT HITS THE PAPERS, THERE'S GOING TO BE SOME DISCUSSION. I THINK IT'S A MOVING TARGET. I THINK WE HAVE DONE

WELL. I THINK PART OF IT IS BECAUSE GEOFF HAS DONE A TERRIFIC JOB IN EDUCATING PEOPLE, TALKING WITH THEM. BUT I THINK AS THE SCIENCE NOW IS TAKING REAL LEAPS TOWARDS MOVING INTO THE CLINICAL ARENA, WE HAVE TO MAKE SURE THAT WE'RE TRYING TO STAY ABREAST.

AGAIN, WE DON'T HAVE TO DO IT ALL TODAY, BUT I THINK WHAT WE MAY WANT TO DO IS SORT OF RAISE SOME ISSUES AND SAY THESE ARE THINGS THAT WE NEED MORE COMMENT, DELIBERATION, AND PUBLIC FEEDBACK ON.

DR. LOMAX: I WANT TO BE A LITTLE BIT CAREFUL, THOUGH, TO SAY WE DO NEED SOME DIRECTION FROM THE WORKING GROUP IN TERMS OF THESE THINGS, WHERE WE SHOULD BE PURSUING.

CHAIRMAN LO: JEFF AND THEN WE TRY AND MOVE ON.

DR. BOTKIN: I GUESS AS I PUT ON MY INSTITUTIONAL HAT, ONE OF THE THINGS THAT IS A FAIRLY FREE-FLOATING ANXIETY IN THIS CONTEXT IS THE FACT THAT THE GRANT AWARDS ARE GOING TO THE INSTITUTION, BUT YET SOME OF THIS -- THE LACK OF NOTIFICATION MIGHT THEN CUT THE INSTITUTIONAL CHECK OUT OF THE NEGOTIATION BETWEEN THE INVESTIGATOR AND THE FUNDER ABOUT EXACTLY WHAT RESEARCH IS GOING TO BE CONDUCTED. SO I HAVE TO SAY THAT THERE'S A CERTAIN AMOUNT OF ANXIETY THERE.

AND AS AN INSTITUTIONAL OFFICIAL, CERTAIN FIDUCIARY RESPONSIBILITY TO SORT OF KNOW WHAT RESEARCH IS GOING ON EVEN IF THERE'S NOT AN ACTIVE ROLE OR A SIGNIFICANT NEED FOR THE OVERSIGHT FOR THAT.

SO I GUESS THE OTHER IMPRESSION I'M GETTING FROM THE DISCUSSION HERE IS THAT THERE'S SORT OF TWO LEVELS OF BURDEN FOR THE OVERSIGHT PROCESS HERE. ONE IS FOR THE INVESTIGATORS, WHICH IS A BURDEN, BUT PERHAPS -- A BIG BURDEN, BUT THEN A SIGNIFICANT BURDEN FOR CIRM TO FIGURE OUT HAVE PEOPLE BEEN COMPLIANT. SO I GUESS I'D BE INTERESTED IN, AS NICOLE WAS SUGGESTING, SOME CREATIVE ADDITIONAL THOUGHT ABOUT ARE THERE WAYS TO REDUCE THE BURDEN TO CIRM FOR DETERMINING COMPLIANCE WITH THE NOTIFICATION AS AN ALTERNATIVE TO ELIMINATING THE NOTIFICATION PIECE.

DR. LOMAX: THAT MESSAGE HAS COME THROUGH. I WOULD ENCOURAGE YOU AT THIS POINT, ONE OTHER THING THAT I'VE BEEN HEARING SORT OF THE VALUE OF NOTIFICATION, I STILL HAVE A QUESTION I HAVEN'T QUITE GOT THE LEAD I COULD USE ON IS, AGAIN, COULD NOTIFICATION INCLUDE THE RESPONSIBLE OFFICIAL? SOMETIMES THERE'S SORT OF THE CONVERSATION GOES TOWARDS WE REALLY THINK THE OVERSIGHT COMMITTEE IS

THE PLACE FOR IT TO BE, OR ARE WE COMFORTABLE IN CERTAIN CIRCUMSTANCES DEFERRING TO SOMEONE AT THE INSTITUTIONAL LEVEL WHO'S INTIMATE WITH OUR REQUIREMENTS, AND THE NOTIFICATION GOES TO THAT INDIVIDUAL AS OPPOSED TO A COMMITTEE. SO THAT'S STILL AN OUTSTANDING QUESTION I DON'T FEEL I HAVE THE DIRECTION THAT I COULD USE FROM THIS COMMITTEE.

CHAIRMAN LO: SO WE'VE DUG OURSELVES INTO A MUCH MORE COMPLICATED PLACE THAN WE PERHAPS THOUGHT WE WERE GOING TO BE.

GEOFF, CAN I ASK A QUESTION ABOUT LUNCH? WE PROBABLY DO NEED A BREAK. BUT I'M NOT SURE YOU GOT THROUGH ALL THE TABLE. WE'VE BEEN SORT OF JUMPING TO ISSUES, AND WE SORT OF STARTED TALKING ABOUT DEIDENTIFIED. DID WE REALLY GET THROUGH THE LAST THREE LINES OF THIS CHART IN TERMS OF YOUR LAYING OUT THE THINKING BEHIND THE PROPOSED NEW REVISIONS? I'M NOT SURE WE DID.

DR. LOMAX: I DIDN'T EXPLICITLY GET THROUGH IT. I HEARD ELEMENTS OF IT COME INTO THE CONVERSATION. I'M HAPPY TO DO THAT IF IT IS OF VALUE. I DID HEAR AS SORT OF -- THE CONVERSATION WAS SORT OF MOVING BETWEEN THESE CATEGORIES QUITE FLUIDLY. I HAD A SENSE THAT PEOPLE WERE CLEAR ON THE DISTINCTIONS.

CHAIRMAN LO: I'M LOOKING AT YOUR LAST SLIDE, WHICH IS F, I GUESS, WHICH DOES START TO ADDRESS -- I'M SORRY. YOU WANTED TO COME BACK TO THAT SEPARATELY. SO LET'S DO D FIRST. SO MY SUGGESTION, IF THERE IS LUNCH THERE -- AND I DON'T KNOW IF THERE IS, COULD SOMEONE PEEK? -- I WOULD SUGGEST WE'VE SORT OF GOTTEN IN SOME REALLY HEAVY ISSUES HERE. I SUGGEST WE MAYBE TAKE A BREAK FOR LUNCH, SORT OF STEP BACK FROM THIS A MINUTE, LET OUR UNCONSCIOUS GENIUS INSIDE US SORT OF SORT THIS ALL OUT, COME BACK TO THIS AFTER A QUICK LUNCH TO SORT OF FOLLOW UP ON THIS WITH A VIEW TO, I GUESS, TWO THINGS.

ONE IS I THINK WE NEED SOME GUIDANCE FOR GEOFF AND SCOTT AND THE CIRM LEADERSHIP AS TO WHAT OUR VIEW IS OF THE PROPOSALS THEY SUGGESTED, I THINK. WE ALSO HAVE SOME QUESTIONS ABOUT ISSUES THAT WE WOULD LIKE TO SEE SOME MORE DELIBERATION AND FEEDBACK ON. IS THAT A FAIR SUMMARY OF WHERE WE NEED TO GET TO AT THE END OF THIS DELIBERATION? YOU REALLY DO WANT TO GO THROUGH THAT CHART AND TO SORT OF GIVE YOU SOME IDEA, NOT A VOTE BECAUSE WE DON'T HAVE A QUORUM, BUT A SENSE OF THE COMMITTEE ON HOW WE'RE THINKING ABOUT THAT.

DR. FEIGAL: THE ANSWER IS, YES, WE DO

WANT THAT.

CHAIRMAN LO: WE HAVE TO --

MR. TOCHER: THE ONLY THING I WOULD JUST ADD TO THAT IS TO JUST EMPHASIZE AGAIN THAT I DON'T MEAN -- I DON'T THINK BERNIE MEANS TO SEQUESTER YOU AWAY IN A ROOM.

CHAIRMAN LO: IT'S GOING TO BE HERE.

MR. TOCHER: IN TERMS OF A FINAL RECOMMENDATION, IT MAY WELL BE THAT IN YOUR CONSIDERED JUDGMENT, YOU'RE NOT READY TO MAKE A FIRM RECOMMENDATION ON SOMETHING ONE WAY OR THE OTHER. AND THAT COULD BE INCORPORATED INTO THE REPORT BACK TO THE ICOC, THAT THIS IS AN ISSUE THAT WARRANTS FURTHER CONSIDERATION AND INPUT THAT YOU'VE IDENTIFIED, EVEN ADDITIONAL AREAS THAT YOU WOULD LIKE TO SEE MORE DATA ON, OR MAYBE SOME DIFFERENT PROPOSALS AND INPUT ON, AND THAT YOU PROPOSE NOT COMING TO A FINAL JUDGMENT ON THAT, BUT BEGINNING THE PROCESS OF GETTING THAT INPUT TO BRING BACK TO COME TO A FINAL RECOMMENDATION.

CHAIRMAN LO: WE CAN ALWAYS SCHEDULE ADDITIONAL EITHER TELEPHONE MEETINGS THAT WOULD BE OPEN TO THE PUBLIC OR, IF NECESSARY, A FACE-TO-FACE. WE NEED TO KIND OF MOVE AHEAD WITH THE IDEA OF GIVING GUIDANCE ON THIS GRAY AND BLACK AND WHITE

TABLE THAT GEOFF BROUGHT UP. OKAY. IS THAT OKAY? SO WE'LL BRIEFLY ADJOURN TO THE FOOD THING THERE.

(A RECESS WAS TAKEN.)

CHAIRMAN LO: I'D LIKE TO RECONVENE. HOPEFULLY YOU ALL HAD A CHANCE TO GET YOUR PLATES FULL, BUT I WOULD LIKE TO SORT OF RESUME BECAUSE ACTUALLY WE HAD A VERY RICH AND THOUGHTFUL DISCUSSION. SO WHAT I WOULD LIKE TO DO IS, FIRST, ASK ELLEN TO MAKE SOME COMMENTS. I WAS GOING TO SUGGEST SORT OF WHAT I THOUGHT THE GROUP WAS SAYING WITH REGARD TO THE DIFFERENT RECOMMENDATIONS FOR REVISIONS THAT GEOFF HAD PROPOSED AND SEE IF WE CAN AT LEAST GIVE A SENSE OF THE COMMITTEE TO THE ICOC.

DR. FEIGAL: I JUST WANT TO MAYBE PROVIDE MORE OF A SUMMARY OF WHAT GEOFF HAS BEEN PRESENTING. I THINK IF YOU LOOK AT HUMAN EMBRYONIC STEM CELL DERIVATION AND USE OF DEIDENTIFIED HUMAN EMBRYONIC STEM CELLS, WE HAVEN'T CHANGED ANYTHING. THERE'S STILL A SCRO REVIEW CURRENTLY AND WE PROPOSE A CONTINUED SCRO REVIEW.

FOR DEIDENTIFIED HUMAN EMBRYONIC STEM CELLS, WE'RE STILL REQUIRING NOTIFICATION OF SCRO OR THE INSTITUTIONAL OFFICIAL. WE DO THAT CURRENTLY. WE ARE PROPOSING THAT STAYS THE SAME.

FOR THE IPS DERIVATION AND IDENTIFIABLE

AND USE OF IDENTIFIABLE AND USE OF DEIDENTIFIABLE, WE ARE ADDING THE OPTION OF IN ADDITION TO NOTIFICATION OF SCRO -- AS GEOFF MENTIONED, SOME INSTITUTIONS DON'T HAVE SEPARATE SCRO'S -- SO WE WANT TO ALLOW AN INSTITUTIONAL OFFICIAL TO BE NOTIFIED AS AN OPTION. SO IT'S REALLY A PRAGMATIC CHANGE AND WHY WE'RE OFFERING THAT ALTERNATIVE.

AND THEN THE OTHER ISSUE THAT WE'RE TALKING ABOUT REALLY IS IN THE USE OF DEIDENTIFIED OR THE USE OF -- BASICALLY DEIDENTIFIED IPS-DERIVED SOMATIC CELLS OR DEIDENTIFIED IPS. CURRENTLY IT'S NOTIFICATION OF SCRO OR INSTITUTIONAL OFFICIAL, AND WE'RE SUGGESTING IN THOSE TWO INSTANCES IT GOES TO NO NOTIFICATION.

THE REASON WHY WHAT WE'D LIKE YOU TO DO IS IF YOU THINK THERE'S A NEED TO NOTIFY THE SCRO OR AN INSTITUTIONAL OFFICIAL, COULD YOU PROVIDE SOME RATIONALE ON WHY THAT'S IMPORTANT AND WHAT YOU THINK IT WOULD ACHIEVE BY HAVING THAT NOTIFICATION? SO WHAT WOULD BE VERY HELPFUL TO US, ONE, I WANTED TO POINT OUT TO CLARIFY WHAT IT IS THAT'S DIFFERENT IN THE PROPOSED VERSUS THE CURRENT AND WHY WE'RE SUGGESTING IT. AND ALSO WE WANT TO CLARIFY, IF WE ARE SUGGESTING IT, IT SHOULD BE BASED ON SOME RATIONALE OF THE STEMNESS. IT SHOULD NOT JUST BE

BECAUSE IT'S UNCOMFORTABLE OR YOU HAVE SOME VAGUE CONCERNS ABOUT IT. IT SHOULD BE BASED ON IS THERE SOMETHING SPECIFIC ABOUT THE TYPE OF CELL THAT'S BEING UTILIZED THAT WOULD MAKE A DIFFERENCE IN TERMS OF WHETHER OR NOT IT REQUIRED NOTIFICATION.

SO MAYBE, BERNIE, IF THE CONVERSATION COULD FOCUS ON THOSE SPECIFIC POINTS, EVEN WITHOUT GAINING CONSENSUS, IT WOULD BE HELPFUL TO HEAR WHAT THE SPECIFIC REASONS ARE OF WHY NOTIFICATION IS REQUIRED, WHAT YOU'D WANT THOSE OFFICIALS OR THE SCRO TO ACTUALLY DO WITH THAT INFORMATION, AND REALLY LET'S NOT TALK ABOUT CAPACITY OF CIRM TO CHECK FOR COMPLIANCE. THAT'S SOMETHING WE CAN DO. I'D RATHER HAVE IT FOCUSED ON WHY ARE WE ASKING FOR IT TO BE DONE.

DR. WAGNER: SO MAYBE IT WOULD BE HELPFUL IF I WALK YOU THROUGH AN EXAMPLE OF HOW THIS HAS BECOME A PROBLEM IN TERMS OF DEIDENTIFICATION. AND IT DOESN'T APPLY TO ALL IPS CELLS. IT APPLIES SPECIFICALLY TO IPS CELLS THAT ARE DERIVED FROM PATIENTS WITH GENETIC DISEASES.

SO IN CONTRAST TO, FOR EXAMPLE, AN ES CELL LINE FOR WHICH WE DON'T HAVE ANY A PRIORI KNOWLEDGE OF A GENETIC DISEASE, FOR EXAMPLE, WHERE WE LOOK AT IDENTITY PERHAPS AS MEASURED BY POLYMORPHISMS TO SAY

THIS IS THE CELL LINE FOR WHICH WE MADE.

IN ANY EVENT, IN CONTRAST, AT LEAST THE PATIENT POPULATIONS THAT I TAKE CARE OF, WHETHER IT BE FANCONI ANEMIA, SICKLE CELL DISEASE, EPIDERMOLYSIS BULLOSA, A VARIETY OF GENETIC DISEASES, PATIENTS THESE DAYS ARE GIVEN A COPY OF THEIR SPECIFIC MUTATION. THE PATIENTS CAN ACTUALLY RECITE TO YOU WHERE THE MUTATION IS IN WHICH EXON OF THE GENE THAT WE'RE TALKING ABOUT.

AND SO AS PART OF THAT CELL LINE, THAT WOULD BE PART OF WHAT IS GIVEN OUT TO THE PUBLIC. I'M MAKING THIS CELL LINE FROM A PATIENT WITH FANCONI ANEMIA WITH THIS SPECIFIC MUTATION. THAT IS NOW PUBLIC KNOWLEDGE. IT IS SOMETHING NOW THAT THE PATIENT CAN IDENTIFY AS MINE BECAUSE THE CHANCE OF SOMEONE ELSE HAVING THAT EXACT SAME MUTATION, ALTHOUGH NOT ZERO, IT'S VERY UNLIKELY.

SO, THEREFORE, WHAT IS DEIDENTIFIED HAS A DIFFERENT MEANING BECAUSE EVEN THOUGH I MAY PUT A DIFFERENT UPN NUMBER AS A METHOD OF DEIDENTIFICATION, IT'S SOMETHING THAT IS STILL IDENTIFIABLE BY THE PATIENT HIM OR HERSELF IN THE FUTURE. SO, FOR EXAMPLE, BECAUSE I'M NOW DEVELOPING AN IPS CELL LINE THAT HAS MULTIPOTENTIAL, PLURIPOTENTIAL POTENTIAL, IF I DO MAKE A HEART, IF I

DO MAKE GAMETES, IF I DO MAKE ANYTHING THAT POTENTIALLY HAS COMMERCIAL VALUE, EVEN THOUGH THEY MAY HAVE TOLD THAT COULD HAVE HAPPENED BEFORE, THE FACT IS THAT IT'S NO LONGER DEIDENTIFIABLE. IT IS NOW MINE. ESPECIALLY IF WE, FOR EXAMPLE, CIRM OR NIH OR ANYBODY ELSE HAS NOW PUT SUFFICIENT RESOURCES INTO A CELL LINE BECAUSE IT HAS SOME VALUE, I THINK WE NEED TO THINK ABOUT -- WE JUST WANT TO MAKE SURE THAT WE DO EVERYTHING WE CAN TO VERIFY THAT WHEN SOMEONE SAYS IT'S DEIDENTIFIED AND THAT SOMEONE SAYS HOW THESE CELLS ARE GOING TO BE USED NOW AND WHAT NEW THINGS COULD DEVELOP IN THE FUTURE, WE JUST HAVE TO BE AWARE THAT THE MEANING OF DEIDENTIFIED IN THIS PARTICULAR CONTEXT MAY NOT ALWAYS BE DEIDENTIFIED.

THAT'S THE ONLY POINT I WANT TO MAKE. IT'S SOMETHING I DIDN'T REALLY REALIZE AND APPRECIATE.

AND THE OTHER THING IS IN CONTRAST TO ES CELL LINES, I THINK, IS THAT ES CELL LINES, THE EMBRYO COMES FROM AN IVF CENTER, WHICH IS SEPARATE, I THINK, THE MAJORITY OF CASES, FROM THE PERSON DOING THE ES DERIVATION. IN CONTRAST, THE PERSON WHO TAKES CARE OF THESE GENETIC DISEASES IS THE ONE MAKING THIS IPS DERIVATION, I WOULD SAY, PROBABLY IN AT LEAST MANY CASES. SO, THEREFORE, I HAVE NOW

TAKEN GREAT LENGTHS TO NOW SEPARATE THE INVESTIGATOR FROM THE DERIVATION. BUT EVEN SO, IT'S STILL DIFFICULT BECAUSE THEY KNOW THAT IT'S AN FA PATIENT OR THEY KNOW IT'S SKIN FROM A PATIENT. THEY KNOW WHEN THAT SKIN WAS OBTAINED. IT'S JUST STILL VERY DIFFICULT EVEN THOUGH I'M NOW PUTTING MYSELF AS AN IN BETWEEN.

JUST SO YOU KNOW. I'M NOT SAYING THAT'S TRUE FOR EVERYONE, BUT IT IS SOMETHING THAT I THINK THAT THE ESCRO OR SOMEONE JUST NEEDS TO BE AWARE OF, THAT I CAN CHECK OFF A BOX AND SAY IT'S DEIDENTIFIED BECAUSE I GAVE IT A UPN NUMBER. THAT'S WHAT WE TYPICALLY WOULD DO IF I'M STORING CORD BLOOD. I CAN SAY IT'S TRULY DEIDENTIFIED, BUT IN THIS CASE I'M AFRAID THAT IT'S NOT ALWAYS DEIDENTIFIED.

DR. FEIGAL: MY INTERPRETATION OF WHAT YOU ARE SAYING, THEN, IS THAT OUR USE OF THE TERM "DEIDENTIFIED" FOR IPS CELLS FROM INDIVIDUALS WITH GENETIC DISEASES IS QUESTIONABLE.

DR. WAGNER: THAT'S RIGHT.

DR. FEIGAL: THAT'S WHY YOU WANT TO TURN IT BACK INTO MORE OF AN IDENTIFIABLE CATEGORY. RIGHT NOW WHAT WE HAVE, EVEN FOR IDENTIFIABLE, IS NO NOTIFICATION OR AN INSTITUTIONAL OFFICIAL AS AN OPTION. YOU WANTED IT AS A MINIMUM THAT OPTION FOR

THE GENETICALLY DEFINED DISEASES.

DR. WAGNER: THAT'S RIGHT. SO I WOULD MAKE IT -- THAT'S INDEED CORRECT. HOWEVER, AS YOU KNOW, I AM ALSO SUGGESTING THAT FOR IDENTIFIABLE, IT SHOULD BE MORE LIKE AT THE TOP LEVEL LIKE THE ES DERIVATION.

DR. FEIGAL: OKAY. THAT'S HELPFUL TO HEAR THAT.

CHAIRMAN LO: LET ME TRY TO HELP ORGANIZE THIS. I WANT TO START BY PROVIDING A LITTLE BIT OF BACKGROUND, ONE, TO PICK UP ON WHAT YOU WERE JUST SAYING WITH REGARD TO IDENTIFIABLE. SO PAT ISN'T HERE, BUT, GEOFF, YOU KEEP ME ON THE STRAIGHT AND NARROW HERE.

SO IDENTIFIABLE HAS A SPECIFIC MEANING IN THE FEDERAL REGULATIONS, 45 CFR 486, THE COMMON RULE, AND THAT CANNOT BE READILY ASCERTAINED BY THE INVESTIGATOR, THE RESEARCHER. AND OHRP HAS INTERPRETED THAT IN CERTAIN REGULATORY WAYS TO SAY THAT IF YOU'VE STRIPPED OFF -- IF YOU HAVE SOMETHING TO WHICH YOU'VE ATTACHED A CODE AND YOU HAVE CERTAIN ARRANGEMENTS, EVEN IF SOMEONE ELSE KEEPS THE CODE, THE PERSON DOING THE RESEARCH DOESN'T KNOW THE CODE, THAT'S DEIDENTIFIED FOR REGULATORY PURPOSES UNDER THE COMMON RULE.

NOW, YOU BRING UP TWO VERY INTERESTING POINTS. FIRST, THAT IF YOU'RE THE CLINICIAN WHO TOOK CARE OF THE PATIENT FROM WHOM THE CELLS WERE DERIVED AND HAVE AN ONGOING INTEREST IN THE RESEARCH, EVEN TO THE POINT OF DERIVING THE IPS CELL LINE, YOU CAN STRIP OFF ALL THE HIPAA IDENTIFIERS YOU WANT, BUT YOU WILL KNOW WHO THAT -- YOU WILL BE ABLE WALK BACK. PROBABLY SOME OF YOUR STAFF, THE NURSES WHO TOOK CARE OF IT. THAT'S ONE COMPLICATION I THINK YOU NICELY POINTED OUT. AND ELLEN SUGGESTED WE COULD FIX THAT BY SAYING, WELL, WE'RE SORT OF GOING TO CHANGE THE DEFINITION OF IT.

YOU ALSO RAISED ANOTHER POINT, WHICH IS HOW ABOUT IF IT'S IDENTIFIABLE TO THE PERSON WHOSE CELLS WERE USED? THEY MAY KNOW, EVEN IF THE RESEARCHER DOESN'T, AND DOES THAT HAVE REGULATORY OR ETHICAL SIGNIFICANCE WHICH ISN'T CAPTURED IN THE CURRENT COMMON RULE? SO THAT'S A WHOLE NEW SET OF ISSUES.

DR. WAGNER: AND IT'S TRUE. THE THING IS THAT THERE'S NO ONE MORE INTERESTED IN THIS RESEARCH THAN THESE PATIENTS WITH THESE DISEASES BECAUSE THEY'RE HOPING, BY GIVING THEIR SAMPLE OF SKIN OR WHATEVER THE TISSUE IS, THAT IT WILL RESULT IN A THERAPY WHICH WILL HELP THEIR CHILD OR THEM. SO

THEY'RE PAYING VERY CLOSE ATTENTION. AND I HAVE PEOPLE ALREADY GUESSING. WHEN THEY SEE REPORTS COMING OUT OF --

CHAIRMAN LO: THIS IS MY CELLS.

DR. WAGNER: THESE ARE MY CELLS THAT YOU'RE REPORTING ON IN *BLOOD* OR IN *STEM CELLS* OR WHATEVER THE PROJECT IS. SO THEY'RE ALREADY DOING IT. AND SO I DIDN'T APPRECIATE THAT WHEN I FIRST GOT INVOLVED IN THIS. I JUST TREATED IT LIKE EVERYONE ELSE AND SO DID THE IRB. ALL THESE STUDIES HAVE BEEN DONE WITH IRB APPROVAL AS BEING DEIDENTIFIED, BUT THEY WEREN'T.

CHAIRMAN LO: SO THOSE ARE SORT OF FOOTNOTES TO IDENTIFIABLE IN ALL THIS.

SECONDLY, I WANT TO POINT OUT, WHICH GEOFF REALLY FOCUSED ME IN ON, IS ONE OF THE SENSITIVE USES OF STEM CELLS HAS TO DO WITH THE CREATION OF HUMAN GAMETES. AND HE REMINDED ME THAT IF YOU LOOK AT 100070(A), IT'S CIRM-FUNDED RESEARCH, BLAH, BLAH, BLAH, INVOLVING THE CREATION OF HUMAN GAMETES MAY NOT COMMENCE WITHOUT SCRO COMMITTEE REVIEW AND APPROVAL IN WRITING. SO WE SORT OF TUCKED THAT INTO ONE OF THE PROVISIONS WHICH SAYS YOU REALLY HAVE TO GET REVIEW AND APPROVAL IN WRITING TO DO ANY WORK DEALING WITH DERIVATION OF -- CREATION OF HUMAN

GAMETES.

AND, IN FACT, THE WAY I READ THIS, GEOFF, IT DOESN'T MENTION IDENTIFIED OR DEIDENTIFIED. SO THAT ONE SORT OF PARADIGMATIC CASE OF SOMETHING SENSITIVE WE'VE SORT OF SINGLED OUT ALREADY IN THE REGULATIONS. IT'S JUST YOU HAVE TO BE AS SMART AS GEOFF TO KNOW WHERE TO LOOK.

DR. LOMAX: THAT WAS, AGAIN, TWO YEARS AGO. THAT WAS DIRECTLY OUT OF THESE DELIBERATIONS, AND WE IMPLEMENTED IT IN A WAY THAT WAS INDEPENDENT OF THIS. IT'S AN EXAMPLE, AGAIN, OF A USE CRITERIA IN TERMS OF THE REGULATIONS.

CHAIRMAN LO: I'M GOING TO SUGGEST -- GEOFF, I THINK THIS WAS VERY -- THIS C AND D IS USEFUL. I'M GOING TO TRY AND WALK US THROUGH THE DIFFERENT LINES. THE TOP LINE, HESC DERIVATION, WE'RE NOT PROPOSING ANY CHANGES, AND I HAVEN'T HEARD ANYBODY SAY THAT WE HAVE CONCERNS.

LET'S TALK ABOUT DERIVATION FIRST AND THEN THE USES. SO IN TERMS OF THE SECOND LINE, DERIVATION WITH IDENTIFIABLE SOMATIC CELLS, I WANT TO REMIND US THAT CIRM IS ISSUING GUIDANCE, SORT OF SUGGESTIONS, BEST PRACTICES, IF YOU WILL, ON HOW TO OBTAIN INFORMED CONSENT FROM PEOPLE DONATING SOMATIC CELLS FOR STEM CELL DERIVATION. SO ON THE SORT OF

EDUCATIONAL BEST PRACTICE FRONT, WE'RE GOING TO WORK ON IT FROM THAT ANGLE.

WHAT IS BEING PROPOSED IS THAT WE NOT WEAKEN, WE NOT REMOVE THE NOTIFICATION OF THE SCRO. IF IT INVOLVES HUMAN SUBJECTS RESEARCH, IT WILL STILL REQUIRE IRB APPROVAL OF THE CONSENT PROCESS. BUT, AS ELLEN SAID, FOR THOSE INSTITUTIONS THAT ACTUALLY DON'T HAVE A SCRO, BUT WANT TO DERIVE IPSC LINES FROM IDENTIFIABLE MATERIALS, WE'RE GOING TO OFFER THE OPTION OF NOTIFYING THE RESPONSIBLE INSTITUTIONAL OFFICIAL.

AND I GUESS JEFF -- I'M TRYING TO REMEMBER THIS RIGHT -- BROUGHT UP THE QUESTION, AND NICOLE. JUST LEAVE IT AT THAT. LET'S TALK ABOUT THAT FIRST WITH IDENTIFIABLE SOMATIC CELL DERIVATION WITH IDENTIFIABLE SOMATIC CELLS. HOW DO WE FEEL ABOUT THAT SUGGESTION WITH GEOFF'S CAVEAT -- WELL, NO, THESE ARE IDENTIFIABLE. AND THEN WE'RE SAYING IT MAY BE A LITTLE BROADER THAN THE NIH DEFINITION OF IDENTIFIABLE.

THOUGHTS ON THIS? DO WE HAVE CONCERNS ABOUT ALLOWING THE RESPONSIBLE INSTITUTIONAL OFFICIAL NOTIFICATION OPTION?

DR. ROBERT TAYLOR: BERNIE, I'M JUST TRYING TO THINK OF WHAT THE SCENARIO WOULD BE HERE.

SO LET'S SAY THIS WOULD BE POTENTIALLY A SMALL OPERATION USING WESTERN IRB TO OBTAIN A SKIN BIOPSY FROM SOMEONE THEY WANT TO MAKE AN IPS CELL OUT OF. IS THAT THE RIGHT SCENARIO? I'M SORT OF WONDERING WHO'S NOT GOING TO HAVE A FUNCTIONAL SCRO THAT WE'RE CREATING THIS EXEMPTION FOR.

CHAIRMAN LO: ELLEN'S EXAMPLE WAS, YOU KNOW THIS BETTER THAN I, SMALL RESEARCH INSTITUTION.

DR. SCHUELE: I'M DR. BIRGITT SCHUELE FROM THE PARKINSON'S INSTITUTE IN SUNNYVALE. SO WE'RE A LITTLE SOUTH OF SAN FRANCISCO ACROSS MOFFET FIELD. SO WE'RE USING OUTSIDE IRB'S LIKE THE EL CAMINO HOSPITAL OR WIRB TO GET IRB APPROVAL FOR OUR STUDIES. AND THEN FOR THE EARLY TRANSLATIONAL GRANT THAT WE GOT THROUGH CIRM, WE HAD INITIALLY SCRO APPROVAL THROUGH THE SERVICE THAT WAS AVAILABLE TILL END OF LAST YEAR.

SO NOW WE ARE KIND OF IN LIMBO AND WE DON'T REALLY KNOW. SO WE HAD -- ARE WE STILL HAVING A GRANT WHERE WE'RE ALLOWED TO DERIVE IPS CELLS FROM HUMAN SKIN CELLS? THEY HAVE BEEN ALL DERIVED NOW, AND NOW WE'RE DOING IN VITRO RESEARCH ON THEM. NO TRANSPLANTATION INTO ANIMALS AT THIS POINT. SO NOW THE QUESTION FOR US IS HOW DO WE HANDLE THIS? THE LINES HAVE BEEN DERIVED AND NOW IN VITRO RESEARCH

HAS BEEN DONE TO LOOK AT DISEASE MECHANISMS FOR PARKINSON'S DISEASE.

DR. LOMAX: I MIGHT ADD FROM THE CIRM PERSPECTIVE, WE'VE GONE OUT AND DONE A SITE VISIT. WE'VE REVIEWED AND THEY HAVE BEEN VERY GENEROUS IN PROVIDING US CONSENT DOCUMENTS THAT HELPED US DEVELOP OUR OWN MODELS, AND WE WILL HAVE A PRESENTATION LATER TODAY WHERE WE'VE ASKED THEM TO REPORT BACK ON THAT EXPERIENCE JUST TO KIND OF GIVE YOU A FEEL FOR HOW WE ENGAGE AND INVOLVE OURSELVES IN THESE SITUATIONS AND TRY TO DEVELOP A SENSE TO WHAT EXTENT THE INSTITUTION ITSELF HAS THE CAPACITY TO OPERATIONALIZE THE TYPES OF THINGS THAT WE'RE LOOKING FOR AS BOTH THE COMMITTEE AND CIRM.

DR. SCHUELE: I WANT TO ADD IN THIS CASE THESE ARE IDENTIFIABLE SOMATIC CELLS, AND WE'RE WORKING ON GENETIC FORMS OF PD. SO THE POINT THAT WAS RAISED, THAT YOU CAN'T TRULY DEIDENTIFY THESE INDIVIDUALS, THAT'S THE CASE HERE TOO. I WAS THE STUDY DOCTOR TAKING THE SKIN BIOPSIES, AND THEN STUDY CODES WERE ASSIGNED, BUT STILL THERE'S NO WAY AROUND TO TRULY DEIDENTIFY SOME OF THOSE INDIVIDUALS.

CHAIRMAN LO: ROB, IS THAT --

DR. ROBERT TAYLOR: THAT WAS SORT OF WHAT

I WAS IMAGINING. THANK YOU.

CHAIRMAN LO: SO YOUR THOUGHTS ON THAT SECOND LINE. DO WE, AS A SENSE OF THE COMMITTEE, AGREE WITH THIS NEW PROPOSAL WITH ALL THE CAVEATS ABOUT WHAT IS IDENTIFIABLE THAT WE'VE DISCUSSED?

DR. WAGNER: CAN I ASK JUST A QUESTION? AND THAT IS THAT IF WE GO THAT ROUTE, CAN YOU TELL ME WHAT THE DIFFERENCE IS OR CAN YOU TELL ME WHY WE NEED AN ESCRO FOR HESC DERIVATION? I'M JUST ASKING THE QUESTION. IF WE'RE STILL TALKING ABOUT PLURIPOTENTIAL STEM CELLS, ONE BEING ES-DERIVED OR EMBRYONIC, ONE BEING FROM ADULT TISSUES, WHAT IS IT ABOUT THE ESC DERIVATION THAT REQUIRES ESCRO? AND HOW IS THAT DIFFERENT FROM IPSC BECAUSE EVEN THOUGH, OF COURSE, SOMEBODY WILL SAY THAT'S OBVIOUS, IT MAY NOT BE ENTIRELY OBVIOUS THE REASONS BECAUSE IF WE REQUIRE ESCRO FOR THAT, WE SHOULD MAKE SURE THAT THERE'S NOTHING THAT IS -- IT'S AT LEAST CONSISTENT BETWEEN THE TWO PLURIPOTENTIAL STEM CELL SOURCES.

DR. LOMAX: THE NATIONAL ACADEMIES ARTICULATION OF THAT IS THAT THERE WOULD NEVER BE AN IRB IN THAT CIRCUMSTANCE BECAUSE IT'S NOT A HUMAN SUBJECT. SO IT'S THE NOTION THAT THERE'S SOME SORT OF CHECKPOINT IN THE DERIVATION PROCESS.

DR. WAGNER: IS THAT THE ONLY REASON?

DR. LOMAX: I WOULD HAVE TO GO BACK AND LOOK AT THE NATIONAL ACADEMIES' REPORT, BUT IT WAS A DRIVING FORCE IN TERMS OF THAT REQUIREMENT, AS I RECALL.

CHAIRMAN LO: SO TO ADD ONTO THAT, I THINK IT'S WHAT JEFF BOTKIN SAID EARLIER ABOUT MISCLASSIFICATION BY INVESTIGATORS. SO THAT I THINK THERE ARE STANDARDS FOR WHAT THE PROCUREMENT AND CONSENT PROCESS NEEDS TO BE FOR STEM CELL DERIVATION IN LIGHT OF THE SENSITIVITY OF EMBRYO RESEARCH. SO EVEN THOUGH THEY'RE DEIDENTIFIED TO THE INVESTIGATOR, THERE'S KIND OF A BACKTRACK TO MAKE SURE THAT THE WOMAN OR COUPLE IN IVF WHOSE EMBRYOS ARE BEING USED GAVE EXPRESS PERMISSION FOR RESEARCH, AND STEM CELL RESEARCH IN PARTICULAR, SO THAT THAT CHECK WOULD NOT NECESSARILY HAPPEN IF WHEN THEY ARRIVE AT THE LAB WHERE THE DERIVATION IS TAKING PLACE, THEY'VE ALREADY BEEN DEIDENTIFIED BECAUSE THE IVF CLINIC GENERALLY HAS STRIPPED OFF THE IDENTIFIERS AND GIVEN THE CODE NUMBER.

DR. WAGNER: AND THOSE TWO THINGS, THEY CLEARLY DIFFERENTIATE BETWEEN ES VERSUS IPS, EXCEPT THAT I THOUGHT YOU MIGHT GO ONE STEP FURTHER, WHICH WAS GOING TO BE HOW THOSE CELLS MIGHT BE USED IN THE CONTEXT OF CHIMERISM IN ANIMAL MODELS. AND ALTHOUGH

WE MAY BE TALKING ABOUT IN VITRO WORK, ISN'T PART OF THE DEFINITION OF AN IPS CELL THAT IT ACTUALLY IS CAPABLE OF DIFFERENTIATING INTO THE THREE LINEAGES IN AN ANIMAL MODEL? SO THERE'S SOME THINGS THAT WE HAVE TO FIGURE OUT. AND AT LEAST IF THE TWO ARE COMPLETELY SEPARABLE AND THE REASONS FOR WHY ONE GETS ESCRO REVIEW AND THE OTHER DOESN'T, WELL, THEN FINE.

I WAS JUST -- THE REASON WHY I WAS A BIT QUESTIONING THAT EARLIER AND GOING BEYOND JUST INFORMING AN INSTITUTIONAL OFFICIAL WAS BECAUSE I COULD IMAGINE WHERE THERE'S OVERLAP BETWEEN THE TWO FOR WHICH AN ESCRO MIGHT BE IMPORTANT.

CHAIRMAN LO: AGAIN, I THINK WHAT I HEARD BEFORE LUNCH IS THE SENSE THAT LET'S SORT OF SEPARATE OUT THE USES AND THE DERIVATION.

DR. WAGNER: I'M JUST TALKING ABOUT DERIVATIONS.

CHAIRMAN LO: FOCUS ON THE DERIVATIONS.

SO WITH ALL THAT, ARE THERE ANY -- LET ME FRAME IT THE OTHER WAY. ARE THERE ANY DEEP CONCERNS OR OBJECTIONS TO THE PROPOSED STANDARD OF ALLOWING THE INSTITUTIONAL OFFICIALS AN OPTION FOR THE NOTIFICATION FOR DERIVATION OF IPSC'S FROM IDENTIFIABLE SOMATIC CELLS? SO IS THE SENSE --

DR. ROBERT TAYLOR: I JUST HAVE TO ADMIT THAT IT SEEMS TO ME THAT KIND OF THE OVERSIGHT THROUGH ONE MECHANISM VERSUS THE OTHER IS QUITE DIFFERENT, AN INSTITUTIONAL OFFICIAL VERSUS A SCRO. IT JUST STRIKES ME THAT THOSE AREN'T THE SAME TYPES OF OVERSIGHT BODIES.

DR. LOMAX: CAN I JUST GIVE ONE RESPONSE TO ROB? AGAIN, THIS IS JUST BASED ON THE EVIDENCE WE HAVE IS THAT TYPICALLY IN A NOTIFICATION SITUATION, THE INSTITUTION WILL GO TO WHOEVER IS ADMINISTERING THE OVERSIGHT COMMITTEE, AND THEY'LL TYPICALLY TAKE A LOOK AT IT, AND IN THEIR TRIAGE IT WOULDN'T BE THIS COMMITTEE LOOKING AT IT. SO THIS IS SUBSTANTIALLY SIMILAR. IT'S SOMEBODY WHO'S BEEN DEPUTIZED BY THE INSTITUTION TO MAKE A DETERMINATION. BECAUSE WE'VE NOT MOVED INTO THAT THRESHOLD OF FULL REVIEW, THE CRITICAL THING AND THE MOST IMPORTANT THING, SCRO OR NO SCRO, IS THAT THERE IS INDIVIDUAL CAPACITY WITHIN THAT INSTITUTION TO LOOK AT THAT, UNDERSTAND IT IN RELATION TO OUR REGULATIONS, AND MAKE THE RIGHT DECISION.

AND, AGAIN, HAVING BEEN TO THE PARKINSON'S INSTITUTE, MY PERSONAL VIEW IS I'M CONFIDENT IN THAT ABILITY. NOW, THE IMPORTANT THING IS TO MAKE SURE, WHEN IT'S BEING DONE, WE CONTINUE TO BE CHECKING.

BUT I WOULD SAY THEY'RE SUBSTANTIALLY SIMILAR. NOTIFICATION OF EITHER THE SCRO OR THE INSTITUTIONAL OFFICIAL OPERATIONALLY IS A SUBSTANTIALLY SIMILAR EXERCISE.

DR. PRIETO: GEOFF, QUESTION ON SOMETHING YOU ALLUDED TO AND THE PARKINSON'S INSTITUTE SPEAKER ALSO DID ABOUT WHAT HAPPENED TO THE ABILITY TO CONTRACT OUT OR USE ANOTHER SCRO? MAYBE I SHOULD KNOW THIS ALREADY AND MISSED SOMETHING.

DR. LOMAX: OUR REGULATIONS ALLOW THE USE OF INDEPENDENT THIRD-PARTY SCRO'S OR COLLABORATIVE SCRO'S. THEY DO NOT NEED TO BE CENTERED WITHIN THE INSTITUTION OR GRANTEE INSTITUTION.

HOWEVER, AT THIS TIME WE ARE NOT AWARE OF ANY CAPACITY OUTSIDE OF THE INSTITUTIONS THAT CAN BE USED. THERE'S NO COMMITTEES, FOR EXAMPLE, OUT THERE. THERE WAS A COMMITTEE THAT WAS DOING CONTRACT SERVICES. WE EVALUATED THEM A NUMBER OF TIMES. THEY WERE DOING OUTSTANDING WORK. THEY ARE NO LONGER OFFERING THOSE SERVICES. SO WHAT WE'RE FINDING IS THE ABILITY FOR INSTITUTIONS THAT DON'T HAVE THE CAPACITY TO CREATE THEIR OWN COMMITTEES IS EXTREMELY LIMITED UNLESS THEY CAN GET INTO A COLLABORATIVE RELATIONSHIP WITH AN EXISTING SCRO, AND THAT'S GETTING TO BE VERY DIFFICULT.

CHAIRMAN LO: WHICH ACTUALLY DOES HAPPEN. SO SAN DIEGO HAS THAT, UCSF ACTS AS THE SCRO OF RECORD FOR UC SANTA CRUZ. SO THOSE ARRANGEMENTS DO EXIST, BUT THEY REQUIRE SOME SORT OF INSTITUTIONAL PARTNERSHIP ARRANGEMENT.

DR. PRIETO: SO IT HAS NOT BECOME IMPOSSIBLE. IT'S JUST BECOME MORE DIFFICULT BECAUSE OF UNAVAILABILITY OF THIS PARTICULAR CONTRACT.

CHAIRMAN LO: THAT'S RIGHT. SO I'M NOT HEARING ANY, GIVEN SORT OF THE FOOTNOTE CAVEATS WE'VE RAISED, AND I GUESS THE OTHER THING I WOULD PUT IN IS PROBABLY WE WOULD LIKE TO SEE SOME MORE THINKING ABOUT DIRECT REPROGRAMMING AS OPPOSED TO IPS, BUT WE THINK THIS AMENDMENT IS FINE.

NOW LET'S THEN SKIP --

DR. WAGNER: JUST WITH ONE CAVEAT. BASED ON WHAT YOU SAID OR WHAT'S BEEN SAID IS THAT IN REALITY, EVEN IF IT'S AN INSTITUTIONAL OFFICIAL, THAT INSTITUTIONAL OFFICIAL WILL SEEK HELP APPROPRIATELY. MAYBE THAT SHOULD BE DEFINED BECAUSE THE THING IS OTHERWISE, IF YOU JUST SAY INSTITUTIONAL OFFICIAL, YOU DON'T HAVE ANY IDEA WHETHER OR NOT IT'S JUST THAT PERSON SAYING LOOKS OKAY TO ME VERSUS ME UNDERSTANDING WHAT THE NUANCES ARE OF THE STEM CELL RESEARCH IN 2013 VERSUS 2012.

IN ANY EVENT, I'M JUST WONDERING IF THERE SHOULD BE SOME STATEMENT THAT SAYS WHAT IS EXPECTED IS A PROCESS -- WHAT THE PROCESS THAT A SCRO WOULD DO IS NOW BEING ASKED OF THIS INDIVIDUAL.

CHAIRMAN LO: GEOFF'S NODDING AND HAS GOT HIS FINGER ON THE PULSE HERE.

DR. LOMAX: IT'S NOT THE EXACT ANSWER YOU'RE LOOKING FOR, BUT THE WAY WE'VE HANDLED THAT IN A REGULATORY CONTEXT IS TO MAKE SOMEBODY REALLY IMPORTANT RESPONSIBLE FOR THAT TO MAKE SURE WITH A VIEW THAT IT'S DONE RIGHT. SO WE SAY THE DEFINITION OF INSTITUTIONAL OFFICIAL IS A CHANCELLOR, CHIEF EXECUTIVE, OR PERSON WITH PLENARY AUTHORITY WHO THEN HAS THE POWER TO DESIGNATE AN INDIVIDUAL. AGAIN, I DON'T KNOW IF THAT SATISFIES YOUR CONCERN, BUT THE IDEA THAT IT'S COMING DOWN FROM SOMEBODY AT HIGH LEVEL EXECUTIVE IN THE INSTITUTION.

CHAIRMAN LO: THE REGULATORY MOVE IS TO SAY HOLD THE HIGH LEVEL OFFICIAL RESPONSIBLE. THEY MAY DELEGATE IT; BUT IF IT'S A PROBLEM, THEY ANSWER TO IT. IT'S KIND OF BEHIND PEOPLE HAVING TO SIGN -- CEO'S HAVING TO SIGN FINANCIAL STATEMENTS. YOU DON'T DO THEM YOURSELF, BUT YOU BETTER BE REALLY SURE THE PERSON YOU DELEGATE IT TO IS RIGOROUS.

DR. WAGNER: ALL I'M SUGGESTING IS THAT

YOU SOMEWHERE IN SOME WAY DEFINE WHAT THAT MEANS. WHEN YOU SIGN THIS, THAT THE EXPECTATION IS YOU'RE DOING THIS, THIS, THIS, AND THIS SO THAT THE PERSON KNOWS. I'M ASKED TO SIGN FORMS FOR OTHER FACULTY ALL THE TIME, AND I'M NOT QUITE SURE WHY I'M SIGNING IT.

CHAIRMAN LO: WHERE IS THE STICKER THAT SAYS SIGN HERE. LET ME JUST SAY, FIRST OF ALL, TO TRY AND PUT IT IN CONTEXT, THERE ARE THESE GUIDELINES FOR CONSENT FOR DONATION TO DERIVE STEM CELL LINES WHICH HOPEFULLY WILL BECOME A BEST PRACTICE. AND I THINK THEN THERE ARE EDUCATIONAL THINGS THAT HAPPEN WHEN GEOFF GOES AND DOES SITE VISITS. SO I THINK IT'S A QUESTION OF HOW MUCH DO WE WANT TO PUT IN A REGULATION AS TO SORT OF USING EDUCATION AND GUIDANCE. BUT I THINK WE SHOULD -- THE TRANSCRIPT WILL REFLECT THERE WAS A CONCERN THAT IS THE NOTIFICATION REALLY -- DO THE PEOPLE TO WHOM NOTIFICATION IS GIVEN REALLY UNDERSTAND WHAT THEY'RE BEING ASKED TO DO.

DR. ROBERTS: AT THIS POINT THE MENTION OF THE IRB, THE IRB MUST APPROVE THE PROTOCOL, WOULD THAT HAVE BEEN A PRIOR APPROVAL, PRIOR TO THIS POINT WHERE THE INSTITUTIONAL OFFICIAL IS NOTIFIED? IN OTHER WORDS, COULD THE IRB APPROVAL TAKE CARE OF

SOME OF THESE CONCERNS ABOUT THE INSTITUTIONAL OFFICIAL NOT UNDERSTANDING AND JUST...

DR. ROBERT TAYLOR: GIVEN THE SCENARIO, THIS IS GOING TO BE A PLACE THAT ALSO DOESN'T HAVE AN IRB.

DR. LOMAX: THAT'S NOT A PROBLEM BECAUSE IRB'S ARE READILY AVAILABLE. THERE'S A HISTORY.

CHAIRMAN LO: INDEPENDENT IRB'S THAT ARE ACCREDITED.

DR. ROBERTS: ALSO I WOULD WANT TO MAKE SURE THAT THIS IS PART OF THE REQUIREMENT, THAT AN IRB DOES APPROVE THE PROTOCOL.

DR. LOMAX: ABSOLUTELY. WE REVIEW THE IRB SUBMISSION. WE LOOK FOR THAT.

WITH REGARD TO THE FRONT PART OF YOUR QUESTION, WE'VE SEEN BOTH SCENARIOS. IT CAN BE A NEW APPROVAL SPECIFIC TO THE PROTOCOL. IT CAN BE AN ADDITION TO AN EXISTING LARGER SCALE, PARTICULARLY A CLINICAL STUDY THAT'S A LARGER STUDY, THE CIRM PIECE CAN COME IN AS PART OF THE EXISTING PROTOCOL. IT WOULD TYPICALLY BE AN AMENDMENT TO THE IRB BECAUSE IT WOULD -- BECAUSE OF THE NATURE -- BECAUSE THE GRANT WOULD BE A CHANGE IN THE PROTOCOL. BUT WE HAVE SEEN A VARIETY OF THINGS. THE MOST COMMON IS AN IRB APPROVAL SPECIFIC TO THE CIRM PROTOCOL, BUT

THAT'S A NOT A HUNDRED PERCENT OF THE TIME.

DR. ROBERTS: IT'S AN AMENDMENT THOUGH. DOESN'T IT HAVE TO GO BACK TO THE IRB FOR APPROVAL?

CHAIRMAN LO: YES.

DR. ROBERTS: SO ONE SUGGESTION I WOULD HAVE IN THINKING ABOUT THIS IS JUST MAKING SURE THAT THE IRB IS INVOLVED AT THE RIGHT TIME TO ADD TO THE INSTITUTIONAL OFFICIAL APPROVING IT.

DR. LOMAX: THAT'S RIGHT. WE HAVE SOME OF THE SCIENCE STAFF HERE. I ALSO TRAIN OUR STAFF IN TERMS OF PRE-AWARD NOTIFICATION. I DON'T KNOW HOW MANY TIMES I'VE SAID OVER AND OVER AGAIN IF YOU SEE HUMAN SUBJECTS RESEARCH, COME TALK TO ME, PLEASE. THOSE ONES ARE IMMEDIATELY ON THE TOP OF OUR LIST TO UNDERSTAND EXACTLY WHAT IS THE NATURE OF THE HUMAN SUBJECTS RESEARCH, AND WE ASK A LOT OF -- I ALWAYS ENCOURAGE THE SCIENCE OFFICERS TO ASK PROBES IF THERE'S ANY UNCERTAINTY BECAUSE I THINK THAT'S THE IMPORTANT PART, THAT SOMEONE IS LOOKING AT THIS, THEY'VE GOT SMART QUESTIONS, AND I THINK THAT SENDS AN IMPORTANT MESSAGE. I THINK THAT'S SOMETHING YOU NOW ALL KNOW WHY I REPEAT THAT OVER AND OVER AGAIN.

CHAIRMAN LO: GEOFF, IF I CAN JUST MAKE A FRIENDLY SUGGESTION, THAT YOU DEVELOP SOME MATERIALS THAT EXPLAIN THIS THAT POINT OUT EXPLICITLY THE

OTHER PROTECTIONS IN PLACE IN ADDITION TO THAT PARTICULAR CLAUSE. SO THE IRB REVIEW HERE, THE EDUCATIONAL ISSUES, THE BEST PRACTICE ISSUES TO PUT IN THE CONTEXT OF THERE'S A WHOLE LOT ELSE GOING ON THAT IS ALL DIRECTED TOWARDS MAKING SURE THAT CONSENT FOR DERIVATION IS ETHICALLY STRONG.

SO I'M HEARING THAT WITH ALL THOSE FOOTNOTES AND QUALIFICATIONS, WE ARE INCLINED, AS A COMMITTEE, TO SUPPORT THIS.

LET'S THEN GO TO THE DERIVATION, THE THIRD LINE DOWN, THE NEW IPSC DERIVATION FROM DEIDENTIFIED SOMATIC CELLS. AND HERE THE CHANGE IS FROM THE CURRENT REQUIREMENT TO NOTIFY EITHER THE SCRO OR THE INSTITUTIONAL OFFICIAL TO SAYING NO, BECAUSE IT'S DEIDENTIFIED SOMATIC CELLS, NO NOTIFICATION IS NEEDED. I'M SKIPPING THE USE BECAUSE I WANT TO DO THE USES TOGETHER.

SO WHAT DO WE THINK OF THAT REVERSAL OF NOTIFICATION FOR THE DEIDENTIFIED? AND I'M TRYING TO PUT IN THE CONTEXT OF WHAT JOHN AND OTHERS HAVE SAID ABOUT, WELL, CLEARLY WE MEAN TO SAY THEY MAY BE TECHNICALLY DEIDENTIFIED; BUT IF, IN FACT, THE RESEARCHER WHO'S DOING THE DERIVATION REALLY KNOWS, THEN IT SHOULD BE BUMPED UP TO THE IDENTIFIABLE CATEGORY. SO THE QUESTION IS IF -- AND THE OTHER

CONCERN WAS, WELL, IT MAY BE DEIDENTIFIED TO THE RESEARCHER; BUT IF I OR MY CHILD HAS A VERY RARE DISEASE AND I KNOW THEY'RE INTERESTED IN STUDYING IT, I REALLY HOPE THEY STUDY IT, AND, IN FACT, AS JOHN SAID, I HOPE THAT THIS WILL EVENTUALLY BECOME VERY WIDELY USED, IT MAY BE DEIDENTIFIABLE TO THE RESEARCHERS, BUT NOT TO THE PERSON. DOES THAT MAKE A DIFFERENCE IN TERMS OF THE DERIVATION NOW?

DR. WAGNER: I THINK THAT IT DOES, AND I THINK IT COULD HAVE A MAJOR IMPACT UPON THE CIRM BANK THAT EVENTUALLY WILL TAKE PLACE.

CHAIRMAN LO: WHY DON'T YOU SAY A LITTLE MORE ABOUT THAT.

DR. WAGNER: JUST BECAUSE, AS I SAID BEFORE, THESE THINGS ARE NOT TRULY DEIDENTIFIED IN ALL CIRCUMSTANCES. AND THIS IS COMPLICATED ENOUGH, THAT WHEN I SUBMIT MY PROTOCOL TO THE IRB TO OBTAIN A PIECE OF TISSUE FOR THE PURPOSE OF DEVELOPING AN IPS LINE, WHICH I HAVE DONE WHERE I HAVE IT FOR DIFFERENT GENETIC DISEASES, I HAVE IT FOR NORMAL CONTROLS, AND I HAVE IT FOR UNRELATED VOLUNTEERS. AND SO EACH ONE IS A BIT DIFFERENT THAN THE OTHER. SO THE UNRELATED VOLUNTEERS, YOU GET A PIECE OF SKIN THERE, THEY REALLY TRULY ARE DEIDENTIFIED. SO THERE'S NO PROBLEM. BUT THE BLANKET STATEMENT

DOESN'T APPLY TO ALL ASPECTS ALL WITHIN THE SAME PROTOCOL.

SO I THINK THAT, YES, YOU COULD EDUCATE THE IRB TO KNOW THIS NUANCE POTENTIALLY, OR YOU NEED TO AT LEAST MAKE AN INSTITUTIONAL OFFICIAL AWARE. I WOULDN'T PERSONALLY MAKE IT LESS THAN ANYTHING -- I WOULDN'T MAKE IT DIFFERENT FROM THE IDENTIFIABLE BECAUSE OF THE POSSIBILITY THAT IT COULD TRULY BE IDENTIFIABLE.

CHAIRMAN LO: SO LET ME TRY AND THINK THIS THROUGH WITH YOU. SO YOUR CONCERN IS THAT IT MAY BE TECHNICALLY DEIDENTIFIED, BUT NOT REALLY. IT'S REALLY IDENTIFIABLE.

DR. ROBERT TAYLOR: I THINK IT'S FAIR TO SAY THAT WITH DEEP SEQUENCING, NOBODY IS DEIDENTIFIED ANYMORE AND NEVER WILL BE INTO THE FUTURE.

DR. WAGNER: EXCEPT THAT YOU DON'T KNOW YOU'RE DEEP SEQUENCING YOURSELF. ONLY CRAIG KNOWS.

DR. LOMAX: COULD I ASK A QUESTION AT THIS POINT? I THINK IF YOU NOTICE FROM THE COMMENTS, A NUMBER OF INSTITUTIONS NOW ARE COMING BACK AND SORT OF ASKING QUESTIONS ABOUT WHAT CATEGORICALLY IS DEIDENTIFIED AND NOT. ONE THING WE COULD DO IS KIND OF GO BACK OUT TO THE INSTITUTIONS AND SEE IF THERE

IS SOME SORT OF WAY TO CREATE A BRIGHT-LINE DISTINCTION BETWEEN STUFF THAT'S REALLY COMING FROM, LIKE, AN OUTSIDE SOURCE THAT'S TRULY DEIDENTIFIED VERSUS INTERNAL MATERIALS. THEY HAVE BEEN ASKING THOSE QUESTIONS. I THINK WE'RE GOING TO HAVE TO FIND A WAY TO THINK THROUGH THAT WITH PEOPLE. WE CAN TAKE A LOOK AT THAT BECAUSE I'M UNDERSTANDING YOUR CONCERNS.

CHAIRMAN LO: JOHN, LET ME FLIP IT AROUND THE OTHER WAY AND SAY THAT YOU'VE RAISED SOME VERY IMPORTANT CONCERNS ABOUT THINGS THAT REALLY ARE IDENTIFIABLE ALTHOUGH THE FEDERAL REGULATIONS MAY NOT THINK SO.

ON THE OTHER HAND, AND WE'VE ACTUALLY HAD PROTOCOLS WHEN I CHAIRED THE SCRO WHERE SOMEONE IS GETTING TISSUE FROM ANOTHER INSTITUTION WHERE IT WAS ACTUALLY -- IT MAY HAVE BEEN A RARE DISEASE, BUT THE TISSUE WAS DERIVED SOMEWHERE ELSE, DEIDENTIFIED, AND THEN SENT TO THE INSTITUTION DOING THE DERIVATIONS. THAT LINK THAT YOU POINT OUT BETWEEN THE CLINICIAN CARING FOR THE PATIENT AND THE PERSON DOING THE DERIVATION ARE DIFFERENT. AND EVEN THOUGH THE PERSON WHO DONATED KNOWS THAT SOME TISSUE WAS OBTAINED, THEY'RE NOT REALLY SURE THAT THEIRS IS THE TISSUE THAT GOT TO THE OTHER INSTITUTION.

IN THAT SETTING, WE HAVE TO THINK ABOUT HOW WE DIFFERENTIATE THE TWO, BUT THAT'S THE EXTREME. WOULD YOU HAVE CONCERNS ABOUT NOT NOTIFYING WHERE YOU REALLY CAN'T -- IT REALLY IS DEIDENTIFIED IN THE SENSE THAT YOU DON'T KNOW ANYTHING ABOUT THE PATIENT EXCEPT THE CODE NUMBER AND I GUESS ANY GENETIC SEQUENCING YOU CAN DO?

DR. WAGNER: THAT'S IT. THE PROBLEM IS WOULDN'T THEY WANT TO HAVE -- IF THEY DIDN'T WANT THE GENETIC INFORMATION, THAT'S A DIFFERENT STORY. BUT IF IT'S A GENETIC DISEASE OR A DISEASE FOR WHICH YOU KNOW THE MUTATION, BECAUSE THAT'S IMPORTANT FOR THEM TO KNOW, THEN THAT'S WHERE EVEN, AS YOU SAID PREVIOUSLY, EVEN IF THEY TRULY ARE DEIDENTIFIED, THE PATIENT CAN RECOGNIZE THEIR OWN CELL POTENTIALLY IN THE FUTURE.

SO MAYBE -- I KNOW WHAT YOU ARE GETTING AT, AND I THINK THAT YOU'RE GETTING CLOSER TO SOMETHING THAT TRULY IS MORE DEIDENTIFIED. IT'S JUST A MATTER OF SOMEONE IS GOING TO HAVE TO ASK THE QUESTION: ARE YOU PROVIDING ANY INFORMATION THAT COULD IDENTIFY THE TISSUE FROM THE SOURCE SUCH AS MUTATIONS?

CHAIRMAN LO: WELL, THERE IS -- LET ME JUST SAY ONE THING AND THEN TURN TO NICOLE. THERE

IS ANOTHER REGULATORY OUT, AND THAT'S IN HIPAA IF YOU LOOK AT THE 17, A UNIQUE BIOLOGICAL IDENTIFIER MAKES AN IDENTIFIABLE SAMPLE. SO YOU COULD ARGUE THAT, IN FACT, IF YOU HAVE A UNIQUE BIOLOGICAL IDENTIFIER, WHICH MAY JUST BE ENOUGH OF THE GENOMIC SEQUENCE THAT YOU CAN IDENTIFY IT, THEN IT MAY NOT BE TECHNICALLY DEIDENTIFIABLE AT LEAST BY ONE SET OF FEDERAL REGULATIONS. AT LEAST WE CAN SORT OF POINT THAT OUT.

DR. WAGNER: AT LEAST POINT IT OUT BECAUSE I CAN TELL YOU THAT UP UNTIL NOW, AT LEAST AT OUR INSTITUTION, IT WAS THOUGHT TO BE DEIDENTIFIED BECAUSE OF THE CLASSIC WAY, AND YET IT REALLY WASN'T. SO IT WASN'T BECAUSE -- JUST NO ONE THOUGHT TO ASK THAT QUESTION. AND THE INVESTIGATOR DIDN'T THINK TO PROVIDE THAT INFORMATION. JUST SAYING I'M COLLECTING SKIN SAMPLES FROM FA PATIENTS. I'M NOT GOING TO KEEP A LINK OF WHO THE PATIENT IS. THAT WASN'T EXACTLY TRUE BECAUSE IT WAS ALWAYS LINKED TO A MUTATION. SO, YES, THEY GOT RID OF THE PATIENT NAME, BUT IT WAS LINKED TO A MUTATION. SO WE JUST HAVE TO POINT THAT OUT THEN.

CHAIRMAN LO: NICOLE, YOU'VE THOUGHT ABOUT THIS A LOT.

DR. LOCKHART: SO IN LISTENING TO THE

CONVERSATION, IT SOUNDS LIKE IT'S GOING TO BE VERY DIFFICULT TO CREATE THIS BRIGHT LINE WHEREBY ONE SET OF DERIVATIONS WILL BE CONSIDERED DEIDENTIFIED AND ANOTHER WOULD BE CONSIDERED IDENTIFIABLE, PARTICULARLY SINCE THE REGULATIONS IN THIS INSTANCE DON'T NECESSARILY ADDRESS SOME OF THE SPECIFIC ISSUES WE'VE RAISED. THEY DON'T ADDRESS CAN THE PATIENT IDENTIFY THEMSELVES. WHAT IF THE PHYSICIAN -- WHAT IF IT'S A PHYSICIAN SCIENTIST KIND OF PROJECT WHERE THE PHYSICIAN THEMSELVES WOULD KNOW, EVEN IF THERE'S NO NAME, WHO THE PATIENT IS?

WHEN WE'RE THINKING ABOUT HOW TO IMPLEMENT, IT SEEMS LIKE, TO ME AT LEAST, IT MIGHT BE EASIER JUST TO HAVE THE POLICY THAT IF YOU'RE DERIVING NEW LINES, YOU NOTIFY. BECAUSE ON THE SIDE OF THE INSTITUTION, IF THERE ARE ALL THESE VERY SPECIFIC IF IT'S THIS, IF IT'S THAT, WHERE IS THE CELL COMING FROM, WHO IS IT IDENTIFIABLE TO, IT SEEMS VERY DIFFICULT FOR THEM TO INTERPRET AND PARSE THAT APART.

AND ALSO IF YOU HAVE NO NOTIFICATION AND YOU'RE IN THAT FOURTH LINE THERE, IF YOU'RE RELYING ON THE PI TO MAKE THAT DETERMINATION AS TO WHETHER IT'S IDENTIFIABLE OR NOT, I THINK THAT'S ASKING THEM TO MAKE A HARD DECISION, PARTICULARLY BECAUSE THIS

IS A MOVING TARGET WITH THE ANPRM COMING OUT WHAT IS CONSIDERED IDENTIFIABLE, AND THERE COULD ALSO BE A POTENTIAL CONFLICT OF INTEREST THERE FOR THEM IF THIS IS THEIR PROJECT. IT'S A LOT EASIER IF IT'S NOT IDENTIFIABLE. I DON'T ACTUALLY KNOW THEIR NAME. YOU WOULDN'T WANT TO BE PUTTING SOMEONE IN THAT POSITION.

DR. PRIETO: THIS BRINGS UP AN INTERESTING POINT. IT MAY ACTUALLY BE LESS OF A BURDEN TO JUST SAY IF YOU'RE DERIVING, NOTIFY. BUT MAYBE WE SEPARATELY NEED TO LOOK AT HOW DOES THAT GET IMPLEMENTED AND HOW DO WE MINIMIZE THE BURDEN.

DR. ROBERT TAYLOR: THAT MIGHT ALSO INCENTIVIZE HAVING AS MUCH INFORMATION ABOUT THE INDIVIDUAL AS YOU CAN HAVE BECAUSE AT THE END OF THE DAY, THE MORE YOU KNOW ABOUT CELLS THAT YOU'RE WORKING WITH, THE BETTER YOU'RE GOING TO DO WITH THEM FOR WHATEVER APPLICATION.

SO IN THIS SETTING WE ACTUALLY SORT OF INCENTIVIZE PEOPLE TO LEAVE DATA OFF THE TABLE THAT MIGHT ACTUALLY BE USEFUL IN TERMS OF ULTIMATE...

DR. LOMAX: AGAIN, NOT TO CHALLENGE ANY OF THE PERSPECTIVE HERE, JUST TO BE CLEAR THAT THE SCIENCE OFFICER DOES -- THERE IS A SCIENCE OFFICE REVIEW OF THOSE PROTOCOLS AS THEY COME THROUGH AS

WELL. SO THERE IS AT LEAST AN EXTERNAL CHECK FROM OUR SIDE, BUT I'M NOT TRYING TO INFLUENCE THE DIRECTION OF THE CONVERSATION. I JUST WANT TO BE CLEAR YOU WOULDN'T HAVE SOMETHING JUST SORT OF SENT IN BY A PI WITHOUT GETTING THE REVIEW FROM OUR END AS WELL.

CHAIRMAN LO: LET ME SAY, GEOFF, ONE THING THAT HAS COME UP IN MY EXPERIENCE IS THAT CIRM GIVES DIFFERENT KINDS OF GRANTS. AND SOME ARE THE EQUIVALENT RO1S TO INDIVIDUALS WHERE THEY TELL YOU THIS IS THE PROJECT I WANT TO DO. OTHERS ARE REALLY TEAM -- ARE MUCH BROADER GRANTS, EITHER TRAINING GRANTS OR SORT OF LONG-TERM PROGRAM-TYPE GRANTS WHERE YOU MAY NOT BE TOLD WHEN YOU GIVE THE FUNDING WHAT EXACTLY IS GOING TO HAPPEN. I'M JUST WONDERING IF THAT ASPECT -- I ACTUALLY SUPPORT THOSE KINDS OF BIG GRANTS BECAUSE IT GIVES FLEXIBILITY AND DIRECTS PEOPLE TO LONG-TERM GOALS AND STUFF.

I'M JUST WONDERING IF THAT HAS IMPLICATIONS HERE BECAUSE MY UNDERSTANDING IS YOU REVIEW THE GRANT AS A WHOLE; BUT THEN WHEN SOME TRAINEE OR SOME SUBPROJECT TAKES PLACE THAT INVOLVES REPROGRAMMING, YOU DON'T NECESSARILY HAVE TO SEE THAT PARTICULAR PART OF THE GRANT.

DR. LOMAX: WE'LL SEE IT IN THE PROGRESS

REPORT. AT THE TIME OF THE PROGRESS REPORT, THE SCIENCE OFFICER IS REQUIRED TO THEN REEVALUATE THE NOTIFICATIONS AND APPROVALS. THAT'S ACTUALLY BECOME -- SO IT'S THE INITIAL AWARDING, THERE IS A CHECK PHASE, AND THEN TYPICALLY WE SPEND -- I GET A LOT OF QUESTIONS IN THE PROGRESS REPORT PHASE. SO BEFORE RENEWAL, AGAIN, OUR SYSTEMS REQUIRE THAT ANY REQUIRED ELEMENTS BE IN PLACE, OR WE'RE NOT GOING TO DO THAT RENEWAL.

CHAIRMAN LO: ACTUALLY YOU MIGHT REVIEW IT AS A SCIENCE PROJECT OFFICER AFTER THE RESEARCH HAS COMMENCED.

DR. LOMAX: YOU'RE EXACTLY RIGHT. ABSOLUTELY THERE'S AN OPPORTUNITY FOR LATENCY BETWEEN OUR LOOK AND THE ACTUAL WORK, BUT THERE WILL BE A LOOK EVENTUALLY. AND IF WE SEE DISCREPANCIES, WE CAN OFTEN COME BACK, AND IT'S A TEACHABLE MOMENT.

DR. BOTKIN: I THINK THIS PROBLEM RAISES SOME UNSETTLED ISSUES CERTAINLY IN THE FIELD. I'M INVOLVED IN A PROJECT OUT OF CASE WESTERN THAT'S LOOKING AT INSTITUTIONAL POLICIES ABOUT BIOBANKING AND HOW IRB'S ARE MAKING DECISIONS AROUND ISSUES LIKE IDENTIFIABILITY. I THINK AT OUR INSTITUTION, AT LEAST WHAT I HOPE IS HAPPENING, IS THAT PARTICULARLY IN THE CIRCUMSTANCE YOU START WITH AN

IDENTIFIABLE TISSUE SET AND SOMEBODY DEIDENTIFIES IT, AND THAT'S A PROCESS THAT MAY OR MAY NOT BE EFFECTIVE OR UP TO CERTAIN STANDARDS. SO I THINK THIS IS A DOMAIN WHERE WE WOULD LIKE THE IRB IN A DEIDENTIFIED RESEARCH SETTING TO EVALUATE THAT PROJECT SUFFICIENTLY TO DETERMINE THAT INDEED IT IS DEIDENTIFIED AND INDEED THE IRB DOES NOT NEED TO BE INVOLVED BECAUSE IT'S NONHUMAN SUBJECTS RESEARCH.

IT SEEMS TO ME THAT, AS THIS IS LAID OUT, THIS DOESN'T REQUIRE AN IRB TO MAKE THE DETERMINATION THAT IT'S ADEQUATELY DEIDENTIFIED AND, THEREFORE, HUMAN NONSUBJECT RESEARCH, PROBABLY A BETTER WAY TO SAY THAT, WOULD IT BE CONCEIVABLE UNDER THESE SORTS OF GUIDELINES FOR SOMEBODY TO TAKE RESIDUAL CLINICAL SAMPLES, DEIDENTIFY THOSE, DERIVE NEW IPSC LINES WITH THAT WITHOUT ANY NOTIFICATION OF ANYBODY WITHIN THE INSTITUTION THAT THAT'S A RESEARCH PROCESS THAT'S GOING ON?

DR. WAGNER: YES. AND IT HAPPENS NOW.

DR. ROBERTS: THAT WAS GOING TO BE MY POINT, THAT UNLIKE WHAT I SAID BEFORE, THAT YOU HAVE THE BACKUP OF THE IRB REVIEW, YOU COULD IMAGINE A SITUATION HERE WHERE THE IRB ISN'T EVEN NOTIFIED AT ALL BECAUSE THE RESEARCHER ALREADY HAS INTERPRETED THAT THIS IS DEIDENTIFIED. SO THAT'S A CONCERN. I

ALWAYS -- IF THERE'S SOME BACKUP LIKE IRB REVIEW, IT HELPS, AND HERE THERE MIGHT NOT BE.

CHAIRMAN LO: JEFF AND DOROTHY, ARE YOU SUGGESTING THAT THERE MIGHT BE VALUE IN HAVING SOMEBODY LOOK OVER THIS PROPOSAL TO DERIVE -- TO REPROGRAM DEIDENTIFIED CELLS TO MAKE SURE THAT THEY REALLY ARE DEIDENTIFIED IN JEFF'S SOMEWHAT BROADER SENSE, BUT JUST TO LOOK AT THAT BECAUSE EITHER IT GETS KICKED UP TO IDENTIFIABLE OR YOU SAY, NO, IT'S OKAY? SO I GUESS THE PURPOSE WOULD BE TO MAKE SURE THEY'VE INTERPRETED THE CONCEPT OF DEIDENTIFIED IN THIS CONTEXT APPROPRIATELY.

I GUESS THEN THE OTHER QUESTION IS WOULD THAT, GEOFF, AT ALL BY NARROWING -- I DON'T KNOW IF THAT ACTUALLY NARROWS THE SCOPE OF THE NOTIFICATION. WILL THAT CUT DOWN ON THE ADMINISTRATIVE BURDENS OR NOT?

DR. WAGNER: WHILE YOU'RE THINKING, DOROTHY, AS YOU'RE SAYING, THE REASON I SAY YES IS IS THAT I HAVE ALL THESE STORED MARROW SPECIMENS ON PATIENTS FOR THE PAST TWO DECADES, NEVER IN A MILLION YEARS EVER IMAGINING IPS. AND YET PEOPLE ARE COMING BACK TO ME AND SAYING CAN I HAVE THESE CELLS, WHICH, OF COURSE, ARE ALL FOR THEIR PURPOSES, FROM THE IRB POINT OF VIEW, WAS ALL OKAYED BECAUSE

IT WAS, QUOTE, IT WILL BE DEIDENTIFIED TO ANYONE I WOULD GIVE THESE CELLS TO. BUT, AGAIN, THEY'RE ASKING FOR THE MUTATION. AND WHEN YOU TAKE IT IN A DIFFERENT CONTEXT, IN MY HEAD THEY WERE DEIDENTIFIED. IT'S JUST THAT I THINK THAT PEOPLE DON'T REALIZE THAT -- PEOPLE AREN'T PURPOSEFULLY MISLEADING THE IRB OR ANY REGULATORY BODY. IT'S JUST THAT IN ANY OTHER CONTEXT IT WOULD HAVE BEEN NOT AN ISSUE. IT'S JUST THAT THE CAPACITY OF THESE CELLS ARE SO BROAD, AND THEN THEY COULD BE -- THERE'S NOT A DEAD END. TYPICALLY I WOULD GIVE THESE LYMPHOCYTES OR THESE BONE MARROW CELLS AND IT WOULD BE AN EXPERIMENT AND IT'S GONE. BUT THE FACT THAT YOU CAN DERIVE THE CELL LINE FROM IT THAT HAS WIDE POTENTIAL AND WILL THEN BE LINKED TO AN IDENTIFIER, A MUTATION CHANGES EVERYTHING, AND THE IRB APPROVAL OCCURRED A DECADE AGO.

DR. BOTKIN: CAN I ADD ONE QUICK POINT TO THAT TOO? I THINK THAT THE DEIDENTIFIED ASPECT OF THAT IS A DETERMINATION THAT IS COMPLICATED AND PART OF THE DISCUSSION. BUT THE OTHER ONE THAT'S NOT REALLY QUITE READY FOR NATIONAL PRIME TIME IS THIS QUESTION OF CELLS THAT WERE DERIVED UNDER A SPECIFIC SET OF RESTRICTIONS. AND FOLKS HAVE FELT FREE TO THEN DEIDENTIFY THEM AND USE THEM FOR SOMETHING

ENTIRELY DIFFERENT THAT'S NOT CONSISTENT WITH THE ORIGINAL CONSENT PROCESS.

I THINK A LOT OF IRB'S HAVEN'T GRAPPLED YET WITH THAT ISSUE TO SAY MAYBE WE OUGHT TO BE ACTUALLY LOOKING AT THE CONSENT FORM EVEN FOR SAMPLES THAT HAVE BEEN DEIDENTIFIED TO MAKE SURE THAT WE'RE HONORING THE COMMITMENT WE MADE TO THOSE DONORS. SO I DON'T THINK THAT'S COMMONLY HAPPENING NOW, BUT WE'LL FIND OUT. BUT AS THIS FIELD CHANGES, I THINK THERE MAY BE REASONS FOR FOLKS TO TAKE A LOOK AT THE CONDITIONS UNDER WHICH THESE THINGS WERE DERIVED BEFORE MAKING A DECISION ABOUT USES EVEN WHEN THEY'RE DEIDENTIFIED.

DR. ROBERTS: SO IT SEEMS LIKE THERE'S TWO ISSUES HERE. ONE IS WHETHER WE COULD BETTER MAKE THE DISTINCTION BETWEEN DEIDENTIFIED AND IDENTIFIED. BUT AS YOU'RE JUST RAISING AND WAS RAISED BEFORE, FOR ETHICAL REASONS IT MAY NOT MATTER WHETHER IT WAS IDENTIFIED OR DEIDENTIFIED. SO IN TERMS OF CONSENT OF THE ORIGINAL DONOR, WHETHER IT'S EVENTUALLY DEIDENTIFIED, IT STILL MAY VIOLATE THEIR CONSENT IF IT'S USED IN A WAY THAT THEY DIDN'T CONSENT TO.

CHAIRMAN LO: SO WHAT I'M HEARING IS A LOT OF SENTIMENT IN FAVOR OF NOT MAKING THIS PROPOSED CHANGE AND KEEPING THE CURRENT SITUATION OF

NOTIFICATION OF SCRO OR INSTITUTIONAL OFFICIAL FOR DEIDENTIFIED DERIVATION AS WELL AS IDENTIFIABLE DERIVATION.

DR. ROBERTS: TREATING THEM THE SAME.

DR. ROBERT TAYLOR: COLLAPSING THE ROWS.

CHAIRMAN LO: HOPEFULLY IN THE TRANSCRIPT THERE'S REASONS FOR WHY WE THOUGHT THAT.

DR. BOTKIN: I PROBABLY DIDN'T UNDERSTAND GEOFF'S RESPONSE TO MY EARLIER QUESTION ABOUT THIS. NOTIFICATION IS A PRETTY THIN TERM. AND SO IT SEEMS SORT OF LIKE A MINIMAL TERM TO SAY THERE'S SOME COMMUNICATION GOING ON. BUT IS THE CONCEPT OF NOTIFICATION UNDER THE CURRENT POLICY SOME SUGGESTION THAT SOME OFFICIAL OR SCRO IS GOING TO ACTUALLY SIGN SOMETHING THAT SAYS WE'VE BEEN NOTIFIED, IT'S OKAY TO GO FORWARD? OR IS THAT UNILATERAL COMMUNICATION ENTIRELY CONSISTENT WITH THE NOTIFICATION REQUIREMENT?

DR. LOMAX: IN TERMS OF IMPLEMENTATION, THERE'S A VARIETY OF APPROACHES. SOME INSTITUTIONS HAVE HIGHLY ESTABLISHED SYSTEMS WHERE THERE'S A NOTIFICATION SORT OF PROTOCOL AND WE GET A COPY OF SORT OF A BLURB ABOUT NOTIFICATION. OTHERS IT'S MORE OF AN E-MAIL COMMUNICATION, BUT THERE IS A CONTACT TO SOMEONE. IN MOST CASES IT'S THE

OVERSIGHT COMMITTEE HISTORICALLY, AND IT'S, AGAIN, A POSITIVE NOTIFICATION. AND, AGAIN, THE INSTITUTIONAL SORT OF SYSTEMS VARY QUITE BROADLY, BUT IT IS, LIKE I SAY, THAT MESSAGE GETTING IN THAT THIS IS A CIRM AWARD AND INVOLVES THIS SORT OF WORK, AND THAT TRIGGERS A SET OF INSTITUTIONAL ACTIONS.

DR. BOTKIN: SO THE PRESUMPTION IS IF THE INSTITUTIONAL OFFICIAL DOESN'T SAY SOMETHING, THAT NOTIFICATION ENTAILS INSTITUTIONAL ACCEPTANCE FOR THEIR RESEARCH TO GO FORWARD?

DR. LOMAX: AGAIN, THEY'RE REQUIRED TO NOTIFY THE APPROPRIATE OFFICIALS. THE APPROPRIATE OFFICIAL THEN HAS TO -- AGAIN, THEIR RESPONSE WILL VARY ON AN INSTITUTION-BY-INSTITUTION BASIS. BUT THEY KNOW, BECAUSE OF OUR REGULATIONS, THAT THE COMMITTEE OR THE INSTITUTIONAL OFFICIAL HAS THE RESPONSIBILITY FOR THEM ASSURING THAT THE RESEARCH IS CONDUCTED IN ACCORDANCE WITH OUR REGULATIONS. SO THEY BECOME THE RESPONSIBLE PARTY BY VIRTUE OF THAT NOTIFICATION. DOES THAT MAKE SENSE?

DR. BOTKIN: THAT HELPS. THANK YOU.

DR. LOMAX: WE WOULD GO TO THEM IF WE THOUGHT THERE WAS SOMETHING A PROBLEM.

CHAIRMAN LO: SO LET'S MOVE AHEAD TO USE OF STEM CELLS. SO THIS IS LINE 3, 5, AND 6. SO USE

OF IDENTIFIABLE IPSC'S. AND, AGAIN, I JUST WANT TO REMIND US, AND I HAD FORGOTTEN THIS EARLIER, THAT IF THE RESEARCH INVOLVES THE CREATION OF HUMAN GAMETES, THERE'S SCRO APPROVAL REQUIRED. IF IT INVOLVES INJECTION OF HUMAN STEM CELLS OR NEUROPROGENITOR CELLS INTO EITHER EMBRYONIC, FETAL, OR POSTNATAL DEVELOPMENT, THERE NEEDS TO BE SCRO REVIEW AND APPROVAL. IF IT INVOLVES HUMAN SUBJECTS IN TERMS OF PUTTING CELLS INTO PATIENTS, IT REQUIRES IRB REVIEW.

SO WE'RE TALKING ABOUT REALLY IN VITRO ONLY USE NOT FOR GAMETE DERIVATION. FOR IDENTIFIABLE IPSC'S, CURRENTLY IT'S NOTIFICATION TO THE SCRO. AND THE PROPOSAL IS TO BROADEN THAT TO NOTIFY EITHER THE SCRO OR RESPONSIBLE INSTITUTIONAL OFFICIAL AS ANOTHER OPTION IN KEEPING WITH THE PARKINSON'S CENTER.

SO ANY CONCERNS ABOUT MAKING THAT AN OPTION? AGAIN, WITH ALL THE CAVEATS ABOUT THIS IS ALL IN THE CONTEXT OF EDUCATION OF OFFICIALS AND SORT OF OUTREACH AND SORT OF SITE VISITS.

SO NOW LET'S GO TO DEIDENTIFIED, THE LAST TWO LINES.

DR. LOMAX: THERE'S NO CHANGE PROPOSED HERE.

CHAIRMAN LO: SO THE DEIDENTIFIED INDUCED

PLURIPOTENT STEM CELLS, AGAIN, IN THAT NARROW CONTEXT OF IN VITRO WORK THAT DOESN'T INVOLVE CREATION OF HUMAN GAMETES, RIGHT NOW IT REQUIRES NOTIFICATION OF EITHER SCRO OR INSTITUTIONAL OFFICIAL. PROPOSAL IS NO NOTIFICATION NECESSARY. THIS IS WHAT WE TALKED A LOT ABOUT BEFORE LUNCH, AND I WANT TO SORT OF BRING IT BACK TO YOU WITH SORT OF TRYING TO REACH ENOUGH CLOSURE TO AT LEAST GIVE SOME GUIDANCE TO THE ICOC. YOUR THOUGHTS?

DR. ROBERTS: WELL, A COUPLE THOUGHTS ARE, ONE, WHETHER WE SHOULD SUGGEST THE SAME THING FOR USE AS WE DID FOR DERIVATION, TREATING DEIDENTIFIED AND IDENTIFIED THE SAME. THE OTHER IS WHETHER THE TWO EXCEPTIONS FOR CREATION OF GAMETES AND INJECTION IN NONHUMAN ANIMALS, WHETHER WE THINK THOSE ARE SUFFICIENT, OR WHETHER THERE SHOULD BE SOME OTHER -- I WOULD REFER TO THE SCIENTISTS WHO KNOW WHAT THEIR ADDITIONAL SENSITIVE USES THAT HAVE COME UP THAT SHOULD BE ADDED TO THAT LIST.

CHAIRMAN LO: SO ONE THING WE COULD CERTAINLY DO IS TO SAY THAT WE NEED TO KEEP UP WITH SCIENTIFIC PROGRESS AND TO SORT OF ANTICIPATE AND DELIBERATE ABOUT OTHER IN VITRO USES THAT MAY INVOKE SENSITIVITIES.

DR. ROBERTS: WHATEVER THAT MEANS,

SENSITIVITY. THAT SEEMS TO BE THE TERM.

CHAIRMAN LO: PAT TAYLOR BEFORE LUNCH, I THINK IT WAS YOU, PAT, SUGGESTED THAT DEVELOPING AN ORGAN FROM STEM CELLS ON A SCAFFOLD ACTUALLY LOOKS LIKE A HUMAN ORGAN, I DON'T SAY PARTICULARLY IT LOOKS LIKE A HEART, MIGHT BE SOMETHING THAT WE WANT TO HAVE SOME AT LEAST NOTIFICATION OR POSSIBLY SOME REVIEW OF EVEN THOUGH IT'S NOT NOW COVERED AS SOMETHING THAT NEEDS TO GO TO OVERSIGHT.

DR. PAT TAYLOR: WHAT I MEANT TO DO WITH THAT EXAMPLE WAS POINT TO SOMETHING THAT IS SORT OF THE COMMONPLACE, BUT AT THE SAME TIME DOES RAISE SOME LEVEL OF CONCERN IN SOME CIRCUMSTANCES, BUT NOT NECESSARILY TO SUGGEST THAT WHATEVER CONCERNS THERE ARE ABOUT TAMING SCIENCE WITH POLICY OUGHT TO NECESSARILY BE RESOLVED THROUGH A SCRO. I THINK IT'S AN INTERESTING QUESTION AS IT EVOLVES.

CHAIRMAN LO: MAYBE IT'S SOMETHING TO HIGHLIGHT FOR EITHER GEOFF, AS A STAFF PERSON, ACTUALLY FOR US AS A COMMITTEE, TO SAY TO THE EXTENT THAT THIS IS ACTUALLY SOMETHING THAT IS PART OF CIRM'S SCIENTIFIC PLAN, THAT WE MAY WANT TO DEVOTE SOME TIME TO THINKING ABOUT THAT, HAVE A MINI WORKSHOP WHERE WE INFORM OURSELVES ABOUT THE SCIENCE, BRINGING PEOPLE WHO THOUGHT ABOUT THE

ETHICS AND POLICY. I DON'T THINK WE WANT TO JUMP TO CHANGING THE REGULATIONS NOW. THIS MAY BE MORE OF A LET'S FOCUS ON THIS IF IT'S IMPORTANT.

DR. PAT TAYLOR: I THOUGHT THE POINT PERSONALLY WAS EXTREMELY WELL TAKEN, THAT TO THE EXTENT THAT THERE'S GOING TO BE CLINICAL TRIALS AND THINGS LEADING INTO CLINICAL PRACTICE, IT GIVES A CERTAIN PERSPECTIVE ON THE BREADTH OF WHAT HAS TO OCCUR SOMEWHERE ALONG THE LINE. AND GIVEN YESTERDAY'S PRESENTATION ABOUT THE PROBLEMS AT THE FDA, SEEMS AS IF THERE'S A BROADER PICTURE ABOUT HOW REVIEW OUGHT TO TAKE PLACE IN THE CONTEXT OF DEVELOPING THE KIND OF STEM CELL PRODUCTS THAT PEOPLE HERE EXPECT.

CHAIRMAN LO: OKAY. SO WITH REGARD TO THE SPECIFIC PROPOSAL, DOROTHY, YOU ARGUED AGAINST ELIMINATING THE NOTIFICATION. OTHER THOUGHTS ON THAT PARTICULAR ISSUE?

DR. BOTKIN: JUST A QUESTION, I GUESS. IS THERE A REASON TO KEEP THINGS PARALLEL BETWEEN THE DERIVATION AND THE USE, OR WOULD FOLKS WANT TO MAKE THE CLAIM THAT THERE'S SUFFICIENT DIFFERENCE AMONG THOSE TWO, THAT THERE CAN BE A DIFFERENCE WITH RESPECT TO THE STANDARD?

CHAIRMAN LO: YOU WANT TO SORT OF SAY A

LITTLE MORE ABOUT HOW YOU THINK.

DR. BOTKIN: I GUESS IT SEEMS TO ME, AND NOT REALLY KNOWING ENOUGH ABOUT THE SCIENCE HERE, THAT IT MAKES SENSE TO HAVE THOSE TWO BE PARALLEL. I DON'T SEE ENOUGH OF A DIFFERENCE BETWEEN THE DERIVATION PROCESS AND THE USE PROCESS TO SAY THAT I SEE ONE WHERE WE WOULD FEEL MOST COMFORTABLE HAVING NOTIFICATION AND THE OTHER NOT. IT SEEMS TO ME THAT IF WE DECIDED FOR THE DERIVATION ONE, THAT NOTIFICATION PROBABLY IS MORE COMFORTABLE AT THIS POINT, THEN IT SEEMS TO ME NOTIFICATION WOULD BE MORE APPROPRIATE FOR THE USE. BUT, AGAIN, IF FOLKS SEE A DISTINCTION THERE BETWEEN THOSE TYPES OF RESEARCH PROJECTS THAT WOULD BE RELEVANT HERE, I'D BE INTERESTED TO LEARN MORE.

DR. LOMAX: ONE OF THE DISTINCTIONS I'VE EXPLAINED TO INSTITUTIONS WHEN THEY ASK ME THE QUESTION WHY ARE WE DOING THIS, ON THE DERIVATION END WE SEE MORE OF AN OPPORTUNITY TO TAKE SOME SORT OF ACTION TO INFLUENCE THE DECISIONS. AGAIN, ON THE IDENTIFIABLE SIDE, I MENTIONED CONSENT. ON THE USE SIDE, IT'S THAT ABILITY TO, ESPECIALLY WHEN YOU GET DOWN TO HERE, WHICH IS REALLY LIKE EVERYTHING, IT'S DIFFICULT TO IMAGINE HOW THE CHOICE AT THIS STAGE, WHAT THE ACTION IS THAT COULD SORT OF CHANGE

SOMETHING. THIS IS REALLY JUST A HUGE -- THIS IS SORT OF THE UNIVERSE OF MATERIALS THAT ARE IN CIRCULATION. AND I'M NOT SURE THAT THERE'S ANY PROCESS WE CAN DEVISE TO INFLUENCE THAT POPULATION OF MATERIALS.

I SUPPOSE THE ONE COUNTER TO THAT WOULD BE AT LEAST IF THERE'S SOMETHING YOU THINK IS PROBLEMATIC IN SOME WAY, AT LEAST OUR FOLKS WOULD BE ADVISED NOT TO USE IT, BUT THAT'S REALLY THE ONLY COUNTER EXAMPLE THERE.

AGAIN, IT WAS THE IDEA OF IS THERE SOMETHING SORT OF ACTIONABLE, AND THIS SEEMS TO BE THE LEAST ACTIONABLE OF THE USES OF THE RESEARCH PROTOCOL.

DR. PAT TAYLOR: THIS MAY SEEM LIKE AN UNUSUALLY BIASED APPROACH, BUT IT DOES SEEM TO ME THAT THERE ARE SOME USES OF IPS CELLS THAT ARE REALLY POTENTIALLY CONCERNING, LIKE SOME USES OF EMBRYONIC STEM CELLS, LIKE CHIMERIC USES AND SO ON. IT IS A FAMILY OF IDENTIFIABLE USES. AND THEN THERE'S AN ADDITIONAL SET OF THINGS THAT PEOPLE HAVE TALKED ABOUT CONCERNS ABOUT THE CLINICAL PRODUCT DEVELOPMENT, FOR EXAMPLE, AND WAYS IN WHICH DERIVATIVES MAY ACTUALLY RAISE ISSUES. IT DOES SEEM TO ME THERE'S A LOT OF THOUGHT THAT NEEDS TO GO INTO

FIGURING OUT WHAT KIND OF REVIEW OUGHT TO BE REQUIRED FOR THIS.

DOES NOTIFICATION ACTUALLY REQUIRE THAT? SO WHAT WE'RE TALKING ABOUT DOING NOW, IF I UNDERSTAND CORRECTLY, IS MAINTAINING THE NOTIFICATION REQUIREMENT FOR THIS QUESTIONABLE POOL EVEN THOUGH, AT LEAST AS FAR AS WE KNOW, INSTITUTIONS ARE NOT DOING ANYTHING WITH THAT NOTIFICATION ALONG THE LINES OF THE KIND OF CAREFUL REVIEW WE'RE DISCUSSING. SO WE HAVE A PERCEPTION ARISING OUT OF THIS EXCELLENT DISCUSSION THAT THERE'S A BODY OF THINGS WE NEED TO EXPLORE.

I GUESS I KIND OF QUESTION WHETHER NOTIFICATION OF INSTITUTIONS IS GOING TO ACCOMPLISH THAT REVIEW, AND WHETHER OR NOT THE RIGHT THING TO DO MIGHT ACTUALLY SIMPLY BE TO PEEL BACK THE NOTIFICATIONS TO THE THINGS WE KNOW OF AND ARE PRETTY WELL ESTABLISHED POTENTIAL USES THAT ARE PROBLEMATIC AND AT THE SAME TIME REALLY WORK THOUGHTFULLY TO TRY AND USE SOME OF THE IDEAS THAT PEOPLE HAVE EXPRESSED HERE TO FIGURE OUT WHAT KIND OF ADDITIONAL REVIEW BEYOND NOTIFICATION MIGHT BE REQUIRED, AND ALSO COMMENSURATE CHANGES IN SCRO QUALIFICATIONS.

THERE IS A LARGE ISSUE OUT THERE ABOUT HOW

CELLULAR PRODUCTS, FOR EXAMPLE, ARE CREATED AND INTERESTING QUESTIONS. BUT NOTIFICATION DOESN'T SEEM TO GET AT THEM, AND I WORRY A LITTLE BIT ABOUT MAINTAINING A NOTIFICATION REQUIREMENT WITH THE THOUGHT THAT WE SOMEHOW HAVE DEALT WITH THE REVIEW OF THESE THINGS BECAUSE I DON'T THINK WE HAVE. IT'S A NEW AND COOL TOPIC.

CHAIRMAN LO: AGAIN, IT'S THIS ISSUE WE TOUCHED ON BEFORE LUNCH WHERE A LOT OF THIS NOW IS REALLY REFERRING TO IN VITRO USES OF STEM CELLS BECAUSE WE'VE SORT OF PUT ASIDE SOME OF THE QUESTIONABLE HUMAN CELLS INTO ANIMALS, WE PUT ASIDE THE CLINICAL TRIALS ASPECT. SO WE'RE SAYING IN VITRO USES THAT DON'T INVOLVE DERIVATION OF GAMETES. THE IMPRESSION THAT WE HAVE IS THAT MOST OF THAT RESEARCH IS REALLY UNPROBLEMATIC, NOT SENSITIVE, BUT THERE ARE SOME THINGS THAT MAY, IN FACT, BE SENSITIVE OR MAY EMERGE AS SENSITIVE. AND I GUESS THE QUESTION IS WHAT REGULATORY SCHEME SHOULD THERE BE.

I THINK, PAT, YOU'RE SUGGESTING THAT FOR SOME THINGS NOTIFICATION MAY NOT BE STRONG ENOUGH. YOU WANT NOTIFICATION WITH SOME DELIBERATION AND REVIEW.

DR. PAT TAYLOR: THIS IS A REALLY

INTERESTING AND POWERFUL DISCUSSION. THE THOUGHT THAT THERE'S SOMETHING OUT THERE WHICH MAY REQUIRE ADDITIONAL REVIEW IS NOT A NEW ONE, BUT IT WAS DEFEATED IN THE CONTEXT OF THE DISCUSSION FROM SCRO'S AND WHETHER IT WOULD BE TOO MUCH WORK FOR THEM TO DO IT AND WHETHER THEY'D BE QUALIFIED AND ALL THAT SORT OF THING. FOR THAT KIND OF ADMINISTRATIVE REASON, I'M NOT AWARE OF ANY PROGRESS ON THE ISSUE OF THIS KIND OF GROWING CATEGORY.

I THINK I'M REALLY INFLUENCED BY YOUR POINT, BERNIE, ABOUT SIMPLICITY. SO FOR IPS CELLS ONE MIGHT THINK THAT CREATING CHIMERIC COMBINATIONS OF IPS CELLS WOULD BE AS PROBLEMATIC POTENTIALLY AS CHIMERIC USES OF EMBRYONIC STEM CELLS. AND SO IT DOES SEEM TO ME THAT WE CAN SIMPLY PARALLEL THE IDENTIFIABLE AND SIMPLE FAMILY OF THINGS WHICH SCRO'S ARE ALREADY REVIEWING OR ABLE TO REVIEW WITH RESPECT TO EMBRYONIC STEM CELLS AND TO TRACK THOSE ON THE IPS SIDE. AND THOSE DO GO BEYOND SOME OF THE NEUROLOGICAL AND THE GAMETE, BUT THEY'RE IDENTIFIABLE AND THEY'RE WELL SETTLED AND OUGHT TO BE UNCONTROVERSIAL, BUT IT IS A GAP THAT'S NOT FILLED.

DR. LOMAX: JUST A QUICK TECHNICAL COMMENT. SO THE DEFINITION OF COVERED STEM CELL

LINE ATTEMPTS TO CREATE THAT PARALLELISM, IF YOU WILL, THAT WOULD APPLY EITHER TO EMBRYONIC OR IPS. SO WE GET THAT OUTCOME IN THE DEFINITION FOR THE MOST PART. JUST TO REMIND FOLKS OF THAT.

DR. PAT TAYLOR: SO THIS, AT LEAST, WOULD GIVE US SOMETHING THAT'S RATIONAL AND SIMPLE AND CONSISTENT WITH THE PERCEIVED QUALIFICATIONS OF SCRO'S TO DEAL WITH THIS MOTLEY SET OF USES. AT THE SAME TIME, PEOPLE THINK HARD ABOUT SOME OF THE OTHER QUESTIONS THAT ARE RAISED.

MR. SWEEDLER: IF I COULD JUST MAKE AN IMPLEMENTATION OBSERVATION BECAUSE, AS SCOTT POINTED OUT, THESE ARE LAW ONCE WE PROMULGATE THESE. SO IF WE'RE GOING TO ASK A SCRO TO RECEIVE NOTIFICATION AND THEREBY DECIDE WHETHER THERE'S SOMETHING THERE THEY NEED TO ACT ON, IT'S REALLY INCUMBENT UPON US TO TELL THEM THE BASIS ON WHICH THEY SHOULD DO THAT. SO WE WOULD NEED TO GO, I THINK, BEYOND SAYING THERE ARE POTENTIAL PROBLEMS THERE. WE SHOULD BE ABLE TO WORK THROUGH, AT LEAST FOR GENERAL, EVEN IF NOT EXHAUSTIVELY, THEN AT LEAST EXAMPLES OF WHAT THE REASON IS.

AND THEN ANOTHER IMPLEMENTATION ISSUE, AND MAYBE UTA OR PAT COULD SPEAK TO THIS BETTER THAN I. MY IMPRESSION IS THAT THAT LAST CATEGORY IS SIMPLY A

MUCH LARGER VOLUME THAN MANY OF THE OTHERS WE'VE BEEN TALKING ABOUT. SO IT'S NOT THAT WE CAN'T HANDLE THE WORKLOAD OR THAT THE ESCRO'S CAN'T NECESSARILY, BUT DOES THAT HAVE THE IMPACT OF REALLY DIVERTING THEIR TIME AND ATTENTION FROM THE THINGS WHERE IT'S MOST IMPORTANT TO THINGS WHERE WE THINK IT'S RELATIVELY UNLIKELY TO MAKE A DIFFERENCE? BUT, AGAIN, I WOULD PREFER TO HAVE ONE OF OUR SCIENTISTS TALK ABOUT JUST HOW COMMON THESE DIFFERENT THINGS ARE IN OUR RESEARCH PORTFOLIO.

CHAIRMAN LO: IAN, MY IMPRESSION FROM HAVING CHAIRED A SCRO IS THAT WE'RE SEEING MORE AND MORE OF THESE IN VITRO USES OF DEIDENTIFIED.

MR. SWEEDLER: THERE'S A LIMITED RANGE OF HESC LINES, AND THEY'RE BEING TRACKED. THERE'S JUST NO -- THERE'S NOTHING COMPARABLE TO THAT WITH IPS.

DR. PRIETO: I GUESS THE REAL QUESTION IS FOR THIS LARGE POOL OF MATERIAL, ARE THE REAL ETHICAL QUESTIONS ALREADY ONES THAT WERE RAISED IN THE DERIVATION PROCESS AND THE DEIDENTIFICATION PROCESS THAT WE'VE TALKED ABOUT? IS THIS DUPLICATION?

CHAIRMAN LO: PAT'S POINT WAS THAT HE THINKS ACTUALLY THERE ARE ISSUES THAT REALLY HAVE TO DO WITH USES THAT ARE DIFFERENT THAN THE ISSUES

HAVING TO DO WITH IDENTIFIABILITY AND CONSENT FOR DERIVATION. AND, IN FACT, THOSE ARE SOME OF THE MORE COMPLEX ISSUES THAT MAY COME UP.

IAN, TO RESPOND TO YOUR POINT, WHAT I'M HEARING IS NOT A WHOLE LOT OF SUPPORT FOR MOVING TO NO NOTIFICATION FOR USE OF DEIDENTIFIED IPSC'S AT THIS POINT UNLESS WE CAN COME UP WITH A BETTER WAY OF SAYING FOR THIS SUBCATEGORY OF IPSC IN VITRO RESEARCH, WHICH MAY, IN FACT, BE THE VAST MAJORITY, IT'S SAFE. SO ABSENT THAT KIND OF SPECIFICATION, I THINK PEOPLE ARE CONCERNED. BUT WE MAY SAY LET'S TRY AND GO BACK TO THE INSTITUTIONS AND SAY CAN YOU HELP US TO COME UP WITH A DEFINITION OF IN VITRO STEM CELL RESEARCH THAT DOESN'T REQUIRE NOTIFICATION AND BY INFERENCE LEAVES OPEN FOR NOTIFICATION POTENTIAL OTHER REVIEWS, OTHER SENSITIVE TOPICS.

THE OTHER THING, I GUESS, IS, PAT, I HEARD YOU SUGGESTING THAT MAYBE WE SHOULD TRY AND BE PROACTIVE AND ON THE OTHER SIDE SAY, AT LEAST AS AN EDUCATIONAL ENDEAVOR, LET'S TRY AND IDENTIFY SOME SENSITIVE USES OF IPSC'S IN VITRO. AND IN THE UK THE ACADEMY OF MEDICAL SCIENCE HAS COMMISSIONED A PANEL THAT MARTIN BOBROW CHAIRED AND WAS WRITTEN UP AND THEY SUMMARIZED THEIR FINDINGS IN *LANCET* WHICH REALLY PUT EXACTLY THEIR FINGER ON THESE CHIMERIC

ISSUES AND SAY A LOT OF THEM ARE NONPROBLEMATIC, AND SOME ACTUALLY ARE OF CONCERN. AND THEY ACTUALLY CALLED FOR A NATIONAL REVIEW IN THE UK. THEY ELECTED TO DO THE NATIONAL REVIEW.

MAYBE WE CAN, GEOFF, SORT OF TRY AND PULL TOGETHER SORT OF OTHER AREAS WHERE PEOPLE HAVE IDENTIFIED SENSITIVE USES OF IN VITRO REPROGRAMMED CELLS, AGAIN, NOT CHANGING THE REGULATION, BUT SORT OF MOVING AHEAD AT LEAST ON AN EDUCATIONAL WORKSHOP FORMAT AND MAKING SURE WE'RE UP TO DATE ON WHAT PEOPLE ELSEWHERE ARE THINKING.

DR. PAT TAYLOR: YOU'RE BEING CHARACTERISTICALLY MODEST, BERNIE. THERE'S A 2009 PAPER, YOU WERE THE SENIOR AUTHOR, WHICH IS A DEFINITIVE LIST OF SENSITIVE USES. IT WAS PROPHETIC, SO IT HASN'T CHANGED. I ACTUALLY READ YOUR WORK.

CHAIRMAN LO: THANK YOU. BUT I'M HEARING THAT WE DON'T WANT TO MOVE TO NO NOTIFICATION FOR THAT LAST LINE. IN FACT, WE'RE THINKING OF SOME CREATIVE THINKING TO IDENTIFY LOW PROBABILITY, BUT HIGH SIGNIFICANCE ISSUES. BUT FOLLOWING IAN'S POINT, YOU NEED TO REALLY SPECIFY WHAT THOSE ARE AND WHY THEY'RE OF CONCERN. AND I THINK, GEOFF, THAT MAY HELP US OUT, BUT IT SEEMS TO ME THAT MAY BE RIPE

FOR COMMENT AND FEEDBACK FROM RESEARCHERS AND INSTITUTIONS AND THE PUBLIC, FOR THAT MATTER, AS WELL AS PERHAPS A THEME FOR US AS A COMMITTEE TO DEAL WITH AT A FUTURE SESSION.

DR. LOMAX: SO IF I'M SUMMARIZING THIS JUST FOR MOVING FORWARD, SO THE CONCEPT OF THE NOTIFICATION, ADDING NOTIFICATION AS AN OPTION BOTH HERE AND HERE IS VIEWED FAVORABLY. WE'RE NOT GOING TO ELIMINATE THE NOTIFICATION REQUIREMENT HERE OR HERE.

MR. SWEEDLER: GEOFF, FOR THE TRANSCRIPT, COULD YOU --

CHAIRMAN LO: JUST SAY WHICH LINES, LINES 3 AND 5.

DR. LOMAX: LET ME JUST STATE IT CLEARLY FOR THE RECORD. SO FOR NEW IPS DERIVATION WITH IDENTIFIABLE SOMATIC CELLS, IT WAS THE SENSE OF THE COMMITTEE THAT IT IS OKAY TO ADD THE INSTITUTIONAL OFFICIAL AS A NOTIFICATION OPTION. AND THE SAME NOTIFICATION REQUIREMENT WOULD APPLY TO USE OF IDENTIFIABLE IPSC CELLS, THAT IT'S OKAY TO INCLUDE THE INSTITUTIONAL OFFICIAL AS AN OPTION.

FOR NEW DERIVATION OF IPSC'S WITH DEIDENTIFIED SOMATIC CELLS, WE WANT TO RETAIN THE NOTIFICATION REQUIREMENT.

AND FOR USE OF DEIDENTIFIED IPSC'S, WE'D LIKE TO RETAIN THE NOTIFICATION REQUIREMENT OF BOTH THE SCRO OR THE INSTITUTIONAL OFFICIAL IN BOTH OF THE LATTER CASES.

CHAIRMAN LO: I THINK THAT'S RIGHT. AND WITH ALL THE COMMENTS ABOUT EDUCATION AND OUTREACH AND THINGS LIKE THAT.

OKAY. LET'S ALL TAKE A BIG DEEP BREATH. CAN WE GO WITHOUT A FORMAL BREAK? TIME IS FLYING AND WE ACTUALLY HAVE A LOT OF INTERESTING THINGS TO TALK ABOUT ON THE SECOND PAGE OF YOUR AGENDA, NO. 5, THE CIRM IPSC BANKING INITIATIVE. AND THERE ARE A COUPLE THINGS WE WANT TO DO HERE.

DR. LOMAX: BERNIE, JUST BRIEFLY BEFORE WE MOVE ON, BECAUSE I KNOW JON THOMAS' TIME IS LIMITED, BUT I KNOW THERE WAS AN INTEREST IN JUST GIVING YOU SOME COMMENTS ON THE INSTITUTE OF MEDICINE REVIEW THAT'S GOING ON. AND ELLEN FEIGAL AND JON THOMAS, I THINK, ARE AVAILABLE WHILE WE HAVE TIME.

CHAIRMAN LO: AGAIN, BECAUSE THIS IS AN ONGOING ACTIVITY AND THE IOM HASN'T ISSUED ITS REPORT, SO JUST SORT OF AN UPDATE AND ANY COMMENTS.

DR. FEIGAL: I'LL KEEP IT REALLY BRIEF. SO THE INSTITUTE OF MEDICINE ACTUALLY WAS CONVENED AT THE REQUEST OF CIRM TO REALLY PROVIDE AN

INDEPENDENT ASSESSMENT OF OUR PROGRAMS, OPERATIONS, STRATEGIES, AND PERFORMANCE SINCE THE INCEPTION OF CIRM. AND SPECIFICALLY THE IOM IS REVIEWING AND ADDRESSING OUR INITIAL PROCESSES, WHAT CAN BE LEARNED FROM OUR HISTORY AND PROCESS OF BUILDING CONSENSUS IN THE PUBLIC AND SCIENTIFIC COMMUNITIES TO SUPPORT THE WORK OF CIRM, OUR PROGRAMMATIC AND SCIENTIFIC SCOPE. DO WE HAVE THE PORTFOLIO OF PROJECTS AND GRANTS, OPPORTUNITIES THAT ARE NECESSARY TO MEET OUR SCIENTIFIC GOALS? HOW COULD WE IMPROVE UPON WHAT WE DO? AND OUR ORGANIZATION AND MANAGEMENT SYSTEMS, DO THEY HAVE THE LEVEL OF TRANSPARENCY AND THE LEVEL OF STAKEHOLDER AND SCIENTIFIC COMMUNITY INVOLVEMENT NEEDED TO MEET OUR PUBLIC RESPONSIBILITIES AND SCIENTIFIC GOALS? OUR FUNDING MODEL, THE IMPACT OF OUR WORK OF THE INSTITUTE, AND WHAT ARE THE ADVANTAGES FOR COVERING LONG-TERM COSTS OF MEDICAL RESEARCH? COULD ASPECTS OF OUR MODEL SERVE AS A PARADIGM FOR OTHER STATES OR COUNTRIES? AND ALSO THEY'LL BE LOOKING AT SOME OF OUR IP POLICIES, INTELLECTUAL PROPERTY POLICIES, AND STRENGTHS AND WEAKNESSES OF THEM.

BUT THE PRINCIPAL OBJECTIVE OF THE IOM REVIEW IS TO REALLY ENSURE THAT ALL ASPECTS OF OUR OPERATIONS ARE FUNCTIONING AT PEAK PERFORMANCE. AND

THEY'RE ALSO ASKED TO MAKE RECOMMENDATIONS REGARDING SHORT, MEDIUM, AND LONG-TERM ACTIONS THAT CAN REALLY IMPROVE THE PERFORMANCE OF OUR INSTITUTE. SO THAT'S AN OVERALL PLAN. AND, J.T., YOU MAY WANT TO ADD SOME ADDITIONAL PERSPECTIVES.

CHAIRMAN THOMAS: THEY'RE UNDERTAKING A HIGHLY COMPREHENSIVE REVIEW. THEY HAVE IMPANELED A NUMBER OF EXPERTS FROM AROUND THE COUNTRY. WE HAVE GOTTEN ANY NUMBER OF INFORMATION REQUESTS TO INFORM THEIR INQUIRY, WHICH WE'VE GONE SORT OF PIECE BY PIECE TO RESPOND TO. THEY'VE HAD A PUBLIC SESSION LAST JANUARY UP HERE IN SAN FRANCISCO WHERE A NUMBER OF MEMBERS OF CIRM AND SOME PI'S AND OTHERS TESTIFIED. JEFF TESTIFIED, ELLEN, I DID, ALAN DID, DUANE DID. AND THEY HAVE A SECOND PUBLIC MEETING ACTUALLY COMING UP NEXT WEEK. IF ANY OF YOU GUYS HAPPEN TO BE IN IRVINE ON TUESDAY AND FIND YOURSELF WITH NOTHING BETTER TO DO, IT SHOULD BE QUITE AN INTERESTING SESSION.

THEY WILL THEN GO INTO A CLOSED SESSION ON THE FOLLOWING DAY AND WILL BE DELIBERATING OVER THE COURSE OF THE COMING MONTHS. WE EXPECT THAT THE REPORT, FOLLOWING A 14-MONTH PROCESS, WILL BE DELIVERED TO US IN DECEMBER OF THIS YEAR. AND WE LOOK FORWARD TO THE INSIGHT AND UNDOUBTEDLY MANY

RECOMMENDATIONS THAT THE IOM BRINGS TO US AS A RESULT OF THEIR REVIEW. SO WE THINK THIS IS A VERY GOOD UNDERTAKING. PARTICULARLY WE'RE SORT OF AT THE MIDPOINT OF OUR FUNDING CYCLE HERE. AND TO HAVE THEM REVIEW ALL ASPECTS IS SOMETHING THAT SHOULD BE VERY HELPFUL.

I'LL NOTE ONE OF THE THINGS THEY'RE REVIEWING, WHICH IS KEY, IS EVERY FEW YEARS WE REVISE OUR STRATEGIC PLAN. AND ELLEN HAS TAKEN THE LABORING OAR AND DONE A GREAT JOB WITH PAT ON THAT. AND THE TIMING OF THAT STRATEGIC PLAN REVIEW WAS REALLY TO COINCIDE WITH THEIR LARGER REVIEW. AND SO WE ANTICIPATE SOME INTERESTING FEEDBACK ON THAT AS WELL.

SO A VERY COMPREHENSIVE, VERY COMPREHENSIVE PROCESS, AND WE'RE LOOKING FORWARD TO HEARING WHAT THEY HAVE TO SAY.

CHAIRMAN LO: GREAT. THANKS, ELLEN AND JON. JON, IF YOUR TIME IS LIMITED, IS THERE ANYTHING YOU WANT TO SAY WITH REGARD TO EITHER WHAT WE JUST TALKED ABOUT WITH THE REGULATION REVISIONS OR WHAT'S COMING UP NEXT WITH THE BANKING INITIATIVE?

CHAIRMAN THOMAS: I'D JUST LIKE TO SAY THAT THIS IS A MOST IMPRESSIVE PANEL AND DISCUSSION.

AND IN TERMS OF THE SUBSTANCE, YOU FOLKS ARE ALL THE EXPERTS ON THAT. AND IT'S BEEN A VERY INTERESTING THING TO HEAR THE GIVE-AND-TAKE BACK AND FORTH. WE GREATLY APPRECIATE YOU SPENDING THE TIME, AND IT JUST DEMONSTRATES, AGAIN, THE HIGH LEVEL OF INPUT THAT ALL OF YOU HAVE. SO I THINK THAT GETTING TO A MEASURED RESULT, AS YOU HAVE, FOLLOWING EXTENSIVE CONVERSATION IS GREAT, AND IT'S EXACTLY WHAT THE DOCTOR ORDERED, AS IT WERE. WE LOOK FORWARD TO HEARING THOUGHTS ON THE IPS CELL BANK COMING UP.

CHAIRMAN LO: GREAT. WITH THAT, LET'S TURN OUR ATTENTION TO THAT. AND THERE ARE TWO THINGS WE WANT TO DO. FIRST, WE JUST WANT TO UPDATE THE SWG ON THE STATUS OF THE INITIATIVE, AND I WANT TO KIND OF REALLY KEEP THAT TO AN UPDATE, IF WE CAN, BECAUSE I REALLY WANT TO FOCUS ON THE CONSENT RECOMMENDATIONS, THE MODEL CONSENT PROCESS THAT GEOFF AND OTHERS HAVE DEVELOPED AND THAT WE TALKED ABOUT IN OUR APRIL 2011 SWG MEETING.

SO WHAT I'D LIKE TO DO IS FIRST HAVE JUST A SUMMARY OF THE FORTHCOMING REQUEST FOR APPLICATIONS WITH REGARD TO THE STEM CELL BANKING AND THEN SOME BACKGROUND ON THE IMPLEMENTATION OF THE CIRM CONSENT RECOMMENDATIONS, REQUIREMENTS FOR IPSC DERIVATION FROM DR. SCHUELE OF THE PARKINSON'S

INSTITUTE. AND THEN FOR US TO REALLY TALK ABOUT THE MODEL CONSENT RECOMMENDATIONS. DO WE HAVE ANYTHING TO REVISE OR ADD, OR DO WE WANT TO RECOMMEND THAT THE ICOC APPROVE THEM?

I ALSO WANT TO MAKE SURE WE HAVE TIME FOR NICOLE TO TALK TO US ABOUT THIS VERY IMPORTANT AND DIFFICULT ISSUE, RETURN OF RESULTS. WE'RE ASSUMING WE GET THE MATERIALS, DO THE IPSC BANK, AND GET A LOT OF INTERESTING RESULTS. WHAT ARE WE GOING TO DO ABOUT RETURNING RESULTS TO THE DONORS GIVEN WHAT JOHN WAGNER SAID ABOUT A LOT OF THESE DONORS REALLY WANT TO KNOW? UTA, WHY DON'T YOU START US OFF WITH THE INITIATIVE THAT CIRM IS GOING TO DO HERE.

DR. GRIESHAMMER: I'M JUST GOING TO GIVE YOU A VERY BRIEF OVERVIEW OF THE INITIATIVE. AS MYSELF, I'M A SCIENCE OFFICER AT CIRM WHO TOGETHER WITH MY COLLEAGUE, SOHEL TALIB, ARE LEADING TO RELEASE THIS SET OF RFA'S FOR OUR IPS CELL BANKING INITIATIVE. I'LL JUST GIVE YOU A BRIEF UPDATE WHERE WE STAND WITH THAT OR WHAT ITS PURPOSE IS.

SO THE GOAL REALLY IS FOR CIRM TO CREATE AN IPS CELL RESOURCE THAT WILL BE AVAILABLE WORLDWIDE FOR PEOPLE TO STUDY THE DISEASES THAT WILL BE INCLUDED IN THIS BANK. I JUST WANT TO POINT OUT, AS YOU ALL KNOW, TO CREATE SUCH A BANKING SITUATION,

OBVIOUSLY YOU NEED TO COLLECT TISSUES, YOU NEED TO DERIVE IPS CELLS, AND THEN YOU NEED TO BANK THEM, AND RELIABLY DISTRIBUTE THEM TO THE RESEARCH COMMUNITY. AND TO CREATE THIS RESOURCE IS THE PURPOSE OF THE CURRENT IPS INITIATIVE.

ONCE THIS RESOURCE HAS BEEN CREATED, THE HOPE IS THAT IT WILL BE WIDELY USED WORLDWIDE INDEED FOR RESEARCHERS TO STUDY DISEASE MECHANISMS THAT HAVEN'T BEEN DISCOVERED YET, TO USE THESE CELLS FOR TARGET DISCOVERY THAT CAN BE USED TO INFORM FUTURE DRUG DEVELOPMENT FOR THE DISEASES THAT ARE INCLUDED IN THIS BANK, AND THEN ALSO POSSIBLY TO USE THE CELLS ACTUALLY FOR SCREENING OF COMPOUND LIBRARIES TO DISCOVER AND DEVELOP DRUGS.

THIS INITIATIVE HAS BEEN ACTUALLY IN THE MAKING FOR QUITE A WHILE. I JUST WANT TO GIVE CREDIT INDEED TO THIS GROUP THAT HAS ALREADY DEALT, AND WE'RE GOING TO TALK MORE ABOUT, WITH THE ISSUES SURROUNDING CREATING SUCH A LARGE RESOURCE. WE ALSO HAD A SCIENTIFIC WORKSHOP A WHILE AGO TO ADDRESS OR TO GET INPUT FROM THE SCIENTIFIC COMMUNITY AS TO WHAT THE NEEDS ARE IN THE COMMUNITY FOR SUCH A BANK.

WE'VE INTERACTED WITH THE NIH MORE RECENTLY BOTH AT THE SCIENTIFIC AS WELL AS POLICY CONSIDERATION LEVEL TO MAKE THE BEST BANK THAT WE

CAN MAKE. AND IN THIS CONTEXT ACTUALLY, THE FIRST PORTION REALLY OF THIS INITIATIVE, CIRM AND THE NIH THROUGH THE INSTITUTE FOR NEUROLOGICAL DISORDERS AND STROKE HAS ACTUALLY ENTERED INTO A COLLABORATION WHERE WE ARE ALREADY NOW CO-FUNDING A PROJECT WHERE IPS CELLS ARE GENERATED FOR HUNTINGTON'S DISEASE, PARKINSON'S DISEASE, AND ALS TO STUDY THESE NEURODEGENERATIVE DISEASES. SO THOSE DISEASES ARE ALREADY, IN EFFECT, COVERED THROUGH A COLLABORATION NOW BETWEEN CIRM AND THE NIH.

NOW GOING FORWARD, WE NOW WILL BE RELEASING ACTUALLY A SET OF THREE RFA'S THAT WILL BE CO-RELEASED IN MID-MAY HOPEFULLY WHERE WE WILL TACKLE -- OR ASK FOR APPLICATIONS FOR PEOPLE TO TACKLE INDIVIDUALLY THESE THREE ASPECTS THAT WILL LEAD TO THE GENERATION OF A HIGH QUALITY RESOURCE OF IPS CELLS.

AND THE FIRST RFA WILL BE FUNDING AWARDS WHERE CLINICIANS AND STEM CELL SCIENTISTS COLLABORATE TO IDENTIFY DISEASES THAT THEY THINK SHOULD BE INCLUDED IN THIS IPS CELL BANK. THE DELIVERABLE OUT OF THESE AWARDS WILL BE INDEED THE TISSUES THAT WILL BE COLLECTED FROM THE PARTICIPATING PATIENTS AND CONTROL INDIVIDUALS. THOSE TISSUES WILL BE PROVIDED TO A DIFFERENT

ENTITY, A SINGLE ENTITY, IN FACT, WHO WILL BE AWARDED THE IPSC CELL DERIVATION AWARD. AND THE JOB OF THAT ENTITY WILL BE TO USE THESE TISSUES THAT WERE COLLECTED HERE AND USE A STANDARD PROCEDURE TO DERIVE HIGH QUALITY IPS CELLS UNDER STANDARD OPERATING PROCEDURES.

AND THEN, FINALLY, ONCE THESE IPS CELLS HAVE BEEN DERIVED, THEY WILL BE HANDED OVER TO A PLURIPOTENT CELL BANK FOR BANKING AND WORLDWIDE DISTRIBUTION.

JUST TO VERY BRIEFLY GIVE YOU A LITTLE BIT MORE DETAIL FOR EACH OF THESE RFA'S, WHAT'S IMPORTANT FOR THE DISEASE MODELING AWARDS, WHICH REALLY ARE ABOUT IDENTIFYING THE PATIENT POPULATIONS FROM WHOM THE TISSUES WILL BE COLLECTED, WE WILL FOCUS THIS SET OF AWARDS ON PREVALENT, GENETICALLY COMPLEX DISEASES. SO THIS IS VERY DIFFERENT FROM SOME OF THE MAIN IPS DISEASE MODELING EFFORTS THAT HAVE BEEN PUBLISHED SO FAR WHERE PEOPLE HAVE CONCENTRATED ON MONOGENIC DISEASES, HIGHLY PENETRANT MONOGENIC DISEASES, AND CIRM REALLY HAS THE VISION TO NOW MOVE THE FIELD EVEN FURTHER FORWARD AND START TO PROVIDE A RESOURCE WHERE PEOPLE CAN GO AFTER REALLY PREVALENT, BUT GENETICALLY COMPLEX DISEASES USING THIS AWARD.

AND THE GOAL IS TO PROVIDE FUNDS TO COLLECT SAMPLES FROM ABOUT 1200 INDIVIDUALS. THE CELL SAMPLES, THEN, FROM THESE 1200 INDIVIDUALS, AS I SAID, WILL BE THEN DERIVED BY USING A SINGLE DERIVATION METHOD BY THE RECIPIENT OF THE SECOND AWARD; WHEREAS, THE RECIPIENT OF THE THIRD AWARD WILL BANK AND DISTRIBUTE THESE LINES. THE RECIPIENT OF THIS AWARD WILL ALSO BE CHARGED TO BANK ADDITIONAL PLURIPOTENT STEM CELL LINES THAT HAVE ALREADY BEEN AND ARE BEING GENERATED IN CALIFORNIA.

THE "I" HAS BEEN DROPPED HERE BECAUSE, AS ELLEN MENTIONED EARLIER, THE GOAL IS ACTUALLY HERE TO CAPTURE HIGH QUALITY LINES GENERATED IN CALIFORNIA, NOT ONLY IPS CELL LINES, BUT ALSO EMBRYONIC STEM CELL LINES THAT HAVEN'T BEEN BANKED YET AND, THEREFORE, ARE MAYBE NOT AS EASILY AVAILABLE AND HIGH QUALITY AVAILABLE TO OTHERS IN THE WORLD. AND THESE WOULD ALSO INCLUDE, FOR INSTANCE, LINES THAT HAVE BEEN GENERATED FROM EMBRYOS THAT WERE IDENTIFIED TO CARRY GENETIC DISEASES SUCH AS MARPHAN'S DISEASE AND HUNTINGTON'S DISEASE.

NOW, MY FINAL SLIDE, I JUST WANT TO POINT OUT THAT THE GOAL OR REALLY REEMPHASIZE THAT THE GOAL OF THIS PLURIPOTENT STEM CELL BANK IS INDEED TO

PROVIDE A VERY HIGH QUALITY RESOURCE WORLDWIDE FOR RESEARCHERS AND DRUG DEVELOPERS TO MODEL DISEASES, DO TARGET DISCOVERY, AND EVEN DISCOVER NEW DRUGS IN PREVALENT DISEASES WHERE THERE IS A REAL NEED AND POTENTIAL FOR GREAT IMPACT FOR DISEASE MITIGATION. BUT I DO WANT TO POINT OUT HERE THAT, IN ADDITION TO THINKING ABOUT THE POTENTIAL SCIENTIFIC UTILITY OF ALL THESE IPS CELL LINES AND OTHER PLURIPOTENT CELL LINES AND THE HIGH QUALITY OF THESE LINES, AS WE'RE THINKING ABOUT THE SET OF RFA'S, AS YOU KNOW, WE'VE, OF COURSE, TAKEN INTO ACCOUNT WORK FROM THIS GROUP ABOUT TISSUE DONOR CONSENT, AND WE'LL TALK MORE ABOUT THAT. WE ARE VERY INTERESTED IN TERMS OF REALLY MAKING THIS RESOURCE AS VALUABLE TO FUTURE DISEASE MODELING AND DRUG DISCOVERY TO INCLUDE AS MUCH MEDICAL INFORMATION ON THE TISSUE DONORS TO INFORM THE IN VITRO STUDIES OF DISEASE PHENOTYPES.

WE'RE ALSO CONCERNED ABOUT THINGS LIKE WE'RE TRYING TO ADDRESS AHEAD OF TIME ISSUES SURROUNDING FREEDOM TO OPERATE. THE IPS INVENTIONS WERE RELATIVELY RECENT. THEY'RE BEING PATENTED, AND WE ARE TRYING TO UNDERSTAND HOW THIS WOULD INFLUENCE FUTURE USES OF THESE CELL LINES. AND SIMILARLY, WE ARE THINKING ABOUT WHAT KINDS OF MATERIAL TRANSFER AGREEMENTS, FOR INSTANCE, WE WOULD TRY TO IMPLEMENT

SO THAT THERE IS -- CERTAINLY THAT THE INTELLECTUAL INPUT THAT CAME INTO THIS BANK IS PROPERLY ACKNOWLEDGED, BUT DOESN'T INHIBIT THE USE OF THESE CELLS FOR DRUG DEVELOPMENT IN THE FUTURE EITHER.

SO IT'S A VERY COMPLEX PROJECT OBVIOUSLY. HAPPY TO ANSWER ANY QUESTIONS YOU HAVE RIGHT NOW.

DR. LOCKHART: JUST TO MAKE SURE I UNDERSTAND, ARE THESE GOING TO BE -- WILL THE THREE DIFFERENT TYPES OF GRANTS BE OPERATING ALL AT THE SAME TIME? THEY'LL BE RELEASED TOGETHER AND FUNDED TOGETHER?

DR. GRIESHAMMER: YES.

DR. LOCKHART: I WAS JUST WONDERING, LOOKING AT THE TIMELINES, IF THE '03 DERIVATION AWARD IS A THREE-YEAR AWARD AND THE BANK IS OPERATING AT THE SAME TIME, WILL THE BANK BE OUT OF FUNDING JUST WHEN THE NEW LINES ARE DERIVED?

DR. GRIESHAMMER: THAT'S A GOOD QUESTION. SO WE ACTUALLY -- AND OBVIOUSLY TO REALLY COORDINATE THESE THREE ITEMS WILL BE QUITE TRICKY. AND ONE REQUIREMENT REALLY OF RECEIVING THESE AWARDS, AFTER OUR BOARD HAS APPROVED THE FUNDING, BUT PRIOR TO RELEASING THE MONEY, WE'RE ACTUALLY GOING TO MAKE SURE THAT ALL THE RECIPIENTS OF ALL THESE AWARDS COME TOGETHER IN A MEETING AND DISCUSS THE LOGISTICS

OF THIS. THERE'S ACTUALLY A LOT OF INFORMATION THAT HAS TO MOVE BETWEEN, FOR INSTANCE, THE DERIVER WILL DETERMINE THE TISSUE COLLECTION PROTOCOL, WHICH THE TISSUE COLLECTOR WILL HAVE TO EXECUTE. SO THERE ARE COMPLEXITIES LIKE THIS.

BUT YOU DO MAKE A GOOD POINT, AND WE'LL HAVE TO THINK ABOUT TO MAKE SURE THAT THERE ARE CONTINGENCIES FOR DELAYS IN ONE AWARD, THAT IT DOESN'T RUIN THE CHANCES FOR THE LAST AWARD TO BE FULLY EXECUTED.

DR. LOCKHART: YOU WOULDN'T WANT THE BANK TO RUN THROUGH MOST OF THEIR MONEY WAITING AROUND. AND ON THE OTHER HAND, IF YOU MADE AWARD AND THEN DELAYED -- YOU SELECTED YOUR GRANTEE, DELAYED GIVING THEM THE MONEY FOR A YEAR BECAUSE THEY DIDN'T HAVE ANYTHING TO DISTRIBUTE, THAT'S NOT GOING TO MAKE THEM HAPPY. SO JUST TRYING TO BALANCE OPERATIONALLY HOW THAT NEEDS TO WORK.

AND THEN ALSO THINKING ABOUT OUT-YEAR FUNDING. THREE YEARS IS NOT VERY LONG IN THE LIFE OF A BIOBANK. SO HOW YOU WOULD HANDLE OUT YEARS AND ALSO THINKING ABOUT LEGACY ISSUES IN TERMS OF THE COLLECTION, MAKING SURE ALL OF THAT'S IN PLACE, MAKING SURE EVERYTHING IS REALLY WELL DOCUMENTED IN THE EVENT THAT YOU DID NEED TO TRANSFER THE

COLLECTION AND THAT YOU HAVE WRITTEN INTO AGREEMENTS WITH THE SITE THAT THEY WILL BE RESPONSIBLE FOR OVERSEEING THAT PROCEDURE SHOULD ANYTHING NEED TO HAPPEN?

DR. GRIESHAMMER: THE RFA'S WILL BE QUITE DETAILED IN TERMS OF REQUIREMENTS. MUCH UNLIKE OTHER RFA'S, WHICH ARE REALLY RESEARCH DRIVEN, WE ACTUALLY HAVE A LIST OF THESE ARE THE REQUIRED ACTIVITIES FOR THE RECIPIENTS. AND WE ARE, FOR INSTANCE -- BANKS OFTEN DO HAVE -- WE'RE HOPING, OF COURSE, THAT THE BANK WILL BE LONG-TERM SUSTAINABLE, AND WE WILL ASK FOR A SUSTAINABILITY PLAN, AND ULTIMATELY THEY'LL BE ABLE TO SELL, HOPEFULLY AT LEAST, SOME OF THESE LINES AND THEREBY MAINTAIN THE OPERATION.

AS A MATTER OF FACT, IT'S A LITTLE BIT UNUSUAL FOR A BANK TO GET REALLY GOOD FUNDING TO START GETTING EVERYTHING IN PLACE, BUT OBVIOUSLY WE ARE EXPECTING THAT THEY WILL BE SELLING LINES FOR HOPEFULLY A LONG TIME TO COME.

DR. FEIGAL: I JUST WANTED TO ADD YOUR CONCERNS ARE THE SAME AS WE HAD ABOUT THE TIMING. SO, FRANKLY, WE'VE DONE A LOT OF THOUGHT ABOUT HOW TO COORDINATE IT SO THAT THINGS ARE -- WHEN THINGS ARE READY TO BE DEPOSITED, THERE OBVIOUSLY IS GOING

TO BE A REPOSITORY TO DO SO. ALSO THERE ARE ALREADY DERIVED LINES THAT ARE READY TO GO IN NOW. SO WE THINK IT WILL SATISFY THAT PURPOSE.

AS UTA MENTIONED, THERE IS DEFINITELY A SUSTAINABILITY PLAN BECAUSE WE DO WANT THIS TO BE A LONG-LASTING RESOURCE. WE DO RECOGNIZE THAT WE DON'T WANT TO START SOMETHING THAT HAS THE VULNERABILITY OF NOT HAVING LONG-TERM POTENTIAL. SO THAT'S DEFINITELY PART OF THE REVIEW CRITERIA.

DR. ROBERTS: I HAVE A QUESTION. AT THE PRIOR END OF IT, THESE PARTLY ETHICAL ISSUES THAT YOU RAISE ABOUT TISSUE DONOR CONSENT, MEDICAL INFORMATION, WHICH RAISES ALL SORTS OF ETHICAL -- EACH OF THEM HAS A SET OF ETHICAL CONCERNS THAT PROBABLY SHOULD BE RESOLVED PRIOR TO THE BEGINNING OF TISSUE COLLECTION. AND I JUST WONDERED IF THAT WAS PART OF THE TIMING CONSIDERATION AS WELL.

DR. GRIESHAMMER: SO I THINK WE WILL BE -- FIRST, I SHOULD SAY THERE IS THE UTILITY OF THE BANK VERSUS THE ETHICAL ISSUES SURROUNDING THE DONORS.

DR. ROBERTS: EXACTLY.

DR. GRIESHAMMER: AND SO THE MODEL CONSENT FORM THAT WAS REALLY DEVELOPED BASED ON THE DELIBERATIONS OF THIS COMMITTEE IS WHAT IS BEING --

ACTUALLY WILL BE PROVIDED IN THIS RFA AS AN EXAMPLE THAT BOTH SATISFIES CIRM'S REQUIREMENTS AND THE REQUIREMENTS OF THE RFA. I'M SURE THERE WILL BE SOME MORE TALK ABOUT IT.

IN TERMS OF THE UTILITY OF THE BANK FOR DOWNSTREAM USE AND PERHAPS DRUG DISCOVERY IN THE FUTURE, AS BROAD A CONSENT, NOT FOR SEEING POTENTIAL USES, BUT ALLOWING THEM WOULD BE, OF COURSE, IDEAL.

DR. ROBERTS: IT WILL BE PART OF THE RFA THEN.

DR. FEIGAL: YES. I JUST WANT TO SAY LAST YEAR THIS COMMITTEE, WE NOW HAVE NEW MEMBERS, ACTUALLY THIS WAS A BIG TOPIC OF DISCUSSION AT LAST YEAR'S. AND ALSO WE'VE BEEN WORKING ACTIVELY WITH THE NATIONAL INSTITUTES OF HEALTH TO MAKE SURE WE HARMONIZE OUR INFORMED CONSENT SO THAT WHAT WE DO CAN BE HARMONIZED ON A NATIONAL LEVEL AS WELL.

CHAIRMAN LO: DOROTHY, IN FACT, SET US UP FOR THE REST OF THE MEETING EXACTLY TO DEAL WITH THOSE TWO QUESTIONS.

CHAIRMAN THOMAS: I'D JUST LIKE TO QUICKLY ADD THAT THIS IS -- WE WERE REQUIRED BY SOME STATE LEGISLATION PASSED IN 2010 TO PRODUCE THIS MARCH 1ST A TRANSITION PLAN. TIMING WAS SORT OF INTERESTING SINCE IF WE GET NO ADDITIONAL FUNDING, OUR LAST

ACTUAL DISTRIBUTION WON'T BE TILL PROBABLY 2021, LAST AWARDS ROUGHLY 2017. SO IT WAS SORT OF AN ARBITRARY DATE WELL IN ADVANCE. BUT IT WAS A USEFUL EXERCISE BECAUSE IT GOT US THINKING ABOUT HOW WE'RE GOING TO HAVE TO TRANSITION ALL SORTS OF STUFF IF AND WHEN IT TURNS OUT THAT WE DON'T HAVE ADDITIONAL FUNDING. AND THAT'S A WHOLE OTHER SEPARATE TOPIC NOT FOR TODAY'S DISCUSSION.

BUT SPECIFICALLY THE IPS CELL BANK WAS ONE OF THOSE TOPICS THAT WAS GIVEN A LOT OF DISCUSSION AND THOUGHT AS TO WHAT WE WOULD DO IF AND WHEN. SO IT'S VERY MUCH ON THE FRONT OF EVERYBODY'S MIND.

CHAIRMAN LO: ONE LAST COMMENT. THEN I WANT TO SORT OF PUSH AHEAD TO GET TO THE CONSENT AND THE RETURN OF RESULTS ISSUES.

DR. BOTKIN: MAYBE A QUICK QUESTION. HOW IS INTELLECTUAL PROPERTY GOING TO BE MANAGED?

DR. GRIESHAMMER: THE LAWYER WHO'S ACTUALLY MOSTLY INVOLVED IN THAT IS NOT HERE RIGHT NOW. SO THERE ARE MULTIPLE INTELLECTUAL PROPERTY ISSUES ASSOCIATED HERE. THERE'S THE INTELLECTUAL PROPERTY IN TERMS OF WHO OWNS THESE LINES, AND I DON'T THINK THAT'S BEEN -- I DON'T KNOW, ELLEN, IF YOU CAN SPEAK TO THAT IN TERMS OF OBVIOUSLY THE PEOPLE WHO MAKE THE DECISIONS ABOUT REALLY THE MOST

INTELLECTUALLY INTERESTING PART OF ALL OF THIS IS TO DECIDE WHICH DISEASES SHOULD BE INCLUDED. ARE THEY GOING TO BE AMENABLE TO MODELING AND WHAT OWNERSHIP WILL BE AT THIS END FOR THE USE OF THE LINES.

BUT THEN THE OTHER INTELLECTUAL PROPERTY ISSUES THAT ARE REALLY ASSOCIATED WITH THIS IS THE DERIVATION ITSELF, WHICH ALREADY HAS PATENTS ISSUED THAT MIGHT ULTIMATELY LIMIT THE USE OF THESE LINES DEPENDING ON HOW THESE PATENTS WERE WRITTEN FOR WHICHEVER DERIVATION METHOD WILL BE USED.

I BELIEVE THAT, IN GENERAL, FOR ANYTHING, FOR ANY -- I KNOW VERY LITTLE ABOUT THIS END OF BANKING, BUT IT'S MY UNDERSTANDING THAT MATERIALS THAT DO GET BANKED, YOU THEN ARE A CUSTOMER AND RECEIVE THE CELL LINES. IF YOU'RE AN ACADEMIC, THERE ARE CERTAIN MATERIAL TRANSFER AGREEMENTS THAT WILL BE PART OF THIS RFA REVIEW WHERE WE WILL KNOW PRIOR TO ESTABLISHING THE BANK WHAT THESE MATERIAL TRANSFER AGREEMENTS WILL LOOK LIKE TO ALLOW ACADEMIC USE.

MY UNDERSTANDING IS THAT IF I WERE A COMPANY WHO HAD AN INTEREST IN USING, LET'S SAY, SOME LINES FROM DIABETES PATIENTS TO SCREEN FOR NEW DRUGS, I WOULD HAVE TO GO BACK TO THE PATENT HOLDERS AND NEGOTIATE LICENSES WITH THEM IN CASE I DO

DISCOVER A DRUG THAT WOULD MAKE IT.

MR. SWEEDLER: AGAIN, I'M ALSO NOT THE CIRM LAWYER WHO'S DEALING WITH THIS MOST DIRECTLY, BUT MY UNDERSTANDING IS THAT THERE'S NO INTENT BY CIRM TO IMPOSE A PARTICULAR IP APPROACH, BUT THAT APPLICANTS WILL BE ASKED TO EXPLAIN WHAT APPROACH THEY WANT TO TAKE. THE OBVIOUS CONCERNS ARE MAKING SURE THAT THERE ISN'T GOING TO BE AN IP APPROACH THAT WOULD UNDERMINE THE UTILITY, MAKE IT NOT ATTRACTIVE OR USEFUL AS A WORLDWIDE RESOURCE, AND AT THE SAME TIME RECOGNIZING THAT SOME OF THAT CAN BE AN IMPORTANT PART OF WHAT MAKES IT AN ECONOMICALLY SUSTAINABLE MODEL.

SO I THINK IT'S GOING TO BE AN APPROACH IN WHICH WE SAY THESE ARE THE OUTCOMES WE NEED TO SEE AND BE OPEN TO DIFFERENT PROPOSALS FOR HOW THAT WOULD BE DONE.

DR. ROBERT TAYLOR: SO JUST KIND OF GIVEN THE COMPLEXITY OF ALL OF THIS, DID YOU THINK ABOUT A PPG, A PROGRAM PROJECT GRANT, KIND OF A MODEL RATHER THAN THREE INDEPENDENT COMPETITIVE MECHANISMS? IT SEEMS TO ME TO MAKE THIS ALL COME ALTOGETHER WITH THREE INDEPENDENT FUNCTIONING GROUPS, WHERE IF YOU WANT TO DISTRIBUTE THE WEALTH ACROSS THE STATE, YOU COULD HAVE INSISTED EACH COMPONENT BE AT A DIFFERENT

SITE. IT WOULD SEEM TO ME THAT SOME COORDINATION UP FRONT WOULD HELP YOU TO RESOLVE SOME OF THESE REALLY THORNY ISSUES THAT I GUESS YOU HAVE A MONTH --

CHAIRMAN LO: YOU KNOW WHAT, FOLKS, I WOULD LIKE TO STRESS WE NOT TRY AND REWRITE THEIR RFP. THAT'S NOT OUR JOB. I WOULD LIKE TO SORT OF SETTLE OR GET SOME MORE INFORMATION FOR GEOFF ON THE IP QUESTIONS. SCOTT, DID YOU HAVE SOMETHING?

MR. TOCHER: I WAS JUST GOING TO ADD -- JUST TO LET YOU KNOW THAT THAT'S THE SUBJECT OF AN UPCOMING MEETING OF A SUBCOMMITTEE OF THE BOARD OF OUR INTELLECTUAL PROPERTY SUBCOMMITTEE TO LOOK AT THE ISSUES THAT IAN JUST DISCUSSED AND POSSIBLE MODIFICATIONS THAT WILL BE REQUIRED OF OUR IP POLICIES CURRENTLY TO MAKE SURE THAT THOSE PROBLEMS DON'T ARISE. IT'S SOMETHING THAT YOU CAN FOLLOW ALONG WITH THE REST OF US.

CHAIRMAN LO: GREAT. I'M GOING TO SUGGEST WE ACTUALLY MOVE AHEAD. WE HAVE WHAT SHOULD BE A VERY INTERESTING PRESENTATION FROM THE PARKINSON'S INSTITUTE THAT HAS ACTUALLY USED THE CONSENT FORM THAT CIRM HAS WORKED ON. AND THEN I WANT TO USE THAT TO SPRINGBOARD TO ACTUALLY TALKING ABOUT THIS MODEL CONSENT AND CONSENT FORM, I GUESS IS IMPORTANT TO STRESS. AND THEN REALLY ALSO THEN MOVE ON TO

HEARING ABOUT THE RETURN OF RESULTS.

DR. LOMAX: I WOULD JUST SAY, IN THE INTEREST OF ACCURATE DISCLOSURE, CIRM HAS BEEN THE BENEFICIARY OF THE PARKINSON'S INSTITUTE SHARING THEIR FORM WITH US. SO I JUST WANT TO LET YOU KNOW ABOUT THE PATHWAYS. SO WE WILL CIRCULATE. WE'VE REALLY RELIED ON OUR GRANTEES TO GIVE US INSIGHTS INTO HOW TO DO THIS. I DON'T WANT TO TAKE CREDIT FOR SOMEONE ELSE'S WORK.

DR. SCHUELE: THANKS, GEOFF, FOR INVITING ME. AND I'LL GIVE YOU A REAL EXAMPLE OF HOW WE USE OUR IRB CONSENT FOR THE DERIVATION OF INDUCED PLURIPOTENT STEM CELLS FROM SKIN CELLS.

GEOFF WANTED THAT I INTRODUCE MYSELF. SO I'M AN ASSISTANT PROFESSOR AT THE PARKINSON'S INSTITUTE. IT'S MY SEVENTH YEAR AT THE PARKINSON'S INSTITUTE. I'M A MEDICAL DOCTOR BY TRAINING, NOT LICENSED HERE IN THE U.S., SO I GOT MY MEDICAL DEGREE IN GERMANY. I DID A POSTDOCTORAL FELLOWSHIP AT STANFORD. SEVEN YEARS AGO I MOVED TO THE PARKINSON'S INSTITUTE.

SO FOR THOSE OF YOU WHO DON'T KNOW WHO WE ARE, WE WERE FOUNDED IN 1988 BY DR. LANGSTON, DR. BILL LANGSTON. WE ARE LOCATED IN SUNNYVALE, CALIFORNIA. IF YOU DRIVE DOWN SOUTH TO SAN JOSE

101, WE ARE RIGHT ACROSS MOFFET FIELD, NASA MOFFET FIELD. I THINK THE UNIQUENESS OF OUR PLACE IS THAT WE REALLY HAVE EVERYTHING UNDER ONE ROOF. WE HAVE A CLINIC, WE HAVE BASIC RESEARCH, AND WE HAVE CLINICAL RESEARCH. SO THAT'S WHAT THIS NOTE SAYS, SCIENCE AND PATIENT CARE ALIGNED. I THINK THAT'S SOMETHING VERY, VERY IMPORTANT, AND NOT MANY INSTITUTIONS HAVE THAT.

IT'S ALSO DIFFICULT TO GET THAT OUT INTO THE COMMUNITY. A LOT OF PEOPLE THINK, OH, WE ARE ONLY A CLINIC OR WE ARE ONLY A BASIC RESEARCH TEAM THAT TRY TO FIND THE CAUSES AND FIND SOME CURES FOR PARKINSON'S DISEASE. NO, WE ARE BOTH. THAT I THINK MAKES US UNIQUE.

SO THE WAY WE WORK IS WE RELY ON GOVERNMENT GRANTS, FOUNDATIONS, ALSO CORPORATE PARTNERS, AND COMMUNITY DONORS. AND MOST OF OUR DONORS ARE PATIENTS THAT COME THROUGH OUR CLINIC. OUR CLINICAL CENTER HAS FIVE NEUROLOGISTS. WE ALSO HAVE PHYSIOTHERAPY, SPEECH THERAPY, AND WE ALSO DO A LOT OF OUTREACH AND EDUCATION. SO THAT MEANS WE HAVE MONDAYS PATIENT SYMPOSIA AND SEMINARS. WE ALSO HAVE, IN ADDITION TO ALL OF THAT, GAIT AND BALANCE CLASSES. WE HAVE A CHOIR. SO WE TRY TO DO MORE THAN THE REGULAR NEUROLOGY CAN DO FOR PATIENTS, AND

WE SPECIFICALLY FOCUS ON PARKINSON'S DISEASE AND RELATED MOVEMENT DISORDERS.

WE HAVE A BASIC RESEARCH DEPARTMENT. DR. BILL LANGSTON IS HEADING THAT AT THIS POINT. WE HAVE FOUR INVESTIGATORS, AND WE'RE TRYING TO EXPAND THAT A LITTLE BIT. WE HAVE A CLINICAL RESEARCH DEPARTMENT HEADED BY DR. CARLIE TANNER. SHE'S VERY INTERESTED IN EPIDEMIOLOGY IN PARKINSON'S DISEASE. SO WHAT ARE THE RISK FACTORS THAT CAN CAUSE THE DISEASE? SO A LOT OF ENVIRONMENTAL STUDIES ARE DONE HERE.

AND THEN WE HAVE A TRANSLATIONAL DRUG DEVELOPMENT PROGRAM HEADED BY DR. IAN IRWIN, AND HE IS TRYING TO TAKE SOME OF THE DISCOVERIES INTO PRECLINICAL DEVELOPMENT.

SO THAT'S KIND OF THE BASIS WHY WE NEEDED AN IRB CONSENT FOR OUR STUDY. SO WE WANT TO MODEL PARKINSON'S DISEASE IN A DISH. AS YOU CAN SEE, WE STARTED WITH A SKIN BIOPSY FROM A PATIENT, GROW THESE CELLS UP, BANK THEM AT OUR PLACE, AND THEN WE USE NUCLEAR REPROGRAMMING TO MAKE AND USE PLURIPOTENT STEM CELLS.

IN THE SECOND STAGE WE DO DIRECTED NEURONAL DIFFERENTIATION INTO DOPAMINERGIC NEURONS AND TRY TO THEN UNDERSTAND DISEASE MECHANISMS

RELATED TO PARKINSON'S DISEASE. ULTIMATELY WE ALSO WOULD LIKE TO USE THESE CELLS, THESE NEURONS IN A DISH, TO DO DRUG DISCOVERY. SO THIS IS HERE NICELY TERMED AS CLINICAL TRIALS IN A DISH.

SO THAT'S KIND OF THE OVERALL BROAD PROGRAM THAT WE HAVE AT THE INSTITUTE. AND THANKS TO AN EARLY TRANSLATIONAL GRANT THAT WAS AWARDED IN 2008, I GUESS, WE WERE LUCKY TO BE ABLE TO START RECRUITING PATIENTS FOR BANKING FOR A FIBROBLAST BANK. AT THIS POINT WE HAVE A TOTAL OF 61 SUBJECTS THAT PUT SKIN IN THE GAME IN THIS CASE. SO WE HAVE SOME GENETIC FORMS. LRRK2 IS ONE OF THE BIGGEST, WE THINK, CAUSES FOR PD. SOME YOUNG ONSET FORMS LIKE PARKIN. THERE'S ALSO GBA, GLUCOCEREBROSIDASE, GENE INVOLVED, AND THERE'S SOME VERY RARE CARRIERS THAT HAVE BOTH, TWO MUTATIONS IN THIS CASE, A GBA AND A LRRK2 MUTATION. AND THERE'S ALSO ALPHA-SYNUCLEIN, WHICH IS A PROTEIN THAT IS FOUND IN LEWY BODIES OF PARKINSON'S DISEASE.

WE ALSO HAVE AN INDIVIDUAL WHO IS CARRYING, IN THIS CASE, FOUR COPIES OF THE WILD-TYPE GENE, AND HE HAS VERY EARLY ONSET PARKINSON'S DISEASE. WE HAVE A WHOLE NUMBER OF SPORADIC CASES, 18 OF THOSE, AND WE ALSO ASCERTAINED MATCHED CONTROLS. AND IN THIS CASE THOSE ARE EITHER

SPOUSES, COMMUNITY MEMBERS, OR RELATIVES. SO TOTAL OF 61.

AND THEN JUST TO GIVE YOU TWO SLIDES AND A FLAVOR OF WHAT WE DO IN OUR RESEARCH. SO IN THIS CASE THESE ARE CELLS FROM THE PATIENT WHO HAS AN ALPHA-SYNUCLEIN TRIPLICATION. AND AFTER WE DERIVED IPS CELLS AND NOW HAVE NEURONS IN A DISH, WE COULD CLEARLY SEE THAT HERE ON THE LEFT PANEL FOR THE ALPHA-SYNUCLEIN TRIPLICATION, THERE'S A LOT MORE ALPHA-SYNUCLEIN IN THOSE NEURONS COMPARED TO THE SIBLING CONTROL.

SO THIS IS THE PATIENT LINE AND THIS IS THE CONTROL LINE. WE WERE ALSO ABLE TO LOOK AT THE PROTEIN BLOCK TO MAKE IT MORE QUANTITATIVE. SO HERE IS ALPHA-SYNUCLEIN MONOMERIC SYNUCLEIN COMPARED TO CONTROL LINES. THAT'S JUST ONE THING, AND IT NICELY REPLICATES WHAT YOU WOULD EXPECT IN A HUMAN BRAIN.

SO THIS IS THANKS TO ANOTHER GRANT FUNDED BY CIRM, A TOOLS AND TECHNOLOGY GRANT. WE ARE ALSO ABLE NOW TO GENETICALLY MODIFY THOSE CELLS. IN THIS CASE WE HAD THIS VERY COMMON LRRK2 G2019S MUTATION. AND IN COLLABORATION WITH SANGAMO BIOSCIENCES, WE WERE ABLE TO USE ZINC FINGER TECHNOLOGY TO CORRECT THIS MUTATION IN THE CULTURE DISH, BASICALLY REPAIRING A MUTATION, THEREFORE, ALSO CURING THE

DISEASE IN THE DISH. SO I THINK THAT IS SOMETHING VERY EXCITING THAT WE'VE NOW ACCOMPLISHED. AND AT THIS POINT WE'RE FRANTICALLY WORKING IN THE LAB TO LOOK AT SOME FUNCTIONAL OUTCOMES TO REALLY SHOW THAT WE HAVE CORRECTED THIS MUTATION AND THEN RESCUED THE PHENOTYPE.

SO NOW GOING TO THE IRB CONSENT AND PROTOCOL AND GIVE YOU A PERSPECTIVE WHAT WE'VE LEARNED THROUGH THE HUMAN IRB CONSENT AT OUR INSTITUTE. SO FIRST OF ALL, WHEN YOU DO A CONSENT PROCESS WITH A PATIENT, YOU HAVE TO EXPLAIN THE PURPOSE OF THE STUDY. AND WHAT I'VE LEARNED, EVEN THOUGH YOU TALK AND TALK AND TALK, IT'S OFTEN MUCH EASIER TO EXPLAIN WHEN YOU HAVE A VISUAL HELP. SO WHENEVER I TALK TO A PATIENT, I HAVE A LITTLE SCHEME THAT SHOWS WHAT WE ARE DOING. BECAUSE INITIALLY WHAT A LOT OF PEOPLE THOUGHT, SO PEOPLE THAT WERE REALLY SAVVY AND WERE TRYING TO READ AT THE INTERNET OR GET OTHER MEDIA TO UNDERSTAND WHAT WE'RE DOING, THEY THOUGHT THESE WERE ADULT STEM CELLS THAT WE WERE EXTRACTING FROM THOSE SKIN CELLS. SO IT WAS REALLY A HELP WITH THIS KIND OF CIRCLE TO SAY NO, NO, WE ARE GOING IN THERE AND WE DO THE REPROGRAMMING AND MAKE THOSE SKIN CELLS PLURIPOTENT. SO THAT WAS VERY IMPORTANT TO EXPLAIN.

THEN THE OTHER TWO QUESTIONS THAT ARE, OF COURSE, COMING FROM PATIENTS WHO WANT TO BE CURED, THEY HAVE VERY SEVERE SYMPTOMS, THEY HAVE TREMOR, THEY HAVE GAIT DIFFICULTIES, THEY HAVE MEMORY PROBLEMS, SOME OF THEM. SO A LOT OF THEM ARE ASKING WHEN WILL THESE CELLS BE READY FOR ME? AND THAT IS SOMETHING THAT WE HAVE TO DISCUSS WITH THEM, AND WE SAY, WELL, THEY MIGHT NEVER BE READY FOR YOU. AND I HAVE TO SAY, EVEN THOUGH YOU SAY THAT AS THE STUDY DOCTOR, SOMETIMES YOU'RE NOT REACHING THE PATIENT BECAUSE THEY DON'T WANT TO HEAR IT. SO I THINK THIS IS SOMETHING THAT WE HAVE TO KIND OF SAY AGAIN AND AGAIN DURING THE CONSENT PROCESS AND ALSO AFTERWARDS WHEN WE SEE THOSE PATIENTS BACK IN THE CLINIC THAT, NO, THESE CELLS MIGHT NEVER BE READY FOR YOU.

AND ALSO THIS IS SOMETHING THAT I ALSO GET ALL THE TIME. WHEN DO WE HAVE A CURE FOR PD, AND WILL STEM CELLS AT SOME POINT IN THE FUTURE BE A CURE FOR ME? AND THIS IS ALSO SOMETHING THAT I CAN'T REALLY ANSWER AT THIS POINT. BUT I CAN JUST SAY SOMETIMES THIS CONSENT PROCESS CAN BE LENGTHY, AND IT CAN BE A REALLY INTERESTING DISCUSSION.

SO WHAT WE'RE TRYING TO DO IS WE TRY TO STAY IN CONTACT WITH OUR SUBJECTS, ESPECIALLY WITH THE PATIENTS THAT WE SEE IN THE CLINIC. AND ONE WAY

TO DO THAT IS TO KEEP THE COMMUNICATION OPEN. AND WHAT WE HAVE, I THINK IT WAS A YEAR AND A HALF AGO, SEPTEMBER 1ST WE HAD A SKIN DONOR EVENT. SO WE INVITED ALL OUR 50 DONORS AT THAT POINT TO COME EXPLORE THE LAB, AND ALSO WE HAD LITTLE PRESENTATIONS AT COMPUTERS, AS YOU CAN SEE HERE, AND THEN EXPLAINING WHAT WE ARE DOING WITH THOSE CELLS. AND I THINK OF THOSE 50 PEOPLE, WE HAD 35 INDIVIDUALS ATTENDING, AND THEY THOUGHT THIS WAS VERY, VERY GOOD.

SO WHAT THESE PATIENTS WANT FROM US, THEY WANT HOPE. THEY DON'T NECESSARILY WANT A CURE TOMORROW, BUT THEY WANT TO BE PART OF THE PROCESS AND THEY WANT TO BE INFORMED. THEY WANT TO HEAR WHAT'S GOING ON. AND SO THIS WAS ONE OF THE WAYS WE'RE COMMUNICATING WITH THEM.

THE OTHER THING, WHAT I'M ALSO DOING WITH THE DONORS, JUST TO KEEP THEM EXCITED AND ENGAGED, IS I ALWAYS SEND THEM A PICTURE OF THEIR CELLS. SO SOMETHING THAT'S VERY PERSONAL. AND EVERY PICTURE LOOKS THE SAME IN A WAY. NO, THESE ARE THE CELLS THAT DERIVED FROM MY LITTLE SKIN BIOPSY. SO THAT IS SOMETHING THAT'S VERY IMPORTANT. EVEN THOUGH YOU THINK AS A RESEARCHER THEY ALL LOOK THE SAME, NO, IT'S SOMETHING VERY SPECIAL. AND IT'S NOT SOMETHING

THAT'S PART OF THE CONSENT PROCESS, BUT IT'S SOMETHING THAT KEEPS PEOPLE INVOLVED. AND I THINK THAT'S IMPORTANT.

AND SINCE WE ARE A SMALL INSTITUTE AND DOWNSTAIRS IS THE CLINIC, I'M IN CONSTANT CONTACT WITH PATIENTS. SOMETIMES ALSO THE NURSE CALLS ME AND SAYS, "BIRGITT, CAN YOU COME DOWNSTAIRS? MR. X IS HERE. HE WANTS TO TALK TO YOU." I THINK THAT'S VERY IMPORTANT TO KEEP PEOPLE ENGAGED AND EXCITED AND GIVE THEM HOPE THAT WE'RE DOING SOMETHING FOR THEM.

SO NOW I'M SWITCHING JUST TO THE DIFFERENT PARTS OF THE CONSENT FORM AND HOW WE WORDED IT. SO WE DIDN'T HAVE ANY RECOMMENDATION FROM CIRM AT THIS POINT, AND THE WAY WE WERE APPROACHING THE IRB CONSENT WAS WE WERE MODELING IT OFF GENETIC FAMILY STUDIES THAT WE DID WHERE WE COLLECTED BLOOD SAMPLES, EXTRACTED DNA. SO THAT WAS KIND OF THE BASE THAT WE WERE USING.

SO HERE IN TERMS OF THE PROCEDURE, WHAT WE SAY, WE ARE USING A FORMULA METER ABOUT THE SIZE OF A LENTIL PUNCH BIOPSY. AND A LOT OF PEOPLE ARE HESITANT INITIALLY BECAUSE THEY THINK IT'S A SURGICAL PROCEDURE, IT'S BLEEDING, THEY GET SUTURES, AND ALL OF THAT, BUT MOST OF THEM SAY, OH, THIS

IS -- EVEN AT THE END, ONCE THEY WENT THROUGH THE PROCESS, IT'S EVEN LESS STRESSFUL THAN A BLOOD DRAW BECAUSE SOMETIMES YOU HAVE TO POKE AGAIN AND AGAIN. AT THE END YOU DON'T WANT ANY MORE. BUT HERE, SINCE WE HAVE THE LOCAL ANESTHESIA, IT'S REALLY NOT VERY STRESSFUL. AND WE CAN USE STERISTRIPS AT THE END OF THE PROCEDURE SO THEY DON'T HAVE TO COME BACK, AND WE DON'T HAVE TO REMOVE ANY SUTURES. SO IT'S VERY EASY AND IT'S KIND OF A WALK-AWAY SITUATION.

THEN THE TYPES OF RESEARCH AND HOW WE EXPLAIN THIS. SO THE CHALLENGE HERE WAS TO INCLUDE AS MANY TYPES OF RESEARCH AS WE COULD THINK OF BECAUSE AT THAT POINT THREE YEARS AGO, WE DIDN'T REALLY KNOW WHAT WAS COMING. SO WE WANTED TO KEEP IT AS BROAD AS POSSIBLE. SO WE'RE STUDYING CHANGES IN STRUCTURE AND FUNCTION. SO THAT INCLUDES LOOKING AT DISEASE MECHANISMS AND IN VITRO RESEARCH. AND THEN HERE WE EXPLAIN HOW WE DO THE REPROGRAMMING PROCESS.

SO WE WANTED TO KEEP IT VERY BROAD SO THAT WE DON'T HAVE TO GO BACK TO OUR IRB EVERY TIME WE'RE MAKING A CHANGE IN OUR RESEARCH. SO WE WANTED TO KEEP IT BROAD.

I ALSO THOUGHT IT WAS VERY IMPORTANT THAT WE KEPT THE FIBROBLAST LEVEL, THAT WE NOT JUST SAID

WE WOULD REPROGRAM AND THEN STUDY IN THE REPROGRAMMED OR DIFFERENTIATED CELLS. WHAT WE'VE DONE IN THE FIRST YEAR AND A HALF, WE WERE ACTUALLY STUDYING THE PATIENT FIBROBLASTS TO LOOK AT DISEASE MECHANISMS. SO YOU CAN ALREADY LEARN A LOT FROM THE SKIN CELLS FROM THESE PATIENTS. SO I THINK THAT IS SOMETHING THAT WE SHOULD ALSO KEEP IN MIND, THAT WE WOULD DO RESEARCH AT THE FIBROBLAST LEVEL AND AT THE IPSC AND DIFFERENTIATED LEVEL.

THEN WE HAD THIS PART IN OUR CONSENT FORM, SHARING OF CELL LINES AND FUTURE USE. ONE THING THAT WE FOUND OUT WHEN WE STARTED TO RECRUIT THESE PATIENTS AND BANK THE FIBROBLASTS, ALL OF A SUDDEN I GOT A LOT OF CALLS FROM A LOT OF PEOPLE ALL OVER THE WORLD ALMOST AND SAID, "OH, CAN YOU SHARE THOSE LINES WITH US? WE ARE INTERESTED IN DOING THIS AND THIS AND THIS." SO THE SHARING PART WAS SOMETHING VERY IMPORTANT FOR US TO HAVE IN HERE. AND THE WAY WE SAID IT WAS, AGAIN, RELATIVELY BROAD. WE SAID THE LINES WILL BE KEPT FOR MANY YEARS AND MAY BE USED FOR FUTURE STUDIES BY US, BUT ALSO MAYBE BY OTHER PEOPLE OR ENTITIES THAT WE CAN'T PREDICT AT THIS TIME.

SO THAT TURNED OUT TO BE FAIRLY BROAD. AND SO WE WERE ALLOWED TO USE THOSE CELLS AND SEND

THEM OUT TO COLLABORATORS. SO SOME OF THE GENETIC CONSENTS DON'T ALLOW US TO DO THAT. SO THAT WAS VERY GOOD. THAT ALLOWED US TO EXPAND THE RESEARCH, TO EXPAND COLLABORATIONS, BUT THEN ALSO TO PARTNER WITH INDUSTRY WHICH THEN ULTIMATELY ALLOWS US TO FIND NEW DRUGS AND POTENTIAL NEW THERAPIES FOR OUR PATIENTS. SO THIS WAS VERY GOOD, AND WE ALSO HAD, I THINK THIS IS SOMETHING THAT NEEDS TO BE IN EVERY CONSENT FORM, THE COMMERCIALIZATION PART.

SO THE TISSUE AND SAMPLES THAT WE ARE COLLECTING MAY BE OF COMMERCIAL VALUE, AND THEN THE PATIENT WILL NOT BE ABLE TO SHARE IN THE PROFITS THAT MAY COME OUT OF IT. SO BY HAVING THIS IN THE CONSENT FORM, WE'RE ALLOWED TO PARTNER WITH, I THINK, THREE INDUSTRY PARTNERS RIGHT NOW. SO THAT WAS ALSO A VERY GOOD THING THAT WE HAD THOUGHT OF IN ADVANCE EVEN THOUGH AT THAT POINT WE DIDN'T KNOW WHO MIGHT BE INTERESTED IN THE FUTURE. SO THOSE ARE MY COMMENTS ON THIS.

BENEFITS, THIS RELATES TO THE POINT WHEN WILL THE CELLS BE READY FOR ME FOR TREATMENT. SO THIS IS KIND OF THE DISCLAIMER, THAT WE SAY THEY ARE NOT INTENDED TO PROVIDE DIRECT MEDICAL BENEFIT EVEN THOUGH EVERYONE BELIEVES IT. SO WE GET A LOT OF CALLS AND OUR RECEPTIONIST SAID, "OH, THERE WAS

AGAIN THIS CALL FROM A PATIENT WHO WANTS TO HAVE THE STEM CELL TREATMENT WITH THEIR CELLS. WHEN ARE THEY READY?" I THINK THAT'S VERY IMPORTANT THAT IT'S IN HERE AND WE KEEP COMMUNICATING THAT. BECAUSE EVEN THOUGH YOU SAY THAT, PEOPLE DON'T WANT TO HEAR IT. AND WE KIND OF SAID IT IN DIFFERENT WAYS, SO WE CANNOT AND DON'T GUARANTEE TO PROMISE YOU YOU WILL RECEIVE ANY BENEFITS FROM THE STUDY. EVEN THOUGH WE PUT IT IN BOLD AND WE SAY IT, PATIENTS DON'T REALLY WANT TO HEAR IT, BUT THIS IS A BIG SECTION THAT WE DEFINITELY WANT TO PUT OUT HERE.

ON THE OTHER HAND, I HAVE TO SAY WE GOT REALLY AN OVERWHELMING RESPONSE. SO WE REALLY HAD MORE PATIENTS THAT WANTED TO PARTICIPATE AND GIVING SKIN SAMPLES THAN WE ACTUALLY WERE ABLE TO INCLUDE. SO OVERALL THIS IS A VERY SUCCESSFUL STUDY. THANKS TO CIRM FUNDING, WE WERE ABLE TO EXPAND THIS BANK. INITIALLY WE SAID WE WOULD DO 18 LINES. NOW WE HAVE 61 LINES. IT'S BEEN VERY SUCCESSFUL. NONE OF THE INDIVIDUALS WHO WERE ENROLLED HAVE WITHDRAWN FROM THE STUDY. WE KEEP THEM ENGAGED. AND THAT'S KIND OF MY PERSPECTIVE ON OUR IRB CONSENT AT THE PARKINSON'S INSTITUTE. THANKS TO ALL THE PATIENTS AND VOLUNTEERS PUTTING THEIR SKIN IN THE GAME. THANKS TO THE LAB, DR. LANGSTON, WHO IS THE

PRINCIPAL INVESTIGATOR OF THIS EARLY TRANSLATIONAL GRANT. THANKS TO THE CLINIC, TO ALL THE DOCTORS THAT HELP ME RECRUITING THE PATIENTS. THANKS TO OUR COLLABORATORS, AND THANKS TO CIRM AND THE PARKINSON'S ALLIANCE AND BLUME FOUNDATION SUPPORTING THIS RESEARCH. AND THANKS TO YOU FOR LISTENING. ANY QUESTIONS?

DR. ROBERT TAYLOR: I'VE GOT SORT OF TWO QUESTIONS. THAT'S A PRETTY OPEN-ENDED CONSENT IN TERMS OF WHAT YOU'RE ALLOWED TO DO WITH IT. I GUESS IN GOING FORWARD, I'VE NEVER USED WESTERN IRB.

DR. SCHUELE: THIS WAS THE EL CAMINO IRB AT THE EL CAMINO HOSPITAL IN MOUNTAIN VIEW WHO APPROVED THIS STUDY.

DR. ROBERT TAYLOR: SOUNDS LIKE WHERE EVERYBODY SHOULD GO TO GET THEIR IRB DONE. SO THAT WAS KIND OF ONE QUESTION. BUT IT STRIKES ME IN THE INSTITUTIONS THAT I'VE BEEN RECENTLY, I THINK IT WOULD HAVE BEEN DIFFICULT TO GET AS OPEN-ENDED AND BROAD. THAT'S GREAT.

AND THE OTHER QUESTION, I GUESS, WE'VE BEEN TALKING ABOUT IT. I'M JUST KIND OF CURIOUS. YOU'RE SOMEBODY WHO'S GOING TO WANT TO BE DOING THOSE SENSITIVE EXPERIMENTS OF PUTTING YOUR STEM CELL POPULATIONS PROBABLY INTO MOUSE BRAIN AT LEAST.

DR. SCHUELE: SO FOR THIS EARLY TRANSLATIONAL GRANT, THIS IS ALL STRICTLY IN VITRO. ALSO, WE HAVE NOT DONE TERATOMA FORMATION. SO WE'VE DONE EMBRYOID BODY IN VITRO DIFFERENTIATION TO SHOW THE THREE GERM LAYER DERIVATION FOR PLURIPOTENCY. FOR THIS GRANT, NO; BUT, YES, FOR FUTURE RESEARCH, WE ARE THINKING OF TRANSPLANTING THEM, BUT AT THIS POINT NO.

DR. ROBERT TAYLOR: IN TERMS OF OUR DISCUSSION BEFOREHAND, YOU'RE GOING TO BE -- BECAUSE YOU WERE IN A SITUATION WHERE IT WAS DIFFICULT TO GET THE SCRO SUPPORT, AND THAT'S GOING TO BE EVEN A BIGGER DEAL THIS NEXT GO-AROUND.

DR. SCHUELE: TO GET THEM INTO. THAT'S NOT A PROBLEM AT THIS POINT, BUT IN THE FUTURE.

DR. LOMAX: SO ONE OF THE THINGS IN DEVELOPING THIS SEGMENT OF THE WORKSHOP, I DID A LOT OF INTERVIEWING OF FOLKS WHO WERE INVOLVED IN THE DEVELOPMENT OF THE CONSENT AND THE PROTOCOL. AND IT'S INTERESTING THAT YOUR OBSERVATION IS THAT IT'S VERY BROAD. THERE WAS A VIEW OUT THERE THAT, IN FACT, THE CONSENT IS VERY SPECIFIC FROM THE STANDPOINT OF IN THE NEAR TERM, THIS IS A PROTOCOL THAT INVOLVES A COLLECTION OF MATERIALS THAT WILL THEN BE TRANSFORMED THROUGH THIS PROCESS.

AND SO THE COUNTERPOINT THERE WAS ACTUALLY IT'S QUITE SPECIFIC WITH REGARD TO THE USE OF THE DONATED MATERIALS. AND THEN, AGAIN, THERE MAY BE DIFFERENT VIEWS IN TERMS OF UNDISCLOSED FUTURE USES. BUT BEING EXPLICIT ABOUT THAT STEP WAS ACTUALLY VIEWED AS A SORT OF CRITICAL FACTOR. AND THERE ARE STILL DIFFERING VIEWS OUT THERE AS TO HOW EXPLICIT YOU ARE ABOUT THE REPROGRAMMING ASPECTS OF IT, BUT THERE IS THAT VIEW THAT THAT, IN FACT, IS QUITE SPECIFIC AND CONSISTENT WITH THE COMMON RULE.

DR. ROBERT TAYLOR: TO BE MORE SPECIFIC, IT WAS THE NUMBER OF POTENTIAL COLLABORATORS AND THE FUTURE STUDIES THAT YOU HAD. THOSE ARE THE TWO ASPECTS THAT WOULD NOT HAVE FLOWN IN MY IRB.

DR. LOMAX: JUST WANTED TO GIVE YOU THE FACT THAT THIS WAS CLEARLY A BACK AND FORTH.

DR. ROBERT TAYLOR: THE DERIVATION PART, THAT SOUNDS STRAIGHTFORWARD.

CHAIRMAN LO: I'D LIKE TO ASK YOU A QUESTION TO GO BEYOND THE CONSENT FORM. YOU INDICATED THAT A LOT OF THESE POTENTIAL DONORS HAVE MISCONCEPTIONS, IN SOME CASES SERIOUS MISCONCEPTIONS, ABOUT WHAT THIS IS ALL ABOUT. AS PART OF YOUR CONSENT PROCESS, NOT THE FORM, BUT THE SORT OF PROCESS, DID YOU DO ANY FORMAL ASSESSMENT OF

WHETHER THEY UNDERSTOOD KEY FEATURES OF THE RESEARCH, FOR INSTANCE, THAT IT REALLY WASN'T -- THIS IS NOT DESIGNED TO OFFER THEM TREATMENT? IF THINGS ARE PATENTED, THEY WOULDN'T GET ANY PAYMENTS, THAT THE CELL LINES COULD BE USED FOR REALLY ALL KINDS OF RESEARCH IF THEY AGREED, NOT JUST PARKINSON'S RESEARCH? DID YOU MAKE ANY PROCESS TO ASSESS WHETHER THEY UNDERSTOOD CERTAIN KEY FEATURES, PARTICULARLY FOR PEOPLE COMING IN WHO SAID WHEN'S MY TREATMENT START. IF THEY AT THE END OF THE CONSENT PROCESS STILL SAID, CAN I MAKE MY APPOINTMENT TO GET THE STEM CELL TREATMENT NEXT MONTH, WOULD YOU ACCEPT THEM AS DONORS TO THIS PROTOCOL?

DR. SCHUELE: NO. NO. ON THE OTHER HAND, WE DON'T QUIZ OUR PATIENTS BEFORE WE ENROLL THEM. SO WE HAVE A LIVELY DISCUSSION. AND WITH THE SCHEME THAT I'M PUTTING OUT, WE'RE GOING THROUGH EVERY STEP AND THEY ARE ASKING QUESTIONS. AND THAT'S HOW WE ARE APPROACHING IT. SO I'M NOT SAYING AT THE END OF THE CONSENT PROCESS THEY SAY, OH, BUT WHEN CAN I SCHEDULE MY NEXT APPOINTMENT FOR THE STEM CELL TRANSPLANTATION. NOBODY IS DOING THAT. BUT WHAT I WANTED TO POINT OUT IS THERE IS THIS URGE OR THEY FEEL THE NEED THAT THEY WOULD LIKE AT SOME POINT TO BENEFIT FROM THIS RESEARCH. I THINK THEY ALL

UNDERSTAND IT'S BASIC RESEARCH AT THIS POINT, BUT KIND OF THEY ARE HOPING THAT WE GET TO THE NEXT STEP QUICKER THAN POSSIBLE.

CHAIRMAN LO: OTHER QUESTIONS?

DR. BOTKIN: I WONDER IF YOU'VE EVER USED OR WOULD ANTICIPATE USING A PATIENT'S LEGALLY AUTHORIZED REPRESENTATIVE TO PROVIDE CONSENT FOR THEIR PARTICIPATION.

DR. SCHUELE: IN CASE SOMEONE IS DEMENTED AND HAVE A SPOUSE CONSENT? NO, WE DIDN'T HAVE THAT. SO PARKINSON'S PATIENTS, IN GENERAL, HAVE -- THEY SAY THEMSELVES I HAVE SLOWED THINKING; BUT WHEN YOU DO A FORMAL COGNITIVE ASSESSMENT, THEY SCORE USUALLY NORMAL. THERE ARE SOME ATYPICAL FORMS OF PARKINSON'S WHERE THERE CAN BE DEMENTIA LIKE MULTIPLE SYSTEM ATROPHY DEMENTIA WITH LEWY BODY. FOR THOSE INDIVIDUALS YOU WOULD HAVE TO HAVE A LEGAL REPRESENTATIVE, BUT WE HAVE NOT ENROLLED THOSE INDIVIDUALS.

DR. LOCKHART: I WAS WONDERING DO YOU REMEMBER WHAT THE CONSENT LANGUAGE RELATED TO WITHDRAWAL OF CONSENT SAID, AND PARTICULARLY WHAT WOULD HAPPEN FOLLOWING WITHDRAWAL? WOULD DISTRIBUTION OF THE DERIVED CELL LINES CEASE? WOULD THE ORIGINAL MATERIAL, THE ORIGINAL SKIN, IF ANY WAS

REMAINING, IF THAT WERE STILL IN THE BANK, WOULD THAT BE DESTROYED? DO YOU REMEMBER KIND OF WHERE YOU CAME DOWN ON THAT ISSUE?

DR. SCHUELE: SO IT SAYS YOU CAN WITHDRAW AT ANY TIME DURING THE STUDY. THE CLINICAL INFORMATION WILL BE DELETED. I THINK THERE ARE SEVERAL POTENTIAL VERSIONS. I WOULD SAY SOMETHING WRONG.

DR. LOCKHART: IT'S A VERY PRECISE QUESTION.

DR. LOMAX: KEEP IN MIND THAT'S NOT THERE.

DR. SCHUELE: IT WOULD BE WRONG, BUT I CAN GO BACK AND FIND IT.

CHAIRMAN LO: SO I WANTED TO ACTUALLY USE THIS AS A WAY OF GETTING INTO OUR NEXT ITEM, WHICH IS REALLY CONSIDERING THE MODEL CONSENT FORM THAT CIRM STAFF HAVE DRAWN UP. I WANT TO THANK YOU VERY MUCH FOR SHARING WITH US YOUR EXPERIENCE AT THE PARKINSON'S INSTITUTE AND FOR THE RESEARCH YOU'RE DOING.

FIVE-MINUTE BREAK.

(A RECESS WAS TAKEN.)

CHAIRMAN LO: I WOULD SUGGEST WE TRY AND AT LEAST START BY KEEPING US ON THE BIG COMMENT LEVEL AND NOT COPY EDIT BECAUSE I DO WANT TO KIND OF

MOVE AHEAD AND SAVE TIME FOR NICOLE TO START US THINKING ABOUT THE RETURN OF RESEARCH RESULTS. SO BIG PICTURE COMMENTS. DOROTHY, I SEE YOU'VE GOT A LOT OF COMMENTS HERE. YOU WANT TO START US OFF?

DR. ROBERTS: I'VE GOT TO THINK OF WHAT ARE BIG PICTURE AS OPPOSED TO --

CHAIRMAN LO: ANYBODY ELSE WANT TO START WHILE DOROTHY IS DELIBERATING HERE?

DR. ROBERTS: I CAN JUST QUICKLY GO OVER JUST -- SO ONE COMMENT. I WAS JUST SCRIBBLING ON WHAT GEOFF SENT OUT. ONE IS, AND THIS IS NO PARTICULAR ORDER, A REVIEW OF MEDICAL RECORDS WILL BE CONDUCTED. IS THERE ANY -- I DON'T SEE ANYTHING HERE ABOUT PROTECTION OF THOSE MEDICAL RECORDS. SO THAT WOULD BE AN ISSUE I WOULD WANT TO RAISE.

THE DISCOMFORTS AND RISKS, THE RISKS SEEM TO ONLY PERTAIN TO THE PHYSICAL RISKS FROM THE BIOPSY ITSELF WITHOUT DISCUSSING THE RISKS OF THE FUTURE USE OF THE CELLS, WHICH I WOULD THINK WOULD BE MORE IMPORTANT THAN THE RISKS OF THE BIOPSY. AT LEAST I WOULD WANT TO INCLUDE MORE ABOUT THOSE RISKS.

THERE'S A PARTICULAR PROVISION FOR CONSENT FOR GAMETE RESEARCH. I JUST WONDERED -- I UNDERSTAND WHY THAT WAS SINGLED OUT BECAUSE, AS WE

SAID IN THE PRIOR DISCUSSION, THERE'S EXTRA SENSITIVITY ABOUT GAMETE RESEARCH, THE CREATION OF HUMAN GAMETES, BUT I WONDER IF THERE AREN'T OTHER USES THAT YOU MIGHT WANT TO ALERT DONORS TO, SOME OF WHICH WE DISCUSSED BEFORE, LIKE INJECTION IN NONHUMAN ANIMALS.

I THINK 7.0, THE DISCLAIMER THAT THE PARKINSON'S DISEASE INSTITUTE, PARKINSON'S INSTITUTE USES IS STRONGER THAN THIS TO MAKE IT CLEAR TO DONORS OR RESEARCH SUBJECTS THAT THEY MAY NOT EVER SEE ANY BENEFIT TO THEMSELVES IN TERMS OF A CURE. SO THE CONSENT FORM, HIGHLIGHTING THAT IN BOLD AND ALSO MAYBE STATING IT IN SEVERAL WAYS SINCE IT SEEMS THAT SOME PARTICIPANTS MAY NOT UNDERSTAND THAT. THAT JUST SEEMS TO BE A PARTICULARLY PROBLEMATIC ASPECT THAT THEY MAY NOT UNDERSTAND, AND SO YOU WANT TO BE VERY CLEAR ABOUT THAT.

THE ANY OTHER BENEFIT, LIKE IT'S CLEAR THEY'RE NOT GOING TO GET -- THEY WON'T BE PAID FOR PARTICIPATION, BUT I WONDER, AND I CAN'T REMEMBER IF WE TALKED ABOUT THIS BEFORE, THAT THEY MIGHT BE ABLE TO USE THEIR CELLS THEMSELVES. THAT MAY HAVE COME UP LAST YEAR AT THE LAST MEETING. I JUST DON'T RECALL. BUT WHETHER IT'S CLEAR THAT HERE THEY'RE NOT ENTITLED TO ANY PROFITS ASSOCIATED WITH THEIR

PARTICIPATION, BUT WOULD THEY BE ENTITLED TO SOME ACCESS TO THEIR OWN CELLS?

THEN I WONDER WITH THE WITHDRAWAL, YOU HAVE A RIGHT TO WITHDRAW. IF YOU DECIDE TO WITHDRAW AFTER YOUR SAMPLE HAS BEEN USED TO GENERATE THE IPSC'S, THEN YOUR MATERIALS WILL BE MADE ANONYMOUS. THAT COULD BE STATED MORE DIRECTLY AS YOU CANNOT WITHDRAW AFTER YOUR SAMPLES HAVE BEEN USED, BUT YOUR MATERIALS WILL BE MADE ANONYMOUS. BECAUSE YOU COULD ARGUE THAT THEY CAN'T WITHDRAW ONCE -- SO THIS COULD BE SEEN AS MISLEADING, MISLEADING THEM INTO THINKING THEY CAN WITHDRAW WHEN REALLY THEY CAN'T WITHDRAW.

AND THEN WHAT HAPPENS -- IT SAYS WE WILL RETAIN THE RESEARCH MATERIALS. IS THAT OR SHOULD THEY -- THEN, AGAIN, HOW ARE THEY WITHDRAWING IF THEIR RESEARCH MATERIALS ARE STILL BEING USED? I THINK WE COULD DISCUSS WHETHER THAT SHOULD -- AND MAYBE WE DID ALREADY -- HOW TO DEAL WITH THAT, BUT I THINK IF THE RESEARCH MATERIALS ARE RETAINED, THEN I THINK IT COULD BE CONSIDERED MISLEADING TO TELL THEM THAT THEY HAVE A RIGHT TO WITHDRAW.

AND I GUESS THE OTHER THING THAT CAME TO MIND WAS RELATED TO OUR DISCUSSION ABOUT DEIDENTIFICATION, MAKING IT CLEARER THAT EVEN IF THE CELLS ARE MADE ANONYMOUS BY REMOVING ALL LINKS TO

THEIR IDENTITY, THAT THEY MAY STILL BE IDENTIFIABLE.

THAT'S JUST WHAT I SCRIBBLED IN. THERE MAY BE MORE THINGS. I DIDN'T READ IT THAT CAREFULLY, BUT THOSE ARE SOME THINGS THAT I NOTICED.

CHAIRMAN LO: THOSE ARE VERY HELPFUL COMMENTS. I'M GOING TO SORT OF JUST MAKE THE OBSERVATION, THOSE OF YOU WHO KNOW MORE ABOUT THE COMMON RULE MAY WANT TO COMMENT ON THIS, BUT I BELIEVE YOU HAVE TO SAY IN HUMAN SUBJECTS RESEARCH THAT YOU HAVE THE RIGHT TO WITHDRAW. BUT AS YOU POINTED OUT, DOROTHY, IN FACT, WE'RE SAYING, YEAH, YOU DON'T BECAUSE WE'RE GOING TO KEEP YOUR CELLS, AND THE IPS CELLS ARE GOING TO CONTINUE TO BE DISTRIBUTED.

DR. ROBERTS: I'M JUST RAISING THAT THERE MAY BE A WAY TO SAY IT THAT IS MORE TRANSPARENT AS TO WHAT ACTUALLY --

CHAIRMAN LO: I AGREE THAT IT'S MORE TRANSPARENT THE WAY YOU DO. I'M JUST WONDERING IF THAT RUNS AFOUL OF THE COMMON RULE. YOU'RE THE LAWYER.

DR. ROBERTS: I HAVE TO THINK ABOUT IT MORE.

CHAIRMAN LO: JEFF, YOU'VE BEEN HERE, AND, NICOLE, YOU'VE BEEN HERE, SO JUMP IN AND FRANCISCO

AS WELL.

DR. BOTKIN: I THINK THAT'S ACTUALLY MY MAIN CONCERN. I THINK OVERALL IT REALLY LOOKS VERY GOOD IN MOST WAYS, BUT I THINK IT SEEMS TO ME THAT FROM WHAT I KNOW ABOUT BIOBANKS IS THE NUMBER OF PEOPLE WHO ACTUALLY WITHDRAW IS VANISHINGLY SMALL. SO WHY NOT JUST TELL THEM IF THEY WANT TO WITHDRAW, WE'LL PULL YOUR SAMPLE AS LONG AS IT'S IDENTIFIABLE. IT SEEMS TO ME YOU CAN MAKE THAT CUT POINT TO SAY ONCE WE'VE DEIDENTIFIED IT, THEN WE CAN'T WITHDRAW IT. BUT IF IT'S STILL IDENTIFIABLE, WE'LL PULL IT AND NOT USE IT ANYMORE. THAT, I THINK, IS MORE CONSISTENT WITH THE NOTION OF BEING ABLE TO ACTUALLY WITHDRAW FROM THE RESEARCH.

DR. FEIGAL: WHAT DO YOU DO WITH THE CELL THAT'S ALREADY BEEN DERIVED?

DR. BOTKIN: WELL, AS LONG AS YOU HAVE IDENTIFIERS ON IT, IS THERE A REASON TO SAY WE WON'T USE IT ANYMORE?

DR. FEIGAL: THIS WAS DISCUSSED ACTUALLY AT THE LAST SWG, ACTUALLY THE ISSUES ABOUT IF YOU'RE TALKING ABOUT THE SAMPLE THAT WAS DONATED OR YOU'RE TALKING ABOUT DERIVED LINE. ONCE THE LINE IS DERIVED, IT COULD HAVE BEEN DISTRIBUTED TO QUITE A FEW INDIVIDUALS. AND YOUR ABILITY TO DO ANYTHING

ABOUT THAT MAY BE QUITE LIMITED. IF YOU ARE TALKING ABOUT THE ACTUAL PIECE OF MATERIAL THAT WAS DEPOSITED, THAT'S A DIFFERENT STORY.

DR. LOCKHART: SO I'M MORE FAMILIAR WITH TRADITIONAL BIOBANKING THAN ANYTHING INVOLVING CELL LINES. AND THE MOST COMMON POLICY IS THAT IF YOU HOLD A LINK AND THERE'S A REQUEST FOR WITHDRAWAL, YOU DESTROY WHAT YOU HAVE IN YOUR BANK, BUT DO NOT GO AFTER THINGS THAT HAVE BEEN DISTRIBUTED. PEOPLE DO IT DIFFERENT WAYS, BUT THAT'S THE MOST COMMON.

I HAVE SOME PROBLEMS OR CONCERNS ABOUT THE LANGUAGE AS WRITTEN, THAT A PERSON WOULD REQUEST WITHDRAWAL, YOU ANONYMIZE, KEEP THEIR TISSUE, AND STILL DISTRIBUTE. I THINK A DONOR WOULD NOT FIND THAT VERY RESPECTFUL. THEY'RE TAKING THE TROUBLE TO COME AND FIND YOU AND SAY I'M NOT COMFORTABLE WITH THIS, I WANT TO WITHDRAW. AND YOU'RE SAYING, OH, WE'RE JUST GOING TO MAKE IT ANONYMOUS AND KEEP DOING IT. NOW, YOU MIGHT BE ABLE TO DRAW A LINE WITH THE CELL LINE AND SAY THERE'S BEEN A SIGNIFICANT INTELLECTUAL INVESTMENT THERE, IT IS DISTINCT, WE'LL DESTROY WHAT'S IN THE BANK, BUT NOT THE CELL LINE. BUT I THINK WE DO NEED TO TRY AND MAKE THIS A LITTLE CLEARER.

AND IF THIS IS GOING TO BE THE POLICY THAT

EVEN IF YOU WITHDRAW, WE WILL KEEP USING AND DISTRIBUTING EVERYTHING, THEN I THINK THAT NEEDS TO BE VERY CLEAR BECAUSE IN THAT CASE YOUR ABILITY TO WITHDRAW IS REALLY VERY TIME DEPENDENT. YOU HAVE TO WITHDRAW BEFORE THE LINE IS CREATED. AND ONCE THE LINE IS CREATED, YOU CAN'T WITHDRAW ANYMORE. SO THAT WOULD NEED TO BE MORE CLEAR IF THAT'S REALLY THE DIRECTION YOU WANT TO GO.

DR. PRIETO: I THINK THAT WAS THE POINT I WANTED TO MAKE, SOMETHING ALONG THAT LINE. THE CONSENT SHOULD BE EXPLICIT THAT, YOU KNOW, UP TO THE POINT WHERE YOUR CELLS ARE DEIDENTIFIED AND FURTHER USES OF CELL LINES DERIVED, DISTRIBUTED, ETC., UP TO THAT POINT YOU CAN WITHDRAW, BUT THOSE SUBSEQUENT PRODUCTS OF YOUR PRODUCTS, WITH BETTER, CLEARER LANGUAGE, CANNOT BE WITHDRAWN. AND THAT SHOULD BE CLEAR FROM THE OUTSET.

CHAIRMAN LO: LET ME TRY AND PARSE THIS OUT. I'M HEARING A NUMBER OF YOU SAY THAT THE ACTUAL SPECIMEN THAT WAS DONATED, AS LONG AS IT'S IDENTIFIABLE, THE PERSON MAY REQUEST IT TO BE WITHDRAWN -- TO WITHDRAW FROM RESEARCH, AND THEN THE SAMPLE WOULD NOT BE USED TO CREATE IPSC LINES OR DISTRIBUTED. IS THAT A FAIR ASSESSMENT, THAT THE UN --

DR. ROBERT TAYLOR: YOU MIGHT WANT TO BE A LITTLE CLEARER BECAUSE IT'S GOING TO BE AT LEAST TWO STEPS THERE. SO YOU'RE GOING TO HAVE YOUR TISSUE SAMPLE, YOU WILL TAKE EXPLANTS FROM THE TISSUE AND PUT THOSE INTO CULTURE TO ESTABLISH A PRIMARY CULTURE. SO THAT'S GOING TO BE SORT OF YOUR SECOND LEVEL OF MATERIAL DERIVED. AND THEN IT'S PROBABLY AT SOME TERTIARY OR QUATERNARY STEP THAT YOU HAD ACTUALLY PROBABLY INTRODUCED YOUR IPS MAGIC SORT OF GROWTH FACTORS AND TRANSCRIPTION FACTORS. I THINK THERE'S GOING TO BE POTENTIALLY -- SO THE ORIGINAL -- YOU PROBABLY HAVE TO SPECIFY WHERE YOU'RE GOING --

CHAIRMAN LO: LET'S TRY AND WORK IT THROUGH. THE EASIEST ONE IS YOU HAVEN'T DONE ANYTHING EXCEPT ARCHIVE IT AND IDENTIFY IT. SHOULD THE PERSON BE ALLOWED TO SAY, NOT GIVE IT BACK, BUT THEY REALLY DON'T WANT IT BACK, BUT DISPOSE OF IT. DOES ANYBODY THINK THAT ONCE THEY GIVE IT TO US, IT'S OURS? SO THAT'S WHAT WE'VE SAID.

DR. ROBERT TAYLOR: DEIDENTIFICATION RIGHT UP FRONT.

CHAIRMAN LO: THIS IS OPTION 1.

DR. ROBERT TAYLOR: SO THAT WOULD MAYBE BE THE --

CHAIRMAN LO: SO I THINK WE HAVE TO SAY THERE'S COMPETING THINGS WE'RE TRYING TO ACCOMPLISH HERE. WE DON'T WANT TO SORT OF SAY TO PEOPLE YOU CAN'T CHANGE YOUR MINDS IF YOU HAVE SECOND THOUGHTS AND JUST SORT OF ITS IRREVOCABLE. ON THE OTHER HAND, YOU DON'T WANT INVESTIGATORS PUTTING SUBSTANTIAL AMOUNTS OF TIME, EFFORT, ENERGY, RESOURCES, CIRM RESOURCES, AND THEN HAVE SOMEONE SAY, OH, WAY DOWNSTREAM I'VE CHANGED MY MIND. STOP EVERYTHING. CANCEL WHAT YOU'VE DONE. AND AS YOU SAID, IT MAY BE IMPOSSIBLE. IT'S ALREADY BEEN DEIDENTIFIED OR IT'S BEEN DISTRIBUTED.

SO WE PROBABLY WANT TO GIVE DIFFERENT WEIGHT TO THOSE GOALS AT DIFFERENT POINTS IN THE PROCESS. I THINK, ROB, YOU'RE POINTING OUT THAT THE PROCESS HAS A LOT OF STEPS, AND THEY'RE INCREMENTAL STEPS AND WHERE IS THE TIPPING POINT? WHERE IS THE TURNING POINT?

THE OTHER THING IS PEOPLE CAN SAY ONCE YOU GIVE IT TO US, WE'RE GOING TO IMMEDIATELY DEIDENTIFY IT. HEY, CAN'T FIND IT. WHICH ONE IS YOURS? SO IT REALLY GETS DOWN TO RESPECT VERSUS UTILITY, USEFULNESS TO SOCIETY. JEFF, HELP US OUT HERE.

DR. BOTKIN: I'M NOT SURE I'M GETTING THE POINT ABOUT WE'VE INVESTED A LOT IN THE CELL LINE;

THEREFORE, WE CAN'T ALLOW YOU TO SAY NO ANY LONGER. IN THE CLINICAL RESEARCH CONTEXT, SOME OF THOSE PATIENTS GET ENORMOUS INVESTMENTS IN THEM, AND THEY STILL CAN SAY NO AT ANY TIME, AND YOU'RE JUST STUCK. IT'S JUST A SHAME. YOU LOSE THAT PATIENT TO THE STUDY.

DR. FEIGAL: YOU CAN STILL USE THE DATA.

DR. BOTKIN: THAT'S RIGHT. YOU CAN USE THE DATA THAT'S BEEN COLLECTED TO DATE, BUT PROSPECTIVELY YOU CAN'T DO ANYTHING ADDITIONAL. BUT HERE WE'RE STILL WANTING TO SAY EVEN IF THE PATIENT SAYS I WANT TO WITHDRAW, WE'RE STILL GOING TO KEEP THAT LINE IN CIRCULATION. AND IT'S GOT SOMEBODY'S NAME ATTACHED TO IT. I GUESS AT THIS POINT I'M A LITTLE MORE COMFORTABLE WITH BITING THE BULLET AND SAYING IT'S REALLY A SHAME. I DON'T THINK IT'S GOING TO HAPPEN BUT A SCANT FEW TIMES, BUT WHY NOT SAY WE'RE GOING TO HONOR YOUR DESIRE TO WITHDRAW AND PULL THAT LINE OUT OF CIRCULATION. USING WHATEVER DATA THAT'S BEEN GENERATED, I THINK, SO FAR IS PERFECTLY APPROPRIATE.

DR. LOCKHART: I THINK JEFF IS RIGHT TO POINT OUT THAT THIS IS LIKELY TO BE A RARE EVENT. I CAN'T REALLY SEE ANY -- PRESUMING THAT YOU DO HAVE A LINK, AND I THINK THAT IS A REASONABLE THING TO

CONSIDER, WERE THE COLLECTION SITE TO BE USING A COMPLETELY ANONYMOUS MODEL, YOU WOULD NEED TO DISCLOSE IN THE CONSENT FORM THAT YOUR SAMPLE WILL BE ANONYMOUS. WE WILL HAVE NO WAY TO WITHDRAW YOUR SAMPLE BECAUSE WE WON'T KNOW WHICH ONE YOU ARE. THAT'S PERFECTLY REASONABLE. YOU WOULD JUST NEED TO BE VERY EXPLICIT THAT THAT WAS THE DESIGN.

SO PRESUMING YOU DO HAVE A LINK, I CAN'T SEE A RATIONALE FOR NOT DESTROYING THE PHYSICAL SKIN OR BLOOD SAMPLE. I CAN'T IMAGINE TELLING SOMEONE THAT YOU'RE GOING TO STRIP IT OF IDENTIFIERS AND HOLD ONTO IT. I DON'T REALLY SEE HOW YOU COULD GET THERE.

THE CELL LINE, IT MAY BE AS DISTINCT. I COULD MAYBE GO EITHER WAY. BUT IF YOU'RE PRESUMING IT'S A RARE EVENT, I THINK IT'S MORE RESPECTFUL TO CEASE DISTRIBUTION. YOU COULD SAY WE MAY HAVE ALREADY GIVEN IT OUT TO RESEARCHERS. WE WILL NOT TRY AND GET IT BACK FROM THEM. BUT IF YOU JUST THINK ABOUT THE OPTICS OF CREATING A CELL LINE, SOMEONE SAYS, YOU KNOW, I NOW HAVE HAD A CHANGE OF HEART, I REALLY DON'T APPROVE OF THIS ANYMORE. AND YOU SAY, WELL, WE'RE GOING TO KEEP DOING IT. WE'RE GOING TO KEEP SENDING IT OUT THE DOOR. KIND OF THINKING ABOUT THAT.

AND JUST ALSO AS YOU GO DOWN THE ROAD, IF YOU WANT TO GET REALLY COMPLICATED, IF YOU'RE THINKING ABOUT USING ANY PEDIATRIC DONORS AND THEY REACH AGE OF MAJORITY AND WANT TO CEASE USE, SAYING, NO, SORRY. YOU TOTALLY DISAGREE WITH YOUR PARENTS DECISION. WE'RE GOING TO KEEP DISTRIBUTING THAT. THAT'S PROBABLY A LESS LIKELY EVENT. BUT TRYING TO THINK OF PEOPLE WHO MAY COME TO YOU WITH VERY LEGITIMATE REASONS AS TO WHY THEY WANT TO CEASE USE AND CEASE PARTICIPATION IN THE PROJECT, I DON'T THINK IT WOULD BE COMMON OR FRIVOLOUS.

CHAIRMAN LO: ANYONE WANT TO ARGUE THE OTHER POSITION, THAT WE'LL GIVE IT BACK IF WE HAVEN'T WORKED ON IT OR MAYBE EVEN IF WE'VE TAKEN AN EXPLANT BECAUSE THAT'S NOT A WHOLE LOT OF WORK? BUT IF WE'VE ACTUALLY GONE AND DERIVED THE STEM CELL, WHICH IS THE MAJOR GOAL OF WHAT WE'RE DOING, WE'RE NOT GOING TO ALLOW YOU TO WITHDRAW THE LINE AT THAT POINT. WE CERTAINLY AREN'T GOING TO ASK FOR THINGS BACK, AND WE CERTAINLY AREN'T GOING -- BECAUSE WE CAN'T PROBABLY BECAUSE WE'VE DEIDENTIFIED THEM TO THE PEOPLE WE'VE SHARED IT WITH, BUT WE WANT TO CONTINUE TO DISTRIBUTE YOUR LINE EVEN THOUGH YOU'VE TOLD US YOU'D LIKE US TO STOP.

SO THIS IS A CONVERSATION WE HAD A YEAR

AGO. ANY THOUGHTS?

DR. ROBERT TAYLOR: I WAS JUST GOING TO SAY THAT YOU HAVE TO SORT OF THINK THIS THROUGH UP FRONT BECAUSE THERE IS LANGUAGE IN YOUR CONSENT THAT ALLOWS RECONTACT. AND IF YOU ARE GOING TO ALLOW RECONTACT, THEN YOU HAVE TO BE ABLE TO GET BACK TO THE SAMPLE. YOU CAN'T REALLY HAVE IT BOTH WAYS.

CHAIRMAN LO: ANONYMIZING, WE DON'T KNOW WHICH IS YOURS, BUT WE WANT TO CONTACT YOU.

DR. ROBERT TAYLOR: SO MY IRB WOULD SAY THAT WAS KIND OF NOT A CONSISTENT MESSAGE. SO THOSE ARE THINGS, I THINK, THAT NEED TO BE.

ANOTHER THOUGHT THAT I HAD REALLY IN LISTENING TO DR. SCHUELE'S PRESENTATION AND THINKING, UTA, ABOUT YOUR PROPOSAL TO DO KIND OF COMMON DISEASES, MULTIFACTORIAL, MULTIGENIC DISEASES, WHICH ARE THE SORTS OF THINGS THAT I'VE KIND OF STUDIED AS WELL, THE MOTIVATION OF PATIENTS TO PARTICIPATE IN SOMETHING LIKE THAT IN MY EXPERIENCE HAS BEEN PROBABLY CONSIDERABLY LESS THAN IN A CONDITION LIKE PARKINSON'S OR WHERE PEOPLE ARE REALLY SUPER-DUPER MOTIVATED. SO JUST KIND OF A FACTOID, I THINK.

DR. FEIGAL: CAN I BRING UP A POINT TOO, AND THIS IS MORE FROM THE RESEARCH END AND JUST TO

PROVIDE ALL THE PERSPECTIVES. THE PURPOSE OF A BANK IS TO HAVE A RESOURCE WHERE RESEARCHERS CAN GO BACK. IF THEY HAVE BEEN DOING A TREMENDOUS AMOUNT OF WORK ON A PARTICULAR CELL, TO BE ABLE TO GO BACK AND GET ACCESS TO IT AGAIN. SO YOU DO NEED TO THINK ABOUT THE PURPOSE FOR WHY WE PUT THE BANK IN PLACE. IT WASN'T REALLY PUT INTO PLACE, AND IF YOU'RE VERY CLEAR IT'S FOR RESEARCH, IT DEFINITELY DIMINISHES THE CREDIBILITY OF BEING A BANK IF THERE'S THE POTENTIAL TO HAVE THE CELL LINE YOU'VE BEEN WORKING ON NO LONGER AVAILABLE.

SO I'M JUST SAYING JUST BALANCE WHAT WE'RE GOING TO BE RECOMMENDING BECAUSE THE PURPOSE OF THIS IS NOT AS A THERAPY. IT'S AS A RESEARCH RESOURCE.

CHAIRMAN LO: SO LET ME MAKE SOME SUGGESTIONS OF HOW WE MIGHT SORT OF THINK ABOUT APPROACHING THIS. SO IT SEEMS TO ME WHY MIGHT PEOPLE WHO CONSENTED ORIGINALLY LATER ON SAY, OH, I'VE CHANGED MY MIND? FIRST, PEOPLE CHANGE, THEIR VALUES CHANGE, THEY CHANGE THEIR MINDS. SECONDLY, I THINK THEY MAY WELL SAY, GEE, I JUST FOUND OUT THAT IN FACT WHAT YOU'RE DOING IS THIS, AND ACTUALLY I THOUGHT YOU WERE DOING SOMETHING VERY DIFFERENT. AND THEN, OF COURSE, THE RECOURSE IS, NO, IT SAYS HERE RIGHT IN BLACK AND WHITE. IT'S NOT WHAT I

UNDERSTOOD.

SO I WOULD SUGGEST A COUPLE -- I'M OFFERING A HYPOTHESIS THAT THE MORE ROBUST WE MAKE THE CONSENT PROCESS UP FRONT, THE LESS LIKELY IT MAY BECOME TO HAVE EVEN A RARER EVENT THAN WITHDRAWAL NOW IS. I WOULD LIKE TO SUGGEST THAT WE THINK ABOUT ASSESSING WHAT PEOPLE UNDERSTAND RATHER THAN JUST SAYING IT'S IN THE FORM.

I THINK THERE'S SOME THINGS THAT I WOULD ACTUALLY FLIP IT AROUND EVEN BEYOND WHAT DARPA DID. I'D SAY YOU WILL NOT GET ANY BENEFIT FROM THIS, PERIOD. NOT THAT WE CAN'T PROMISE IT OR WE CAN'T GUARANTEE IT. IT SAYS, YOU KNOW, YOU AND I, WINK, WINK, KNOW THAT THIS IS GOING TO HELP YOU, BUT I CAN'T SAY THAT. I CAN'T TELL YOU THIS THE BEST DEAL ON THE CAR EVER. SO I WOULD REALLY GO OVERBOARD AND SAY, NO, THIS IS REALLY FOR RESEARCH.

I THINK WHERE ELSE PEOPLE GET UPSET IS WHERE THEY THINK THERE'S MONEY INVOLVED AND THEY'RE NOT GETTING ANY. SO TO REALLY ASCERTAIN THAT'S WHAT'S GOING TO HAPPEN. AND I THINK YOU COULD CONSIDER A WAITING PERIOD, A COOLING-OFF PERIOD. SIGN IT, THINK ABOUT IT, AND WE'RE GOING TO, WHATEVER, A WEEK, THREE DAYS LATER COME BACK AND WE'RE GOING TO ASK YOU TO GO OVER IT AGAIN.

WE CONSIDERED THIS FOR THE OOCYTE DONATION, AND WE ULTIMATELY REJECTED IT, BUT WE THOUGHT ABOUT IT. I'M JUST OFFERING THAT AS ANOTHER WAY OF TRYING TO MINIMIZE THE NUMBER BECAUSE I AGREE COMPLETELY WITH ELLEN, THAT ONCE YOU PUT IT IN THE BANK AND WANT IT TO BE USED, THEN YOU REALLY WANT TO HAVE IT THERE FOR FUTURE RESEARCHERS.

AND THEN I GUESS THE OTHER THING IS HOW DO YOU KEEP THE LINKS BETWEEN OVERT IDENTIFIERS AND THE LINES? ONE WAY TO SAY IS WE'LL MAKE IT REALLY A BANK IS TO SAY AT SOME POINT IT GOES INTO THE BANK, IT'S ANONYMIZED, AND WE REALLY CAN'T TRACE IT BACK. IT ALSO MEANS WE CAN'T GIVE YOU RESULTS BACK. WE CAN'T WALK BACK AND ASK FOR SPECIMENS FROM YOUR RELATIVES. SO THERE'S A DETRIMENT TO THAT. SO THERE ARE ALL THESE TRADE-OFFS, AND I GUESS THEY DO INVOLVE HOW MUCH WE RESPECT PEOPLE'S RIGHT TO CHANGE THEIR MINDS VERSUS HOW MUCH WE'RE REALLY INVESTING IN SOMETHING THAT WE WANT TO BE USEFUL FOR THE SOCIETAL GOOD AND FOR THE RESEARCH KNOWLEDGE.

DR. LOCKHART: SOME OF THOSE POINTS YOU JUST BROUGHT UP ARE ALSO REALLY RELATED TO THE SCIENTIFIC DESIGN. ARE YOU DEALING WITH A POPULATION WHERE YOU WANT TO DO FOLLOW-UP AND GO BACK AND GET MORE MEDICAL INFORMATION ABOUT HOW IS

THEIR DISEASE PROGRESSING, DO YOU HAVE AFFECTED SIBLINGS, ALL OF THAT? SO YOU NEED TO MAINTAIN THAT LINK SCIENTIFICALLY. AND THEN YOU'RE ASKING FOR A MUCH DIFFERENT RELATIONSHIP WITH THE PATIENT THAN IF IT'S MAYBE A HEALTHY DONOR OR A MORE COMMON DISEASE WHERE THAT'S LESS NEEDED FROM A SCIENTIFIC RATIONALE. AND SO SOME OF THAT, THE SCIENCE WILL DRIVE SOME OF THOSE KIND OF DESIGN DECISIONS ABOUT HOW LINKS ARE MAINTAINED AND ALL OF THAT.

AND I COULD BE -- ABOUT WHETHER TO WITHDRAW THE CELL LINE, I'M KIND OF ON THE FENCE. SO I COULD BE PERSUADED NOT TO WITHDRAW THE CELL LINE AS LONG AS IT'S CRYSTAL CLEAR. AND IF THIS IS GOING TO BE AN ASSESSMENT OF UNDERSTANDING, I WOULD NOMINATE THAT TO BE ONE OF THE POINTS, THAT THEY UNDERSTAND WE WILL NOT BE ABLE TO WITHDRAW THE CELL LINE. AND MAYBE EVEN INCLUDE A SENTENCE OR TWO ABOUT WHY, ABOUT WHY IT'S SO BENEFICIAL TO THE SCIENCE WHY THAT WON'T HAPPEN. SO THAT WOULD NEED TO BE SOMETHING THAT WOULD BE VERY CLEAR. AND SOMEONE COULD DECIDE WHETHER THEY'RE COMFORTABLE WITH THAT.

CHAIRMAN LO: OTHER THOUGHTS, COMMENTS?

DR. ROBERT TAYLOR: I WAS JUST GOING TO SAY THAT I'VE SPENT REALLY ABOUT THE LAST 20 YEARS

DOING THIS KIND OF CLINICAL TRANSLATIONAL RESEARCH AND HAVE COLLECTED PROBABLY CLOSE TO 3,000 PATIENT SAMPLES. I'VE HAD TWO REQUESTS TO WITHDRAW FROM THE BANK. I THINK THIS REALLY IS -- THEY'RE NOT -- SOME OF THESE ARE KIND OF TRANSIENT PREECLAMPSIA PREGNANCY COMPLICATIONS THAT GET BETTER, SO PEOPLE GO ON AND THEY DON'T REALLY THINK ABOUT IT SO MUCH AS OPPOSED TO SORT OF CHRONIC DISEASES WHERE THEY MIGHT HAVE A DIFFERENT PERSPECTIVE. BUT I DO THINK THIS IS GOING TO BE QUITE A RARE PROBLEM, AND I THINK HAVING THE ABILITY TO, I WOULD ARGUE, SORT OF KEEPING IN THE LINKS, ALLOWING THOSE PATIENTS THAT WANT IT TO PULL THINGS BACK, TO PULL THEM BACK AS FAR AS YOU'RE KIND OF WILLING TO GO, A COUPLE OF STEPS, AND TO HAVE THE OPPORTUNITIES TO GET LONG-TERM FOLLOW-UP AND THAT SORT OF THING, I THINK THAT WOULD BE THE BETTER MODEL.

CHAIRMAN LO: SO BOTH JEFF AND ROB HAVE SAID THEY THINK IT'S GOING TO BE REALLY RARE THAT PEOPLE WANT TO WITHDRAW. NICOLE, IS THAT WHAT OTHER BIOBANKS ARE FINDING?

DR. LOCKHART: I THINK IN GENERAL IT IS VERY RARE.

CHAIRMAN LO: ONE IN A THOUSAND?

DR. LOCKHART: PROBABLY. IT ALSO DEPENDS

WHAT POPULATION GROUP YOU'RE WORKING WITH. I THINK IT'S ALSO HARD TO TELL BECAUSE THERE ARE SOME WITHDRAWALS THAT HAPPEN FOR CLINICAL REASONS. SO IF YOU'RE A CANCER BIOBANK AND YOU HAVE THE TUMOR BLOCK THAT THAT PATIENT NEEDS TO GET ON A TRIAL SOMEWHERE, BECAUSE YOU HAVE A FROZEN SPECIMEN AND THEY NEED A FROZEN SPECIMEN, THERE CAN BE A WITHDRAWAL FOR THAT REASON. BUT I THINK IT WOULD BE UNLIKELY THIS BANK WOULD HAVE THAT KIND --

CHAIRMAN LO: THE FIBROBLAST SPECIMENS. THEY NEED TO SPIN OFF A FEW.

DR. LOCKHART: SO IT'S UNLIKELY THERE WOULD BE A WITHDRAWAL FOR THAT REASON. I WOULD THINK IT WOULD BE RARE. I WOULD THINK YOU'D WANT TO BE CAREFUL ABOUT HOW YOU DESCRIBE THIS THOUGH. I WILL AGREE TO MOST RESEARCH PROJECTS. I WOULD HESITATE TO SIGN THIS AS WRITTEN BECAUSE THE RIGHT TO WITHDRAW IS SO CONFINED.

CHAIRMAN LO: SO I GUESS THE OTHER QUESTION IS IS IT WORTH DOING SOME FIELD TESTING WITH GOING TO PROSPECTIVE DONORS, SAYING, LOOK, WE'VE GOT THE DILEMMA HERE, OR JUST RANDOMIZING PEOPLE TO SAY, TAKE A LOOK AT THIS FORM AND GIVE OTHER PEOPLE ANOTHER FORM AND SEE HOW PEOPLE REACT. I THINK THIS IS A WORK IN PROGRESS. YOU ARE GOING

TO MAKE IT BETTER AND BETTER. I THINK ASSESSING WHAT WORKS AND WHAT DOESN'T AND WHAT PEOPLE HAVE TROUBLE UNDERSTANDING THE RATIONALE FOR OR UNDERSTANDING WHAT THEY'RE SIGNING UP FOR IS MAYBE IMPORTANT.

DR. BOTKIN: I THINK OHRP HAS SOME GUIDANCE ON THIS THAT'S RELATIVELY RECENT. YOU MAY REMEMBER, NICOLE, OR, BERNIE, BETTER THAN I DO EXACTLY WHAT THAT SAYS, BUT I'M NOT SURE THAT THIS IS CONSISTENT WITH THAT.

BUT I GUESS THE OTHER QUESTION IS THIS WILL BE A RECOMMENDED FORMAT THAT THE INSTITUTIONS THEMSELVES. SO PERHAPS RATHER THAN GOING DIRECTLY TO POTENTIAL PARTICIPANTS TO LOOK AT THE LANGUAGE, YOU MAY WANT TO GO TO SOME OF THE INSTITUTIONAL IRB'S AROUND THE STATE AND SAY WOULD THIS PASS MUSTER? DO YOU GUYS HAVE CLEAR EXPECTATIONS ABOUT THE WITHDRAWAL ISSUE THAT THIS ISN'T GOING TO FLY WITH?

CHAIRMAN LO: OF COURSE, ANOTHER WAY TO LOOK AT THAT, JEFF, IS TO SAY THE IRB'S ARE STRUGGLING WITH THIS, AND IT MAY BE THAT THEY WOULD WELCOME A DOCUMENT WITH YOUR ANNOTATIONS, JEFF, AS TO WHY -- WE KNOW THIS IS A COMPLEX TOPIC. THIS IS WHY WE CHOSE TO DO IT THIS WAY. WE CONSIDERED THIS

ALTERNATIVE, THAT ALTERNATIVE. WE CHOSE NOT TO AND, IN FACT, WE TALKED TO SOME PATIENTS AND THEY SEEM TO AGREE WITH US.

DR. LOCKHART: THE POINT ABOUT THE OHRP GUIDANCE IS AN EXCELLENT ONE. YOU WOULD WANT TO LOOK AT THAT. I THINK THE OHRP GUIDANCE WOULD SUPPORT WITHDRAWING SAMPLES, SO THE ORIGINAL SAMPLES THAT ARE IN THE BANK IF YOU MAINTAIN A LINK. IT DOESN'T ADDRESS CELL LINES. I'M NOT AWARE OF ANY GUIDANCE THAT ADDRESSES CELL LINES. SO I'M NOT SURE WHETHER HOW THEY WOULD CONSIDER THAT BASICALLY. IT IS STILL TIED TO A PATIENT, BUT HAS BEEN MANIPULATED. SO IT WON'T REALLY HELP YOU OUT, I WOULDN'T THINK, ON WHAT TO DO WITH THE CELL LINES.

AND ABOUT TALKING TO INSTITUTIONS AND IRB'S, I THINK THAT WOULD BE VERY VALUABLE. AND I THINK THEY REALLY WOULD LIKE JEFF'S ANNOTATED APPROACH, PARTICULARLY IF YOU'RE TRYING TO HARMONIZE ACROSS INSTITUTIONS AND HAVE THEM USE SIMILAR CONCEPTS AND SIMILAR TEMPLATES. TO THE EXTENT THAT YOU CAN TELL THEM THE RATIONALE BEHIND LANGUAGE, THAT CAN BE HELPFUL.

DR. LOMAX: I THINK THAT'S THE END POINT. WE WANT TO HAVE THAT AVAILABLE, BUT WE ARE AT A SORT OF POINT SLIGHTLY FURTHER BACK IN OUR GLIDEPATH, AND

THESE COMMENTS ARE PERFECT FOR THE PLACE WE'RE AT AT THIS TIME, AND WE HAVE AN OPPORTUNITY TO GIVE IT ONE MORE ITERATION. THAT WAS THE WHOLE PURPOSE OF LAST YEAR'S WORKSHOP. THIS IS, I THINK, A BIG STEP FORWARD. AND NOW WE NEED TO PROCESS THIS FEEDBACK. AND I FEEL COMFORTABLE IN TERMS OF THE TRAJECTORY OF THIS ONE.

CHAIRMAN LO: THIS IS NICELY DONE AND REALLY GOES WELL BEYOND WHAT WE WERE TALKING ABOUT A YEAR AGO. THANKS TO GEOFF FOR SPEARHEADING.

DR. LOCKHART: I HAVE OTHER COMMENTS IF WE HAVE TIME JUST QUICKLY. I THINK THIS IS REAL IMPORTANT TO GET THROUGH. THE FIRST THING I NOTED, AND I DIDN'T HAVE A CHANCE TO REALLY CHECK OFFICIALLY, BUT THE READING LEVEL SEEMED VERY HIGH TO ME. SO I THINK YOU COULD PROBABLY ADDRESS THAT AT LEAST INITIALLY THROUGH DOING A LOT OF SENTENCE SHORTENING. THERE'S A LOT OF LONG SENTENCES WITH MANY CLAUSES, WHICH ARE QUITE DIFFICULT TO GET THROUGH. SUPPOSED TO BE EIGHTH GRADE LEVEL. I DIDN'T CHECK IT. I'M SURE IT'S AT LEAST 12, I WOULD BET. SO TRY AND TAKE A LOOK AT THAT.

ALSO INCLUDING SOME DEFINITIONS. I DON'T THINK GENE IS DEFINED AT ALL. SOME THINGS LIKE THAT AND MAKING SURE YOU DEFINE CLOSE TO FIRST USE

BECAUSE I THINK PLURIPOTENCY IS PROBABLY USED A COUPLE TIMES BEFORE IT'S DESCRIBED, AND WORDS LIKE THAT ARE VERY INTIMIDATING.

I AGREE WITH ALL OF DOROTHY'S COMMENTS ABOUT TALKING MORE ABOUT PRIVACY PROTECTIONS AND CONFIDENTIALITY PROTECTIONS BECAUSE THAT INFORMATION OCCURS MUCH LATER THAN WHERE YOU ACTUALLY MENTION REVIEW OF THE MEDICAL RECORD. SO TRYING TO BRING THAT MORE IN ALIGNMENT. YOU MIGHT WANT TO TALK ABOUT GENETIC PRIVACY SINCE GENETIC SEQUENCING IS MENTIONED.

DR. LOMAX: CAN I JUST SAY ONE THING BECAUSE WE GOT COMMENTS IN ADVANCE ON THIS AS WELL. I THINK WE KIND OF SET OURSELVES UP THERE. WE ARE NOT ASSUMING A PRIORI THAT MEDICAL RECORDS WILL BE INVOLVED. IT WAS ACTUALLY KIND OF PUT IN THERE AS A -- IN THE OTHER DOCUMENT YOU WILL SEE IT SAYS ARE YOU CONSIDERING MEDICAL RECORDS, AND IT WAS SORT OF MORE OF A PLACEHOLDER. WE ANTICIPATE THERE COULD VERY WELL BE PROTOCOL WHERE YOU WOULDN'T NEED A MEDICAL RECORD. THERE COULD JUST BE SOME DIAGNOSTIC ASSAY. SO THAT'S WHY WE MOVED TO THAT MEDICAL INFORMATION CONSTRUCT.

I APOLOGIZE. IT'S COME UP SO MANY TIMES, AND I REALIZE WE PROBABLY SHOULD HAVE BEEN BETTER

ABOUT LETTING YOU KNOW THAT IT'S NOT NECESSARILY A MEDICAL RECORD DRIVEN PROTOCOL, BUT WE CAN'T RULE IT IN, WE CAN'T RULE IT OUT.

DR. LOCKHART: EVEN IF THERE ISN'T MEDICAL RECORD ACCESS, STILL THE SECTION 8.0 DEALING WITH PRIVACY AND CONFIDENTIALITY, I THINK IT WOULD STILL BE GOOD TO SAY A LITTLE BIT MORE ABOUT WHO HAS -- IF THE LINK TO IDENTITY WILL BE MAINTAINED AND WHO WOULD HOLD THAT LINE. THAT'S NOT REALLY DESCRIBED. I KNOW IT'S DIFFICULT WHEN YOU'RE WRITING A TEMPLATE DOCUMENT AND YOU DON'T YET KNOW WHAT THE STUDY LOOKS LIKE, SO THERE MIGHT ALSO BE A LIST OF THINGS YOU PUT ON THE SIDE TO ADDRESS ONCE YOU'RE FURTHER DOWN THE ROAD BECAUSE IT IS HARD TO WRITE A CONSENT FOR A HYPOTHETICAL STUDY.

DR. ROBERT TAYLOR: I THINK YOU MIGHT BE SORRY IF YOU TAKE IT OUT, THE MEDICAL RECORDS ACCESS. I WOULD ARGUE ON THE SIDE OF INCLUDING IT.

DR. LOMAX: THAT WAS THE IDEA. JUST TO SAY THIS IS WITHIN THE REALM OF POSSIBILITY.

DR. ROBERT TAYLOR: BUT YOU HAVE TO DISCUSS THE PRIVACY ISSUES.

DR. LOCKHART: I ALSO NOTED THE CONSENT FOR GAMETE RESEARCH, I THINK IT PROBABLY -- I THINK YOU DO NEED TO SEEK AN EXPLICIT CONSENT FOR THAT. I

FOUND IT A LITTLE ALARMING WHEN I WAS READING IT. I WOULD MAYBE SUGGEST SOMETHING THAT SAYS IF YOU DO NOT CONSENT TO GAMETE RESEARCH, THAT RESEARCH WILL NOT BE PERFORMED, TO MAKE THAT VERY, VERY CLEAR. I'M A LITTLE AFRAID THAT SOMEONE WILL HIT THAT SECTION AND WANT NOTHING FURTHER TO DO WITH THIS STUDY. I FIND IT KIND OF SCARY.

DR. ROBERT TAYLOR: IN MY PLACE IT WOULD BE LIKE GENETICS WHERE YOU ACTUALLY NEED A SEPARATE SIGNATURE FOR THAT COMPONENT OF THE CONSENT.

CHAIRMAN LO: SO ALMOST AFTER YOU'VE DONE THE MAIN CONSENT, SAY, AND BY THE WAY, THERE'S SOME OTHER ADD-ON THAT YOU MAY OR MAY NOT WANT TO PARTICIPATE IN.

DR. LOCKHART: AND PUTTING THOSE ADDITIONAL SIGNATURES OR THOSE ADDITIONAL CHECKS AT THE END MIGHT KIND OF MAKE THAT CLEARER. YOU CAN THINK ABOUT WHETHER RESTRUCTURING IT THAT WAY WOULD HELP A LITTLE BIT.

IN 6.0 THERE'S A STATEMENT, YOU HAVE THE RIGHT TO PLACE ADDITIONAL RESTRICTIONS ON HOW YOUR SPECIMENS ARE USED. I WAS A LITTLE SURPRISED AT THAT, AND I WAS UNCLEAR AS TO WHAT WAS MEANT BY THAT BECAUSE THERE AREN'T REALLY ANY OTHER CHOICES HERE ABOUT HOW YOUR SPECIMEN CAN BE USED. I DIDN'T KNOW

IF SOMEONE CAN JUST WRITE ON THEIR FORM NO USE FOR SCHIZOPHRENIA RESEARCH. WHAT DOES THAT MEAN? IF YOU'RE GOING TO PUT THAT THERE, THEN I SUDDENLY WANT THE RIGHT TO MAKE ALL KINDS OF DECLARATIONS.

DR. LOMAX: AGAIN, THAT IS SOMETHING THAT WE PUT FORWARD ALREADY IN OUR STANDARDS ORIGINALLY. SO PART OF WHAT THIS DOCUMENT IS TRYING TO ACCOMPLISH IS TO PROVIDE A TEMPLATE THAT'S ALSO VIEWED AS COMPLIANT WITH OUR REGULATIONS. THE WAY OUR REGULATIONS ARE CURRENTLY WRITTEN, IT INDICATES YOU HAVE TO TELL PEOPLE THAT. SO I APPRECIATE YOUR COMMENT. I JUST WANTED TO LET YOU KNOW THE GENESIS OF THAT STATEMENT.

DR. ROBERT TAYLOR: GEOFF, YOU ALSO HAVE LANGUAGE THERE THAT SAYS YOU CAN'T RESTRICT WHO MIGHT RECEIVE CELL THERAPY THAT COMES FROM YOUR CELL LINE. SO IT'S A LITTLE BIT OF A...

DR. LOMAX: THIS WORKING GROUP CAN PERHAPS REVISIT THAT IN THE FUTURE AND DECIDE HOW BEST TO PROCEED.

DR. LOCKHART: I THINK ALL THE OTHER MAIN COMMENTS I HAD IS UNDER 7.0, INCIDENTAL FINDINGS ARE DISCUSSED, AND THEY'RE LISTED THERE AS -- THEY APPEAR UNDER THE SECTION ARE THERE ANY POTENTIAL BENEFITS. I WOULD REALLY FEEL MORE COMFORTABLE WITH

NOT PUTTING THAT UNDER BENEFITS. IT MAKES IT APPEAR LIKE A BENEFIT, AND I THINK THERE YOU REALLY INCREASE THE RISK OF A THERAPEUTIC MISCONCEPTION, THAT SOMEONE IS GOING TO THINK THEY SHOULD BE IN THIS STUDY BECAUSE OF THE CHANCE THEY MIGHT FIND OUT SOMETHING. SO TO THE EXTENT YOU CAN PUT THAT IN A SEPARATE SECTION, I THINK THAT MIGHT HELP.

AND ALSO, I'M NOT SURE IF YOU REALLY WANTED TO STICK TO JUST INCIDENTAL FINDINGS OR IF YOU ALSO MEAN RESEARCH RESULTS. I DON'T KNOW IF THE DISTINCTION THERE WOULD REALLY BE MEANINGFUL TO A PATIENT.

DR. LOMAX: SO YOU MEAN SORT OF GENERALIZED RESULTS, SORT OF GENERAL UPDATES?

DR. FEIGAL: WOULDN'T INCIDENTAL BE THINGS THAT ARE OUTSIDE THE SCOPE?

DR. LOCKHART: YES.

DR. ROBERT TAYLOR: JEFF, YOU MIGHT BE THE EXPERT ON THIS ONE. I REMEMBER WHEN THIS CAME UP WITH HIV RESEARCH. CERTAIN ACCESS TO NON-CLIA DATA AND THINGS LIKE THAT THAT WERE COMING FROM -- IT WAS A PRETTY HOT-BUTTON TOPIC, IT SEEMS TO ME, BACK A DECADE AGO WHERE I THINK ONE OF THE THINGS THAT WE HAD IN OUR CONSENT FORMS WERE THAT IF IT WASN'T COMING FROM A CLIA-CERTIFIED LABORATORY, WE HAD NO

RIGHT OR WE HAD NO OBLIGATION TO TRANSMIT THE DATA FROM THOSE STUDIES TO THE DONORS ESSENTIALLY. I THINK THERE WAS A BIG PUSH REALLY FROM ACT UP TO REALLY KIND OF CHANGE ALL OF THAT, AND I DON'T FRANKLY KNOW WHERE WE STAND TODAY WITH SOME OF THOSE ISSUES.

DR. LOMAX: IF I CAN JUST JUMP IN THERE. THE POINT OF, AS I UNDERSTAND IT, STILL YOU CANNOT COMMUNICATE A RESULT TO SOMEONE THAT HAS NOT COME FROM A CLIA-CERTIFIED LAB. SO THE POINT OF THIS SUBCONSENT IS TO SAY IF SOMEONE HASN'T CONSENTED, THEN YOU WOULD NOT MOVE FORWARD ON THE EXPENDITURE OR THE EFFORT TO DO THE VERIFICATION BECAUSE THERE'S NO ABILITY TO DO THE RECONTACT. SO THAT'S THE CONCEPTUAL RATIONALE FOR HIGHLIGHTING THE -- IT'S SPECIFICALLY IN PART, I WOULDN'T SAY SOLELY, BUT IN PART BECAUSE OF THAT NEED TO DO VALUE-ADDED ASSAYS.

DR. LOCKHART: THIS LANGUAGE ACTUALLY IS NOT VERY SPECIFIC ABOUT WHAT THOSE FINDINGS WOULD BE. IT'S CONSTRUED AS NEW INFORMATION ABOUT YOUR INDIVIDUAL HEALTH, WHICH IS REALLY BROAD. SO YOU MIGHT WANT TO THINK ABOUT WHETHER YOU WOULD WANT TO SAY SERIOUS OR SIGNIFICANT OR IMPORTANT TO YOUR HEALTH OR SOMETHING. OTHERWISE INFORMATION ABOUT YOUR HEALTH WILL BE ALMOST ANYTHING.

CHAIRMAN LO: THIS IS WHAT YOU ARE GOING TO TALK TO US ABOUT, WHETHER IT HAS TO BE ACTIONABLE OR NOT OR CLINICALLY SIGNIFICANT.

DR. FEIGAL: I WAS JUST GOING TO COMMENT THERE'S BEEN A LOT OF CONVERSATION ABOUT THIS REGARDING GENOMIC TESTING. AND ACTUALLY THERE'S QUITE A BIT WRITTEN ABOUT IT. I ACTUALLY JUST CAME FROM A PANEL ON THAT AT THE AMERICAN ASSOCIATION FOR CANCER RESEARCH WHERE THEY TALKED ABOUT SOME OF THESE EXACT ISSUES. AND WHETHER THE INCIDENTAL FINDINGS WERE SOMETHING THAT COULD ACTUALLY BE IMPACTFUL OR HAVE SOME -- THERE'S SOME EITHER MEANING INTERVENTION OR THERE'S SOMETHING THAT IMPACTS ON YOUR FAMILY AND FAMILY COUNSELING. SO THERE IS, MAYBE NOT IN STEM CELL, BUT IN OTHER AREAS OF TECHNOLOGY, THERE HAS BEEN QUITE A BIT WRITTEN ABOUT THIS.

CHAIRMAN LO: THERE'S A LOT OF THOUGHT ACTUALLY THAT THERE'S SO MUCH THAT YOU ARE GOING TO FIND IN SOMETHING LIKE THIS, YOU DON'T WANT TO SORT OF GIVE THINGS OUT THAT ARE UNVERIFIED, MAY NOT HAVE CLINICAL SIGNIFICANCE, MAY NOT AFFECT CLINICAL DECISION-MAKING.

DR. BOTKIN: MY POINT HAS PROBABLY JUST BEEN MADE BY ELLEN AND BERNIE. I THINK THESE KINDS

OF PROTOCOLS ARE PRETTY MUCH ZERO RISK FOR PARTICIPANTS UNTIL YOU GET TO THE POINT WHERE SOMEBODY DECIDES TO GIVE SOME INFORMATION BACK. AND IT MAY BE INFORMATION BACK THAT'S WRONG, UNWANTED, MISINTERPRETED, ETC. SO I VERY MUCH AGREE THAT THIS SHOULDN'T BE IN THE BENEFIT SECTION. AND I WOULD GET AWAY FROM A TERM LIKE "INCIDENTAL" AND MAYBE CALL IT UNANTICIPATED OR SOMETHING AND EXPLICITLY SET THE BAR HIGH, TO SAY IF WE COME ACROSS SOMETHING THAT MIGHT SERIOUSLY IMPACT YOUR HEALTH, DO YOU WANT TO HEAR ABOUT IT KIND OF THING, AND NOT LET INVESTIGATORS STRUGGLE WITH THE MINOR STUFF.

ONE OTHER POINT, MORE OF AN ADMINISTRATIVE THING. OUR IRB HAS TRIED TO GET AWAY FROM THE SO-CALLED TIERED CONSENT MODEL, WHICH THIS IS, LOTS OF DIFFERENT CHOICES INTERNALLY BECAUSE WE REALIZED WE DIDN'T HAVE THE SOFTWARE SUPPORT TO BAR CODE THE CONSENT FORMS IN A WAY THAT WE CAN FIGURE OUT WHO SAID WHAT. WE REALLY DON'T WANT PEOPLE HAVING TO PULL OUT THE PAPER FORMS AND FIGURE OUT WHO SAID WHAT FOR WHAT.

SO I THINK IT WOULD BE A GREAT CONTRIBUTION TO THE COMMUNITY IF GUYS HAVE A SOFTWARE SUPPORT KIND OF SYSTEM THAT YOU COULD HELP SHARE WITH INSTITUTIONS THAT WOULD ENABLE THEM TO

USE THESE TYPES OF TIERED CONSENTS IN AN EFFICIENT WAY.

CHAIRMAN LO: PAT, DIDN'T YOU AND THAD COHANE WRITE SOMETHING SAYING THAT YOU GUYS HAD AN I.T. SUPPORT SYSTEM THAT COULD DO THAT?

DR. PAT TAYLOR: NOT TO A GREAT LEVEL OF INTRICACY. I THINK CERTAINLY THE TREND IS TO AVOID TIERED CONSENTS. WHETHER CLARITY IS LOST IN THE PROCESS IS AN OPEN QUESTION.

DR. LOCKHART: I THINK FOR SOME THINGS LIKE THE GAMETE RESEARCH, YOU MAY NEED TO HAVE A SEPARATE CONSENT FOR THAT OR RISK LOSING A LOT OF PEOPLE. BUT THEN IN YOUR RFA YOU WOULD WANT TO MAKE CLEAR THAT THEY WILL NEED TO TRACK VARIOUS THINGS, INCLUDING THEY'LL TRACK WITHDRAWAL AS WELL SHOULD THAT RARE EVENT OR ANY OTHER KIND OF RARE EVENT HAPPEN. IT'S POSSIBLE -- YOU CAN THINK ABOUT WHETHER YOU WANT TO DO A SEPARATE CONSENT FOR RETURN OF INCIDENTAL FINDINGS. IN THAT INSTANCE YOU HAVE TO BE PREPARED TO NOT RETURN ANYTHING EVEN WERE IT SOMETHING WHERE YOU FELT A DUTY TO RESCUE WAS INVOKED. IF THEY SAY THEY DO NOT WANT TO KNOW, THEN YOU HAVE TO FEEL COMFORTABLE WITH NOT TELLING THEM.

CHAIRMAN LO: OKAY. MORE COMMENTS, THOUGHTS?

DR. PAT TAYLOR: I'LL DEFER MINE UNTIL AFTER I SEE GEOFF'S MAGNUM OPUS. I LIKE TO UNDERSTAND THE REASONS FOR THINGS BEFORE I VOTE. MAYBE I'LL AGREE WITH THEM ALL.

DR. LOMAX: LIKE I SAY, A NUMBER OF THESE COMMENTS ARE TERRIFIC. AGAIN, THEY ALL MAKE -- THE VAST MAJORITY OF THINGS, I THINK, WE CAN INCORPORATE AND SO WE'LL JUST UPGRADE IT.

I JUST WANT TO POINT OUT I FEEL A LITTLE BAD IF YOU SENSE THAT YOU JUST GOT HIT WITH THIS. IT WAS IN ONE OF MY EARLY E-MAILS, THE LINK TO IT. MAYBE PERHAPS YOU GET A BIT OF E-MAIL FATIGUE, BUT WE REALLY DO TRY TO GET YOU ALL -- I ALWAYS ASSUME YOU'RE GOING TO READ IT ALL ON THE PLANE, SO WE TRY TO GET YOU AS MUCH AS POSSIBLE FOR THE PLANE RIDE.

DR. PAT TAYLOR: I ENJOYED READING IT. I WANT MUCH MORE TO READ AS WELL IS THE POINT. ACTUALLY, YOU KNOW, THERE'S SO MANY DIFFERENT WAYS OF WRITING CONSENTS, I ALWAYS TRY AND DEFER TO REASONABLE EXPLANATIONS.

DR. LOMAX: I THINK AT SOME POINT WE COULD COME BACK AND DO SOME KIND OF FOCUS GROUP WITH PEOPLE WHO HAVE EXPERIENCE WITH THIS DONOR POPULATION. THAT'S THE KIND OF THING WE ROUTINELY DO WITH OUR GRANTEES. SO I THINK WE'RE ON THE RIGHT

GLIDEPATH HERE.

CHAIRMAN LO: THE OTHER THING YOU MAY WANT TO THINK ABOUT, GEOFF, IS BEST PRACTICES AROUND THE WHOLE SUPPORTING INFRASTRUCTURE SO THAT WE HEARD HOW IMPORTANT IT IS TO SORT OF KEEP UP TIES WITH THE DONOR POPULATION AND SORT OF NEWSLETTERS AND UPDATES AND LET THEM KNOW WHAT'S GOING ON IN A GENERAL SENSE CAN BE REALLY HELPFUL IN TERMS OF BUILDING GOODWILL, AND I WOULD ARGUE MAKING IT LESS LIKELY PEOPLE SAY I DON'T LIKE WHAT THEY'RE DOING BECAUSE THEY KNOW WHAT YOU ARE DOING AND THEY CAN SAY, OH, IT'S KIND OF INTERESTING.

WITH THAT, LET'S TAKE A DEEP BREATH. WE COULD TAKE A BREAK OR WE COULD JUST TAKE INDIVIDUAL BREAKS, BUT FRANCISCO JUST GAVE ME THE LET'S GO ON SIGN. YOU WANT THE BREAK. LET'S TAKE A FIVE-MINUTE BREAK. THERE'S, I HOPE, SOMETHING LEFT STILL TO EAT. WE'RE GOING TO COME BACK, AND NICOLE'S GOING TO START US ON A DISCUSSION OF THIS TOPIC WE JUST BROACHED, WHICH IS WHAT ABOUT RETURNING RESULTS TO DONORS.

(A RECESS WAS TAKEN.)

CHAIRMAN LO: WHY DON'T WE RECONVENE. WE'RE HEADING TOWARDS IMMINENT ADJOURNMENT, BUT WE HAVE A LOT OF INTERESTING THINGS TO THINK ABOUT

BEFORE THEN. NICOLE, WHO HAD A LOT OF EXPERIENCE WITH BIOBANKS OF VARIOUS SORTS, HAS VOLUNTEERED TO SORT OF HELP US REALLY THINK ABOUT THIS THORNY, COMPLICATED ISSUE OF RETURN OF RESULTS TO RESEARCH SUBJECTS OR DONORS. OBVIOUSLY WE'RE NOT GOING TO SOLVE THIS BETWEEN NOW AND 4 O'CLOCK, BUT I THINK IT WOULD BE GOOD TO HELP US TO GET STARTED THINKING ABOUT THIS PARTICULARLY AS TO HOW IT MIGHT BE SALIENT WITH THIS RFP THAT'S COMING OUT WITH A THREEFOLD RESEARCH SET OF PROPOSALS THAT CIRM IS GOING TO FUND.

THERE IS IN YOUR BRIEFING BOOK A SHEET THAT LOOKS LIKE THIS ON WHICH IS SUMMARIZED SOME OF THE RECENT THINKING ON THIS TOPIC OF RETURN OF RESEARCH RESULTS. SO, NICOLE, THANKS VERY MUCH FOR DOING THIS, AND WE LOOK FORWARD TO HAVING YOU HELP US THINK ABOUT THIS.

DR. LOCKHART: SURE. I SHOULD SAY IT'S TITLED "ILLUSTRATIVE OVERVIEW" FOR A REASON. THERE WAS FAR TOO MUCH TO TRY AND FIT IT ALL INTO ONE TABLE, SO I TRIED TO COVER BOTH SOME OF THE MAJOR RECENT PUBLICATIONS AS WELL AS SOME OF THE MORE KIND OF OPPOSING VIEWS THAT ARE OUT THERE. AND FOR THOSE WHO ARE REALLY INTERESTED IN THE TOPIC, THERE IS AN ENTIRE ISSUE OF *GENETIC MEDICINE* WHICH IS COMING OUT

IN APRIL, I BELIEVE, BUT IS CURRENTLY ALL AVAILABLE AS E-PUBS DEVOTED TO RETURN OF RESULTS IN BIOBANKING.

AND THEN IN THE WINTER 2011 EDITION OF *JOURNAL OF LAW, MEDICINE, AND ETHICS* WAS ALSO ENTIRELY DEVOTED TO RETURN OF RESEARCH RESULTS AND INCIDENTAL FINDINGS. SO I PULLED SOME OF THE PAPERS FROM THOSE ISSUES, BUT NOT ALL BECAUSE IT WOULD HAVE BEEN 15 OR 20 PAPERS.

AND THERE'S ALSO SOME EMPIRICAL LITERATURE IN THIS AREA WHICH I DID NOT COVER DUE TO I DIDN'T HAVE A LONG ENOUGH FLIGHT, AND I WAS COMING FROM THE EAST COAST, SO IT TOOK SOME TIME ANYWAY.

AND THIS, AS BERNIE SAID, IS NOT SOMETHING WHERE THERE'S GOING TO BE AN ANSWER TODAY. IT'S REALLY JUST TO TRY AND KIND OF GENERATE SOME DISCUSSION AS TO WHAT SOME OF THE CURRENT THINKING IS. AND THIS IS SOMETHING THAT IS PROBABLY ONE OF THE MOST CHALLENGING ISSUES AROUND RIGHT NOW.

SO IF YOU KIND OF LOOK AT SOME OF THE KEY FINDINGS AND SUMMARY ITEMS FOR THE FIRST PROBABLY FOUR PUBLICATIONS, YOU WILL NOTE THAT THERE'S A LOT OF SIMILARITY THERE IN TERMS OF SOME OF THE KEY THINGS THAT WOULD NEED TO HAPPEN IN ORDER FOR A RESULT TO BE RETURNED, THE ANALYTIC VALIDITY, SOME

CALLING OUT SPECIFICALLY THAT RETURNED REPORTS COMPORT WITH APPLICABLE LAW, INCLUDING CLIA, THAT THE RESEARCH PARTICIPANT OPTED TO HAVE THE FINDINGS, THE FINDINGS REVEAL ESTABLISHED AND SUBSTANTIAL RISK OF A SERIOUS HEALTH CONDITION, AND THE FINDINGS ARE CLINICALLY ACTIONABLE. SOMETIMES DIFFERENT WORDS ARE KIND OF CHOSEN AS TO HOW THOSE DIFFERENT CRITERIA ARE DESCRIBED, BUT THOSE ARE COMMONLY NOW STARTING TO BE A CONSENSUS THAT THOSE ARE THE FACTORS THAT WOULD NEED TO BE THERE BEFORE SOMETHING COULD BE RETURNED.

HOWEVER, WHEN YOU GET INTO THE AREA OF BIOBANKING, THINGS CAN GET TO BE MORE COMPLEX LARGELY BECAUSE IT STARTS TO BE A MORE COMPLEX SYSTEM. IT'S MUCH DIFFERENT THAN IF YOU HAVE AN INDIVIDUAL RESEARCHER WHO HAS A SAMPLE AND IS DOING RESEARCH AND THEY KNOW WHO THE PATIENT IS. NOW YOU MAY HAVE A PARTY WHO'S INTERCEDING THERE. SO IT COULD DEPEND ON WHO HOLDS THE LINK. IN SOME CASES A SPECIMEN IS COLLECTED AT A COLLECTION SITE, STORED CENTRALLY AT A BIOBANK, THE BIOBANK THEN DISTRIBUTES THE SPECIMEN. THAT'S NOT ALWAYS THE CASE. SOMETIMES THE BIOBANK HAS THE LINK TO IDENTITY, BUT THERE'S NOW MAYBE THREE DIFFERENT ENTITIES INVOLVED.

AND SO WHO'S GOING TO DO THAT RETURN

ACTION? WHO'S GOING TO DO THAT REIDENTIFICATION? THOSE ARE ALL THINGS THAT, IF YOU DO HAVE A PLAN TO RETURN RESULTS, YOU WOULD NEED TO HAVE WORKED OUT AS WELL AS ALL OF THESE FINDINGS. EVEN THE ONES WHO ARE MORE OPPOSED TO RETURN WOULD SAY YOU NEED TO HAVE A PLAN. YOU NEED TO FIGURE OUT WHAT YOU ARE GOING TO DO ABOUT THIS ISSUE SO YOU CAN TELL PATIENTS. YOU CAN TELL PATIENTS WHAT THEY SHOULD EXPECT AND KIND OF WHERE ARE YOU GOING TO DRAW THAT LINE.

THERE ARE SOME KIND OF COUNTERPOSING PAPERS OUT THERE NOW, MOST NOTABLY ELLEN CLAYTON'S RECENT PAPER AS WELL AS MARIANNA BLEDSOE'S RECENT PAPER THAT ARE MUCH MORE NEGATIVE ON RETURN OF RESULTS, ISSUING A LOT OF CAUTION AND CONCERNS. AND I THINK THOSE ARE ALSO VERY IMPORTANT TO HIGHLIGHT BECAUSE THERE ARE A LOT OF THESE CONSENSUS DOCUMENTS WHICH ARE REALLY KIND OF BUILDING MOMENTUM TO RETURN RESULTS.

I THINK IT'S ALSO KIND OF GOOD TO THINK ABOUT, WELL, THERE'S THESE OTHER PEOPLE ALSO QUITE SMART WHO HAVE SOME HESITATION. SO WHAT ARE THEY KIND OF THINKING?

ELLEN CLAYTON ARGUES THAT THE EXPANSION OF THE SCOPE TO RETURN INDIVIDUAL RESEARCH RESULTS MAY

RESULT IN FAR-REACHING ETHICAL AND LEGAL DUTIES. SO HERE SHE'S WORRIED THAT THE CONSENSUS, IF THERE'S THIS BUILDING CONSENSUS TO RETURN RESULTS, THAT THAT COULD LEAD TO A NEW STANDARD OF CARE, THAT IT'S NOW PERCEIVED THAT THE STANDARD OF CARE IS TO RETURN. AND IF YOU DO NOT RETURN, THEN YOU ARE NEGLIGENT. AND SO SHE'S KIND OF WORRIED ABOUT THESE DOWNSTREAM EFFECTS.

ALSO TRYING TO DRAW THE LINE BETWEEN WHAT IS RESEARCH AND WHAT IS CLINICAL CARE. THE PURPOSE IS RESEARCH IS TO PRODUCE GENERALIZABLE KNOWLEDGE, AND THAT ENDORSING RETURN CAN GENERATE MORE -- INCREASES THE RISK OF A THERAPEUTIC MISCONCEPTION ON THE PART OF PATIENTS. IF YOU'RE TELLING THEM THEY'RE GOING TO RECEIVE ALL THESE RESULTS, YOU CAN SEE HOW THEY WOULD START THINKING THAT THIS RESEARCH IS FOR THEM. IT'S TO HELP THEM. YOU ARE GOING TO TELL THEM THINGS, INFORMATION THEY WOULD HAVE NO OTHER WAY OF GETTING POSSIBLY.

THERE ARE ALSO CONCERNS ABOUT COST. AND I THINK THIS POINT, THAT'S REALLY DIFFICULT TO KIND OF IMAGINE WHAT COST WOULD LOOK LIKE IN THIS INSTANCE. BUT YOU DO NEED TO START THINKING ABOUT, FOR EXAMPLE, ESPECIALLY IN A BIOBANKING SYSTEM, YOU NEED SOMEBODY TO DETERMINE WHAT TO RETURN. SO THERE'S

GOT TO BE SOME KIND OF BODY, SOME DELIBERATIVE BODY WHO MAYBE IS MAKING THESE DECISIONS. THERE WOULD NEED TO BE SOMEONE WHO'S HAVING THAT CONVERSATION WITH PATIENTS. PRESUMABLY YOU WOULD WANT THAT PERSON TO BE TRAINED IN A RELEVANT FIELD. SO MAYBE THEY'RE A GENETIC COUNSELOR. THAT WOULD ALL NEED TO COME FROM SOMEWHERE.

ALSO REPEAT TESTING, OF COURSE, IS ANOTHER HUGE ONE. MOST RESEARCH DOES NOT HAPPEN IN A CLIA-APPROVED LAB. THERE'S SOME OTHER THINGS RELATED TO THAT I'LL GET TO FROM BLEDSOE'S PAPER.

AND THEN JUST THAT WHEN YOU THINK ABOUT RETURN OF INDIVIDUAL RESEARCH RESULTS AND DOING THAT WELL WITHIN THE CONFINES OF OUR HEALTHCARE SYSTEM, WE HAVE MISCOMMUNICATIONS AND PATIENTS NOT GETTING THE INFORMATION THEY NEED FROM THEIR PHYSICIANS IN OUR CURRENT HEALTHCARE SYSTEM. THIS IS A WHOLE OTHER TYPE OF DUTY, AND IT WOULD MOST LIKELY BE ABOUT INFORMATION THAT PHYSICIANS ARE NOT AS FAMILIAR WITH. SO IF YOU HAND A PRIMARY CARE PHYSICIAN A RISK PORTFOLIO AND SAY COMMUNICATE THIS TO YOUR PATIENT, THAT'S NOT WITHIN THEIR CURRENT BOUNDS OF PRACTICE OR KNOWLEDGE. IT WOULD BE VERY CHALLENGING FOR THEM.

SO TRYING TO THINK ABOUT HOW THIS WOULD

FIT INTO CURRENT CLINICAL PRACTICE SO THAT IT IS EFFECTIVE FOR PATIENTS. THOSE ARE ALL KINDS OF -- I THINK WE CAN ALL KIND OF INTUITIVELY UNDERSTAND WHY RETURN OF RESULTS MIGHT BE A GOOD IDEA, BUT YOU DO NEED TO THINK ABOUT SOME OF THE DOWNSTREAM RAMIFICATIONS AS WELL.

THE PIECE FROM BLEDSOE IS REALLY KIND OF THE BIOBANKER PERSPECTIVE. ALL OF THOSE AUTHORS ARE VERY INVOLVED IN ISBER, THE INTERNATIONAL SOCIETY FOR BIOLOGICAL AND ENVIRONMENTAL REPOSITORIES, WHICH IS THE MAJOR BIOBANKING PROFESSIONAL SOCIETY. A COUPLE OF THEM ARE PAST PRESIDENTS, SO THEY'RE VERY MUCH ON THE GROUND BIOBANKER KIND OF PEOPLE.

SO THEY RAISE A LOT OF MORE IMPLEMENTATION CHALLENGES FROM THEIR EXPERIENCES FROM BIOBANKS THEY'RE FAMILIAR WITH ABOUT THINGS THAT WOULD BE VERY CHALLENGING.

ONE THING I DON'T THINK PEOPLE NECESSARILY THINK ABOUT IS JUST IF YOU'RE GOING TO RETURN RESULTS, AS WE MENTIONED BEFORE, YOU NEED TO MAINTAIN A LINK TO THE PARTICIPANT IDENTITY. YOU NEED A NAME AND YOU NEED SOME CONTACT INFORMATION. SO THAT TO SOME PEOPLE MIGHT POSE AN INCREASED PRIVACY RISK. YOU MIGHT NEED TO MAKE SURE THAT INFORMATION IS UP TO DATE. YOU COULD, OF COURSE,

PUT IN PLACE VARIOUS FIREWALLS OR KIND OF TRUSTED INTERMEDIARY PEOPLE TO HOLD THAT INFORMATION, BUT IT IS SOMETHING TO CONSIDER.

IN KIND OF RELATION TO THE NEED TO REPEAT TESTING IN CLIA, THERE'S ALSO A LOT OF REQUIREMENTS AROUND CHAIN OF CUSTODY. SO IF YOU ARE GOING TO RETURN RESULTS, YOU NEED TO VALIDATE THAT YOU ARE PROPERLY TRACKING, LABELING, ALL OF THAT, YOU KNOW WHAT HAPPENED FROM WHEN THE SPECIMEN WAS COLLECTED, WHO HAS TOUCHED IT SO THAT YOU CAN MAKE SURE YOU'RE RETURNING RESULTS TO THE RIGHT PERSON. AND YOU NEED, IF YOU ARE GOING TO RETURN AND YOU'RE GOING TO REDO THE TEST IN A CLIA-APPROVED LAB, YOU MAY NEED SOMETHING TO RETEST. SO IF IT'S A BLOOD DRAW, IT'S NOT A BIG DEAL. IF IT'S A TISSUE SPECIMEN, IT MIGHT BE A BIGGER DEAL. SO JUST MAKING SURE THAT THOSE KIND OF CHAIN-OF-CUSTODY QUESTIONS ARE ADDRESSED.

FROM THE BIOBANKING PERSPECTIVE, SOME BIOBANKERS HAVE CONCERNS ABOUT LEGAL LIABILITY, PARTICULARLY WHEN THE RESULTS ARE GENERATED BY SECONDARY RESEARCHERS OVER WHOM THEY HAVE NO CONTROL. THEY DON'T NECESSARILY WANT TO BE THE ONES TAKING ON THE ONUS OF THAT RESPONSIBILITY AND VOUCHING FOR THEM.

GENERAL KIND OF INFRASTRUCTURE

REQUIREMENTS FOR RETURN, WHICH I ALREADY TALKED ABOUT A LITTLE BIT. THE RELATIONSHIP QUESTION, WHO HOLDS THE RELATIONSHIP WITH THE SPECIMEN? THIS IS PARTICULARLY IF YOU'RE THINKING ABOUT WHAT IS THE ROLE OF THE BIOBANK IN THIS PROCESS. THEY MAY OR MAY NOT HAVE ANY RELATIONSHIP WITH THE PATIENT. IT DEPENDS. THERE'S SOME LONGITUDINAL COHORT STUDIES WHERE THE BIOBANK DOES HAVE A CLOSE RELATIONSHIP WITH THE PATIENTS. BUT IN OTHER CASES, THEY MAY HAVE ABSOLUTELY NO RELATIONSHIP. THEY MAY JUST BE THE CENTRALIZED STORAGE FACILITY. SO THAT CAN BE KIND OF DIFFICULT AS WELL.

AND THEN, AGAIN, JUST THE QUESTION OF RESOURCES. BUT EVEN BLEDSOE, THIS GROUP WHO IS MUCH MORE CAUTIOUS ABOUT RETURN, THEIR KIND OF OVERALL TAKE-HOME RECOMMENDATION IS THAT BIOBANKS DO NEED TO DEVELOP AN ETHICALLY DEFENSIBLE POLICY AND PROCEDURES FOR IF, WHEN, AND HOW TO RETURN RESULTS. SO THAT'S KIND OF THE THING THAT PRETTY MUCH EVERYONE CAN AGREE ON. YOU NEED A PLAN ABOUT WHAT YOU'RE GOING TO DO IN REGARDS TO THIS ISSUE. YOU CAN COME AT IT FROM A LOT OF DIFFERENT PERSPECTIVES, BUT IT'S NOT REALLY SOMETHING TO IGNORE AT THIS POINT. YOU NEED TO FIGURE OUT HOW YOU WILL ADDRESS IT.

ONE OTHER KIND OF ARTICLE I PULLED OUT BECAUSE I THOUGHT IT WAS INTERESTING WAS THIS ARTICLE BY BESKOW ABOUT OFFERING AGGREGATE RESULTS TO PARTICIPANTS. AND THEY HAVE SOME RECOMMENDATIONS AROUND HOW TO DO THAT. AND I THINK THAT, AS THE INDIVIDUAL FROM THE PARKINSON'S INSTITUTE POINTED OUT, THAT THAT CAN ALSO BE A VERY REWARDING THING FOR PARTICIPANTS TO JUST LET THEM KNOW HOW THEIR CONTRIBUTION IN GENERAL IS ADVANCING SCIENCE. AND IT'S SOMETHING THAT PEOPLE TALK ABOUT A LOT. EVERYONE AGREES AGGREGATE RESULTS OR GENERAL RESULTS SHOULD BE RETURNED. IT'S NOT DONE VERY WELL OR VERY OFTEN. SO THINKING ABOUT HOW THAT CAN HAPPEN IN A BETTER, MORE COMPREHENSIVE WAY BECAUSE SOMEONE MAY NEVER GET AN INDIVIDUAL RESEARCH RESULT. IN MANY WAYS, IF THEY DID, IT MAY NOT BE GOOD NEWS. BUT KNOWING THAT THEIR LITTLE SKIN BIOPSY GREW INTO A CELL LINE AND IT IS DOING GREAT THINGS AND IT'S GROWING WELL, AND IF THERE'S SOMEONE WHO IS VERY ENGAGED IN THAT RESEARCH, IF THEY HAVE A DISEASE OR THEIR FAMILY MEMBER HAS A DISEASE, I THINK THAT WOULD BE VERY REWARDING TO THEM TO KNOW THAT, HEY, THEY ARE USING MY SPECIMEN AND I CONTRIBUTED IN A VERY REAL WAY.

THE LAST THING I PUT TOGETHER WAS JUST A

SAMPLE, NOT REPRESENTATIVE OR INCLUSIVE LIST, OF DIFFERENT PROJECTS THAT ARE CURRENTLY IMPLEMENTING RETURN OF RESEARCH RESULTS IN SOME WAY. AND MAYBE GEOFF CAN SEND OUT THE ACTUAL WORD FILE FOR THIS BECAUSE IT'S ALL HYPERLINKED. SO IF YOU'RE INTERESTED IN A PARTICULAR PROJECT, YOU CAN GO TO THE PROJECT WEBSITE. IF THEY HAVE A PUBLICATION, I LISTED IT JUST TO KIND OF GET A FEEL FOR WHAT'S HAPPENING IN THE COMMUNITY BECAUSE I THINK THERE'S REALLY GOING TO BE A LOT OF KNOWLEDGE GAINED AS PEOPLE TRY TO START DOING THIS IN A REAL WAY. A LOT OF EMPIRICAL RESEARCH HAS BEEN MORE HYPOTHETICAL IN NATURE. WHAT DO PEOPLE WANT, BUT A LOT OF THAT IS WHAT DO THEY THINK THEY WANT.

SO I THINK ONCE RESEARCHERS ARE ON THE GROUND GIVING BACK THIS TYPE OF INFORMATION, SEEING HOW PEOPLE ACTUALLY FELT ABOUT IT, WHAT DID THEY UNDERSTAND, HOW COULD IT BE IMPROVED, I THINK THERE WILL BE A LOT TO LEARN AS THOSE EVOLVE.

DR. LOMAX: JUST ONE THING TO POINT OUT, UNLESS ANYONE HAS ANY OBJECTIONS, WHAT I WILL ACTUALLY DO IS WE'LL ASSOCIATE THESE DOCUMENTS WITH THE MEETING AGENDA, AND THEY'LL BE AVAILABLE ON THE WEB. SO THAT WAY IT AVOIDS HAVING TO SEND EVERYTHING OUT, BUT WE STILL MAINTAIN ACCESS.

ONE OTHER THING, YOU REMINDED ME OF THIS, IT WAS A CONVERSATION WITH ONE OF OUR INSTITUTIONS WHEN YOU WERE KIND OF TALKING, GOING THROUGH THE POINTS ABOUT IT'S EXPENSIVE, ALL THE THINGS THAT MAKE IT UNLIKELY THAT YOU WOULD GO THAT PATH. SOMEBODY ELSE ALSO POINTED OUT IN VERY PARTICULAR TERMS. IT'S ONE THING TO HAVE THIS DISCUSSION WHERE YOU ARE USING PRIMARY SAMPLES; BUT IF WE'RE TALKING ABOUT THE USE OF IPS CELLS, WE DON'T EVEN KNOW WHAT THAT CELL REPRESENTS ANYMORE. THE TRANSFORMATIVE NATURE OF THE SAMPLE MEANS THAT WE WOULD -- HIS VIEW WAS HE COULDN'T IMAGINE A SCENARIO WHERE YOU WOULD EVEN INITIATE THE PROCESS BECAUSE YOU'RE NOT DEALING WITH SOMETHING THAT IS ANY LONGER ASSOCIATED WITH THE INDIVIDUAL. IT'S A TRANSFORMED ENTITY.

DR. ROBERT TAYLOR: UNLESS IT WERE GENOTYPE BASED.

DR. LOCKHART: THAT WAS KIND OF A QUESTION I HAD FOR YOU ALL BECAUSE I'M NOT ENOUGH OF AN EXPERT IN THAT AREA TO KNOW WHAT THAT CORRELATION WOULD BE. AS YOU THINK THROUGH THIS, THAT MIGHT BE -- THAT SEEMS LIKE AN EXCELLENT RATIONALE FOR LIMITING WHAT YOU RETURN. IF A LOT OF THINGS THAT PEOPLE ARE GOING TO FIND ARE NOT GOING TO BE RELATED TO THE PERSON ANYMORE, THIS IS A TRANSFORMED CELL

LINE, SO YOU MIGHT WANT TO DRAW -- KIND OF THINK THROUGH WHAT ARE THE KINDS OF RESULTS PEOPLE WOULD FIND AND WOULD IT RELATE TO THE PERSON ITSELF? I DON'T KNOW ENOUGH ABOUT THE SCIENCE THAT WOULD BE CONDUCTED TO SEE WHAT THAT WOULD LOOK LIKE, BUT I THINK THAT'S A REALLY GOOD POINT IS IF YOU'RE MOSTLY THINKING ABOUT POLICIES FOR THE CIRM IPSC BANK, THAT'S MUCH DIFFERENT THAN PROJECTS WHERE THEY'RE TAKING A PRIMARY SAMPLE, PLANNING ON DOING HUGE AMOUNTS OF IN-DEPTH GENOMIC SEQUENCING, IT'S A VERY DIFFERENT KIND OF RESEARCH. YOUR PLAN NEEDS TO BE BASED ON WHAT YOU ANTICIPATE DOING.

CHAIRMAN LO: LET ME GIVE AN EXAMPLE THAT WAS ACTUALLY PUBLISHED FROM A GROUP OF RESEARCHERS IN MUNICH WHO ARE STUDYING IPS CELLS AS A MODEL OF A CERTAIN TYPE OF FAMILIAL CARDIAC ARRHYTHMIA ASSOCIATED WITH SUDDEN DEATH, AND THEY DERIVED CARDIOMYOCYTES FROM IPS CELLS. YOU COULD PROBABLY DO IT BY DIRECT REPROGRAMMING NOW. WENT ON TO DO ACTUALLY EVOKED POTENTIALS ON THE INDIVIDUAL CELLS AND THEN TESTED THE CELL'S RESPONSIVENESS TO CERTAIN STANDARD DRUGS AND TREATMENT AND SHOWED THAT, IN FACT, THOSE WERE VERY SENSITIVE TO A CERTAIN STANDARD DRUG THAT'S COMMONLY USED.

ONE CAN IMAGINE GOING FURTHER AND ALSO

FINDING OUT IT ACTUALLY IS NOT RESPONSIVE TO OTHER DRUGS OR THAT THERE'S AN ADVERSE REACTION.

I GUESS THE QUESTION IS, WELL, TO WHAT EXTENT ARE THESE REALLY RELATED TO THE ORIGINAL DONOR? COULD YOU SOMEHOW IN THE REPROGRAMMING HAVE CHANGED THINGS? SO THAT'S THE KIND OF UNCERTAINTY. OR DO YOU WANT TO SHARE THAT UNCERTAINTY WITH THE PATIENT OR THE DONOR, PRESUMABLY THE PHYSICIAN? DIFFERENT PEOPLE MAY HAVE DIFFERENT LEVELS OF WANTING TO KNOW THAT IT MAY NOT RISE TO THE LEVEL OF SORT OF ACTIONABLE BY A SORT OF EXPERT CONSENSUS COMMITTEE.

BUT I THINK YOUR QUESTION OF WHAT SORTS OF INFORMATION FROM THE TYPES OF RESEARCH THAT WOULD BE DONE ON THIS WOULD MEET CRITERIA SORT OF BROADLY BASED FOR SAYING IT WOULD BE REASONABLE TO OFFER THIS BACK TO PATIENTS, TO DONORS WHO MAY ALSO BE PATIENTS WHO MAY WANT TO KNOW.

DR. LOCKHART: JUST IF YOU THINK A LITTLE BIT ABOUT THAT SCENARIO, HOW COULD YOU REPRODUCE THAT EXPERIMENT IN A CLIA LAB. THERE'S NO WAY TO DO THAT. IT'S JUST A MUCH DIFFERENT KIND OF RESEARCH THAN I THINK WHAT HAS BEEN DISCUSSED TO DATE. TODAY A LOT OF IT FOCUSES ON GENETIC RESEARCH, AND THIS IS KIND OF MUCH MORE REMOVED.

CHAIRMAN LO: COMMENTS, THOUGHTS? JEFF THEN FRANCISCO.

DR. BOTKIN: THIS IS A REALLY HELPFUL SUMMARY FOR ME, AND I'M GLAD TO SEE SOME MORE LITERATURE EMERGING THAT SORT OF PUSHES BACK BECAUSE I'VE BEEN IN THE CLUB OF FOLKS TO SAY THIS IS A CAN OF WORMS. AND AS AN ETHICAL OBLIGATION TO RESEARCH PARTICIPANTS, WE HAVE A STRONG OBLIGATION NOT TO MAKE THEM WORSE, BUT NOT SO MUCH OF AN OBLIGATION TO MAKE THEM BETTER. SO IF YOU DON'T RETURN ANYTHING, YOU'VE NOT MADE ANYBODY WORSE OFF. YOU'VE JUST PERHAPS MISSED AN OPPORTUNITY TO HELP THEM.

AND SO I'M VERY MUCH IN THE CLUB OF FOLKS WHO THINK YOU NEED TO SET A VERY HIGH STANDARD FOR RETURN OF RESULTS, AND THAT THESE SORTS OF CRITERIA MAKE A LOT OF SENSE, BUT YOU CAN SET THAT BAR PRETTY HIGH TO SAY AN HNPCC MUTATION OR BRCA 1 OR SOMETHING OF THAT MAGNITUDE IS WHAT WE'RE TALKING ABOUT HERE.

THE OTHER WRINKLE THAT I'VE NOT SEEN ANY LITERATURE ON THIS PIECE OF IT IS HOW DO YOU START THIS CONVERSATION WITH PEOPLE? IN CLINICAL TESTING CONTEXT, YOU'VE GOT A HIGH RISK FAMILY. YOU CAN SAY DO YOU WANT GENETIC TESTING OR NOT, AND WE KNOW LOTS OF PEOPLE SAY NO. I'M NOT INTERESTED.

IN THIS CONTEXT, YOU CALL THEM UP AND SAY

REMEMBER THAT SKIN BIOPSY YOU GAVE US FIVE YEARS AGO? WELL, WE FOUND SOMETHING. YOU WANT TO KNOW WHAT IT IS? HOW IS SOMEBODY GOING TO SAY NO TO THAT? EVEN WHEN THEY MAY BE OF A PERSONALITY TYPE WHO IS ACTUALLY NOT INTERESTED IN THIS KIND OF STUFF, BUT YET YOU'VE FUNNELED THEM INTO THIS SYSTEM WHERE PRETTY MUCH THEY'VE GOT TO KNOW WHAT IT IS THAT YOU FOUND.

SO I'VE NOT SEEN GOOD LITERATURE ON ACTUALLY HOW THAT CONVERSATION, HOW THAT CONTACT WORKS TO GIVE PEOPLE A FAIR CHOICE TO SAY NO.

DR. PRIETO: I THINK I HAVE TO AGREE WITH JEFF. AND THIS SORT OF MAKES ME THINK AS A CLINICIAN. AND I WOULD WANT US TO KIND OF PUSH BACK AGAINST THIS NOTION OF HAVING TO REPORT EVERYTHING. UNLESS THERE'S SOMETHING SERIOUS, VERIFIABLE, AND/OR SOMETHING THAT INDICATES AN IMMINENT RISK, PUT THOSE TOGETHER, THAT'S A BAR YOU'RE ALMOST NEVER GOING TO REACH, PROBABLY NEVER GOING TO REACH. WE'RE MUCH BETTER OFF NOT RUNNING THAT RISK OF POTENTIALLY HARMING PEOPLE, AND THERE'S A REAL RISK OF HARMING PEOPLE, BUT OFFERING THEM ACCESS TO THEIR AGGREGATE RESULTS. I THINK THE MAIN PSYCHOLOGICAL BENEFIT ANYONE DERIVES FROM ANY OF THIS IS HOPE, HOPE THAT THEY ARE ADVANCING THINGS FOR THE FUTURE. AND BY

GIVING THEM AGGREGATE RESULTS, YOU'RE HELPING THEM SUPPORT THAT.

DR. LOMAX: CAN I ASK A QUESTION THEN BASED ON THE DOCUMENT BEFORE YOU? ANY TIME YOU PUT SOMETHING IN A DOCUMENT, IT SORT OF GETS A LIFE OF ITS OWN. WOULD WE BE BETTER SERVED IN REMOVING THAT SECTION FROM THIS DOCUMENT AND MAKING AN ANNOTATION TO SAY WE RECOGNIZE THERE IS THIS ISSUE ABOUT RETURN OF RESULTS. WE URGE YOU TO CONSIDER IT, BUT WE HAVE NOT INCLUDED IT IN THE BODY OF THIS DOCUMENT BECAUSE WE THINK WE'LL HAVE TO SORT OF DESCRIBE THAT. SEE WHAT I'M SAYING? THE DIFFERENCE BETWEEN -- IT'S ALMOST ONCE IT'S IN THE MODEL, IT ALMOST HAS A SORT OF -- MIGHT BE PERCEIVED AS ADVOCATING THAT OPTION; WHEREAS, WHAT I'M HEARING NOW IS THE HIGH BAR ARGUMENT, THAT WE CAN ACKNOWLEDGE THAT IT COULD BE OUT THERE, BUT WE'RE DEFERRING IT BACK TO THE PEOPLE DEVELOPING THE PROTOCOL, BUT TAKE IT OUT OF THE BODY OF THE DOCUMENT. WOULD THAT BE A BETTER WAY TO GO IN THE MIND OF THE WORKING GROUP?

CHAIRMAN LO: GEOFF, BY DOCUMENT, YOU MEAN THE MODEL CONSENT FORM, NOT NICOLE'S CHART?

DR. LOMAX: YEAH.

DR. ROBERT TAYLOR: I THINK YOU COULD CERTAINLY DO THAT. I THINK IT CAN BE JUSTIFIED.

ONE OF THE MORE COMPELLING THINGS IN THIS REPORT, I THINK, IS THIS IDEA OF WHO HAS THE CONTACT WITH THE PATIENT, WHO HAS THE RELATIONSHIP WITH THE PATIENT. AND I THINK IF THE BIOBANK IS KIND OF PHYSICALLY REMOVED, AND IT SORT OF SOUNDS LIKE THAT'S A BIT OF YOUR STRUCTURAL PLAN, IT'S A BIT -- THIS MAY BE KIND OF A DODGE, BUT I THINK IT GIVES YOU AN OUT TO SAY WE ARE NOT -- WE DON'T HAVE THE DIRECT RELATIONSHIP WITH THE DONORS TO THIS PROGRAM. AND YOU WILL HAVE TO SORT OF ESTABLISH SOME SORT OF A POLICY, BUT I THINK IT GIVES YOU AN EXCUSE REALLY TO NOT PROVIDE THAT PRIMARILY.

DR. LOMAX: THE OTHER THING I PICKED UP ON IS I'VE HEARD A SERIES OF COMMENTS NOW WHICH SUGGEST TO ME THAT THERE'S ACTUALLY MORE DOWNSIDE THAN UPSIDE OF EVEN IMPLYING THIS. SO WE REALLY NEED TO DEFER TO SOMEONE WHO'S MUCH MORE FAMILIAR WITH THE EXACT PROTOCOL TO EVEN SORT OF GO THERE. SO WE WOULDN'T LEAD WITH IT. WE WOULD ALLOW SOMEONE TO BRING IT IN ONLY UNDER A VERY LIMITED SET OF CIRCUMSTANCES.

DR. PRIETO: I REALLY DON'T THINK IT'S A DODGE. I THINK IT'S THE FACT THAT YOU DON'T HAVE A RELATIONSHIP WITH THE INDIVIDUAL AS THE BIOBANK. AND THE PERSON WHO DOES, GENERALLY THEIR CLINICIAN,

MAY NOT KNOW WHAT TO DO. NO ONE MAY KNOW WHAT TO DO WITH THE KIND OF INFORMATION WE'D RETURN IF WE RETURNED INDIVIDUAL INFORMATION. SO THERE IS THAT VERY SERIOUS DOWNSIDE AND, I THINK, VERY, REMOTE POSSIBILITY OF UPSIDE.

DR. ROBERT TAYLOR: I THINK GEOFF HAS COMMENTED THERE IS A FAIR AMOUNT OF PRESSURE OUT THERE. AND WHEN I WAS ON THE GRC HERE IN SAN FRANCISCO, THERE WAS A LOT OF PUSH FROM PATIENT ADVOCACY GROUPS TO SORT OF GET ACCESS TO DATA THAT WERE BEING GENERATED THAT POSSIBLY COULD HAVE BENEFITED THEM. SO I THINK -- I DON'T KNOW WHERE THE PENDULUM IS RIGHT NOW, BUT I THINK YOU JUST HAVE TO BE SORT OF SENSITIVE TO THAT.

DR. LOCKHART: I THINK THE OTHER THING TO CONSIDER HERE, AS WE KIND OF TOUCHED ON, IS THAT A LOT OF THE DATA GENERATED MAY NOT BE ABOUT THE PERSON. IT WOULD BE ABOUT THE CELL LINE. BUT I THINK EVEN IF YOU DON'T INTEND TO RETURN, I THINK IT'S STILL WORTH PUTTING SOMETHING INTO CONSENT THAT YOU DON'T INTEND TO RETURN RESEARCH RESULTS BECAUSE I THINK THAT'S IMPORTANT FOR PATIENTS TO UNDERSTAND, PARTICULARLY IF YOU'RE WORKING WITH PATIENTS FROM A DISEASE POPULATION WHO, AS POINTED OUT BY THE PARKINSON'S INSTITUTE, MAY NOT UNDERSTAND THAT THE

RESEARCH ISN'T FOR THEM. SO WHATEVER THE PLAN IS, TRYING TO DESCRIBE THAT.

AND THE OTHER THING I WOULD SAY IS IF YOU'RE GOING TO HAVE COLLECTION AT MULTIPLE SITES, TRYING TO HAVE AS HARMONIOUS A POLICY AS POSSIBLE BECAUSE YOU WOULDN'T -- YOU WOULD WANT TO TRY AND AVOID A SITUATION WHERE COLLECTION SITE A IS RETURNING RESEARCH RESULTS AND COLLECTION SITE B IS NOT, AND PARTICIPANTS POSSIBLY WITH THE SAME DISEASE EVEN ARE BEING TREATED DIFFERENTLY.

DR. PAT TAYLOR: IT IS A FIELD VERY MUCH IN FLUX. THERE IS A VERY STRONG MOVEMENT TO DECLARE A LEGAL DUTY TO REPORT TO PEOPLE THOSE FINDINGS THAT A CLINICAL GENETICIST WOULD ORDINARILY REPORT, MEANING SOME GENE POLYMORPHISMS THAT ARE ASSOCIATED WITH SOME DEFINITE CONDITION. SO SOME PEOPLE CERTAINLY BELIEVE, IN FACT IT'S THEIR INTENTION, THAT ALL BIOBANKS, EVEN THOUGH THEY LACK THAT RELATIONSHIP, EVEN THOUGH IN A SENSE THEY LACK PARTICULAR GENETIC INTERPRETIVE SKILL, OUGHT TO HAVE A DUTY, DO HAVE A DUTY TO RELEASE INFORMATION THAT IS SO DEFINITIVE AND IS SITTING IN A SENSE IN THEIR LIBRARIES AND OTHERWISE IS UNAVAILABLE. I THINK THEY FORESEE A SITUATION WHERE THE KNOWLEDGE SITS SOMEPLACE INSIDE A BIOBANK AND NOBODY ELSE HAS IT,

BUT IT'S IMPORTANT TO THE DONOR AND NOTHING HAPPENS.

THAT'S A VERY DIFFERENT SITUATION, THOUGH, THAN THE GENETIC FINDINGS THAT ARISE FROM NOVEL RESEARCH. WEAK ASSOCIATIONS WHERE THE ENVIRONMENTAL RESULTS ARE VERY UNKNOWN.

THE DISCUSSIONS GET VERY CONFUSED, INCLUDING ISSUES OF AMBIGUITY OF INTERPRETATION. SO SOME PEOPLE THINK, FOR EXAMPLE, THAT SAYING, NO, WE'RE NOT GOING TO DO IT IS A VIABLE APPROACH. OTHER PEOPLE THINK IT ACTUALLY VIOLATES A POLICY. THEY MAY BE REQUIRED OF DOING SOMETHING JUST AS ABUSE OF NEGLECT IS SORT OF AN EXCEPTION OFTEN TO CONFIDENTIALITY. SO I THINK IT'S HARD TO TELL WHAT TO DO.

PERSONALLY I WOULDN'T ACTUALLY ADDRESS IT IN ANY WAY AT THIS POINT ONE WAY OR ANOTHER, BUT I RECOGNIZE THAT'S BECAUSE I THINK THEY'RE ACTUALLY REALLY SMART. IT MAY NOT HOLD WATER ULTIMATELY. IT MAY BE A DUTY THAT CAN'T ACTUALLY BE FOREGONE.

DR. ROBERTS: IT SEEMS LIKE SOMETIMES WE'RE TALKING ABOUT RETURN OF RESEARCH RESULTS, AND OTHER TIMES WE'RE TALKING ABOUT RETURN OF UNANTICIPATED FINDINGS ABOUT A PARTICULAR PERSON'S CELLS.

DR. PAT TAYLOR: THEY REALLY ARE QUITE

DIFFERENT. INCIDENTAL FINDINGS ARE YOU'RE DOING THE RESEARCH TODAY ABOUT SOMETHING, AND IN THE COURSE OF IT, YOU DISCOVER THEY HAVE A GENE THAT'S WELL-KNOWN TO DO X, AND EVERYBODY KNOWS THAT. THAT'S THE KIND OF THING THAT IS SORT OF A CENTER OF THE DEBATE AROUND WHETHER OR NOT THERE'S AN ABSOLUTE DUTY IN BIOBANKS. AND THERE'S THE OTHER STUFF, THE NEW RESEARCH STUFF, WHERE ONE COULD IMAGINE SAYING THIS MIGHT MEAN THIS, BUT IT MIGHT MEAN A LOT OF OTHER THINGS, AND TOO MUCH HARM TO RESEARCH PARTICIPANTS. THE TWO GET VERY CONFLATED.

DR. ROBERT TAYLOR: I THINK BERNIE'S EXAMPLE IS INTERESTING. IF YOU REALLY DO MAKE A HEART CELL OUT OF A CELL IN A DISH AND IT ENDS UP BEING SUPER SENSITIVE TO DIGOXIN, THEN MAYBE IT'S ETHICALLY APPROPRIATE TO TELL THAT PATIENT THAT SHE MIGHT BE AT RISK OF HAVING A WORSE ARRHYTHMIA.

DR. PRIETO: OR MIGHT NOT, WHICH MAY OR MAY NOT BE TREATABLE BY DRUG X. THAT'S WHY I MADE MY COMMENT ABOUT THE BAR. YOU KNOW, IT SHOULD BE SERIOUS, VERIFIABLE, AND KNOWN TO BE --

DR. ROBERTS: AND TREATABLE ALSO. ACTIONABLE. IS THAT THE TERM USED? ACTIONABLE. BUT TO ME BERNIE'S HYPOTHESIS SOUNDED LIKE SOMETHING YOU WOULDN'T WANT TO -- YOU WOULD JUST CONFUSE

PEOPLE BECAUSE YOU DON'T EVEN KNOW WHAT YOU FOUND.

DR. PRIETO: I'LL TELL YOU EVEN AS A PHYSICIAN, IF SOMEONE GAVE THIS TO ME, I WOULD SAY WHAT DOES THIS MEAN? AND WHO DO I TURN TO? TO MY FRIENDLY CARDIOLOGIST? HE'S NOT GOING TO KNOW EITHER.

DR. PAT TAYLOR: EMPIRICAL DATA SHOWS A REAL DIVIDE BASED ON ROLE. SO PEOPLE WHO MANAGE BIOBANKS OR CLINICIANS HAVE THIS PROBLEM DON'T SAY ANYTHING. WE DON'T KNOW WHAT IT MEANS. BUT IF YOU ACTUALLY ASK PATIENTS, THEY WANT A LOT. THEY WANT UNCERTAINTY, AND THEY SAY WE MANAGE THIS ALL THE TIME. DON'T PATRONIZE US. PATIENTS OFTEN TAKE A VERY DIFFERENT VIEW.

DR. ROBERT TAYLOR: BRCA GENE MUTATIONS, NOT EVERYBODY WITH THAT MUTATION IS GOING TO GET A BREAST CANCER. I THINK WE'RE CONFUSED ON A NUMBER OF LEVELS HERE ABOUT WHAT WE DO WITH THE INFORMATION.

DR. ROBERTS: I THINK THERE'S A DIFFERENCE BETWEEN LETTING PATIENTS KNOW INFORMATION WHERE THERE IS AN ABILITY OF SOMEBODY TO FIGURE OUT WHAT IT MEANS AND TO ASSESS RISKS AND BENEFITS, THAT SORT OF THING. I BELIEVE IN PATIENT AUTONOMY AS ANYBODY ELSE, BUT BERNIE'S HYPOTHETICAL SOUNDED AS IF YOU

COULDN'T -- YOU WOULDN'T EVEN BE ABLE, EVEN THE BEST EXPERTS WOULDN'T BE ABLE TO ADVISE ON WHAT IT MEANS. AND THAT'S DIFFERENT THAN WHAT ARE YOU TELLING THE PATIENT.

DR. PAT TAYLOR: I PERSONALLY THINK BERNIE'S HYPOTHETICAL IS BRILLIANT BECAUSE IT'S JUST LIKE THE SITUATIONS I SEE AT CHILDREN'S. PEOPLE WHO ARE LOOKING FOR AN AUTISM GENE AND THEY KNOW IT'S NOT GOING TO BE LOCKED UP, BUT THEY'RE EAGER TO CONTRIBUTE, AS SOMEONE SAID, AND THEY'RE CERTAINLY EAGER TO KNOW IF SOMETHING EXISTS. THEY KNOW IT DOESN'T MEAN SOMETHING DEFINITIVE, BUT THEY KNOW IT MEANS SOMETHING. THAT'S ENOUGH IN THE CONTEXT WITH PEOPLE WHOSE CLINICAL LIVES ARE BUILT AROUND UNCERTAINTY IN THE FATE OF THEIR CHILDREN.

DR. ROBERTS: BUT THEN WHAT YOU'RE REPORTING IS GENERAL RESEARCH RESULTS. AGAIN, THAT'S DIFFERENT FROM TELLING A PATIENT.

DR. PAT TAYLOR: WE SHOULDN'T LIE WHEN WE GIVE THESE RESULTS.

DR. ROBERTS: GIVING THEM SOME SENSE THAT A CURE FOR YOU, OR THIS IS SOME DIAGNOSIS OF YOUR CONDITION, THAT'S WHAT I DON'T THINK --

DR. PAT TAYLOR: YOU'RE ABSOLUTELY RIGHT. YOU JUST DEMARCATED THE FIELD IN A WAY MUCH BETTER

THAN SOME OF THESE OTHER DEBATERS. TELL THE TRUTH ABOUT GENETICS.

CHAIRMAN LO: SO THE TIME IS DRAWING NIGH TILL FOUR. WE HAD PROMISED THAT WE WOULD GET YOU OUT IN TIME TO MAKE A FLIGHT. SO I THINK, FIRST OF ALL, THANKS TO NICOLE FOR SORT OF GIVING THIS VERY NICE OVERVIEW. THIS IS SOMETHING I SUSPECT WE MAY WELL WANT TO COME BACK TO IF ONLY TO SAY HOW CAN WE UPDATE THE THINKING AS SORT OF MORE THINGS GET WRITTEN.

THIS ALSO MAY BE SOMETHING THAT WE WANT TO DO KIND OF A WORKSHOP OR AN EDUCATIONAL OUTREACH FOR THE PEOPLE WE FUND TO HELP THEM THINK THROUGH THESE ISSUES BECAUSE THEY'RE PROBABLY GETTING CONFLICTING ADVICE AND OPINIONS.

I WANT TO WRAP UP BY SORT OF, FIRST OF ALL, THANK GEOFF AND STAFF FOR SORT OF REALLY DOING THE BACKGROUND FOR THIS MEETING.

(APPLAUSE.)

CHAIRMAN LO: I WANT TO THANK ALL OF YOU FOR REALLY INTERESTING, SPIRITED, AND THOUGHTFUL DISCUSSION. I HOPE WHEN WE GET THE TRANSCRIPT, GEOFF, YOU CAN SORT OF SORT THROUGH THIS AND GET SOME USEFUL STUFF. WE MAY WELL COME BACK TO YOU, BUT THERE WILL BE SOME THINGS PROBABLY THAT WE'LL

WANT TO COME BACK AND DISCUSS FURTHER. AND CERTAINLY SOME OF THE THINGS THAT WE MENTIONED WHICH WE'RE GOING TO GO AHEAD IN TERMS OF THESE REGULATIONS AND SORT OF GETTING MORE FEEDBACK, WE'LL DEFINITELY GET BACK TO YOU.

BUT THANKS VERY MUCH. AND I WISH EVERYBODY A WONDERFUL TIME HERE IF YOU'RE STAYING. IT LOOKS LIKE NICE WEATHER. IF NOT, SAFE TRAVELS HOME.

DR. LOMAX: THANKS, EVERYONE.

(THE MEETING WAS THEN CONCLUDED AT 03:57 P.M.)

REPORTER'S CERTIFICATE

I, BETH C. DRAIN, A CERTIFIED SHORTHAND REPORTER IN AND FOR THE STATE OF CALIFORNIA, HEREBY CERTIFY THAT THE FOREGOING TRANSCRIPT OF THE PROCEEDINGS BEFORE THE SCIENTIFIC AND MEDICAL ACCOUNTABILITY STANDARDS WORKING GROUP OF THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE IN THE MATTER OF ITS REGULAR MEETING HELD AT THE LOCATION INDICATED BELOW

SAN FRANCISCO COURTYARD DOWNTOWN
299 SECOND STREET
SAN FRANCISCO, CALIFORNIA

ON

APRIL 6, 2012

WAS HELD AS HEREIN APPEARS AND THAT THIS IS THE ORIGINAL TRANSCRIPT THEREOF AND THAT THE STATEMENTS THAT APPEAR IN THIS TRANSCRIPT WERE REPORTED STENOGRAPHICALLY BY ME AND TRANSCRIBED BY ME. I ALSO CERTIFY THAT THIS TRANSCRIPT IS A TRUE AND ACCURATE RECORD OF THE PROCEEDING.

BETH C. DRAIN, CSR 7152
BARRISTER'S REPORTING SERVICE
160 SOUTH OLD SPRINGS ROAD
SUITE 270
ANAHEIM, CALIFORNIA
(714) 444-4100