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

REGULAR MEETING

LOCATION:	2121 AVENUE OF THE STARS GROUND FLOOR CONFERENCE ROOM LOS ANGELES, CALIFORNIA
DATE:	APRIL 2, 2015 12:30 P.M.
REPORTER:	BETH C. DRAIN, CSR CSR. NO. 7152
BRS FILE NO.:	97344

I N D E X

LOS ANGELES, CALIFORNIA; THURSDAY, APRIL 2D, 2015

12:30 P.M.

DR. LOMAX: WE WILL START WITH A ROLL CALL. SO WE'LL GET THE FOLKS ON THE PHONE LINE AS WELL. SO WHY DON'T WE START AND WE'LL GET A ROLL CALL.

SHERRY LANSING.

CO-CHAIR LANSING: HERE.

DR. LOMAX: BERNIE LO.

CHAIRMAN LO: HERE.

DR. LOMAX: JEFFREY BOTKIN.

DR. BOTKIN: HERE.

DR. LOMAX: BENHUR LEE.

DR. LEE: HERE.

DR. LOMAX: MARIANNA BLEDSOE.

DR. BLEDSOE: HERE.

DR. LOMAX: FRANCISCO PRIETO. TED PETERS. DOROTHY ROBERTS.

MS. ROBERTS: HERE.

DR. LOMAX: JEFF SHEEHY.

MR. SHEEHY: HERE.

DR. LOMAX: PATRICK TAYLOR. ROBERT TAYLOR.

DR. TAYLOR: HERE.

DR. LOMAX: ART TORRES. JOHN WAGNER.

DR. WAGNER: HERE.

CHAIRMAN LO: OKAY. SO IT'S MY PLEASURE TO CALL THE MEETING TO ORDER, TO WELCOME EVERYBODY, BUT I REALLY WANT TO TURN THIS OVER TO SHERRY FOR THE REAL WELCOME. BUT I WANTED TO THANK HER AND HER STAFF FOR MAKING THE ARRANGEMENTS AND FOR ARRANGING THE NICE WEATHER FOR THOSE OF US WHO HAVE SPENT TIME ON THE EAST COAST. IT'S NICE NOT TO HAVE TO WEAR GALOSHES.

SHERRY, IF I MAY, LET'S JUST GO AROUND THE ROOM AND THEN ALSO ON THE PHONE AND PEOPLE INTRODUCE THEMSELVES. I'M BERNARD LO AND I'M THE CO-CHAIR OF THIS FROM THE GREENWALD FOUNDATION.

DR. LOMAX: I'M GEOFF LOMAX. I'M THE CIRM STAFF PERSON WHO FACILITATES THE STANDARDS WORKING GROUP.

DR. MARSALA: MARTIN MARSALA, UCSD STEM CELL PROGRAM.

DR. BLEDSOE: MARIANNA BLEDSOE. I'M ADJUNCT ASSISTANT PROFESSOR OF DEPARTMENT OF CLINICAL RESEARCH AND LEADERSHIP AND DEPARTMENTS OF PATHOLOGY AT GW.

DR. BOTKIN: JEFF BOTKIN, PEDIATRICS AND MEDICAL ETHICS AT THE UNIVERSITY OF UTAH.

DR. LEE: I'M BENHUR LEE. I WAS FORMERLY PROFESSOR AT UCLA ON THE SCRO COMMITTEE, AND I'VE BEEN RECRUITED TO MT. SINAI IN THE LAST YEAR.

DR. GRIESHAMMER: UTA GRIESHAMMER. I'M A SCIENCE OFFICER AT CIRM.

MR. TOCHER: SCOTT TOCHER. I'M COUNSEL AT CIRM.

DR. MILLS: RANDY MILLS, PRESIDENT OF CIRM.

DR. ROBERTS: DOROTHY ROBERTS. I'M A PROFESSOR AT UNIVERSITY OF PENNSYLVANIA.

DR. MILLAN: MARIA MILLAN FROM CIRM.

DR. TAYLOR: ROB TAYLOR. I'M VICE CHAIR FOR RESEARCH IN THE DEPARTMENT OF OB-GYN AT WAKE FOREST UNIVERSITY.

MR. SHEEHY: I'M JEFF SHEEHY. I'M A MEMBER OF THE GOVERNING BOARD OF CIRM. I'M ONE OF THE PATIENT ADVOCATE MEMBERS.

CO-CHAIR LANSING: I'M SHERRY LANSING. I'M A MEMBER OF THE BOARD OF CIRM. I'M A PATIENT ADVOCATE IN THE AREA OF CANCER AND I HAVE MY OWN FOUNDATION.

BUT MOSTLY I WANTED TO WELCOME ALL OF YOU AND SAY WHAT A PLEASURE IT HAS BEEN TO CO-CHAIR THIS COMMITTEE SINCE THE VERY BEGINNING BECAUSE OF

BERNIE, HE'S JUST BEEN AN EXTRAORDINARY CO-CHAIR, AND ALSO OBVIOUSLY BECAUSE OF THE ENTIRE CIRM STAFF. AND ALSO, AND MOST IMPORTANTLY, BECAUSE OF ALL OF YOU.

SO I WANT TO THANK WHAT I WILL REFER TO AS THE OLDER MEMBERS. BY OLDER I DON'T MEAN AGE. I JUST MEAN THAT SOME OF YOU HAVE LITERALLY BEEN HERE SINCE THE BEGINNING. AND THE DEDICATION, THE TIME, AND THE COMMITMENT THAT YOU PUT TOWARDS THIS COMMITTEE I KNOW WE ARE ALL EXTREMELY GRATEFUL FOR. BUT I ALSO WANT TO WELCOME THE NEW MEMBERS AND TELL YOU THAT I AM PERSONALLY VERY, VERY GRATEFUL FOR THE TIME AND THE COMMITMENT THAT I KNOW YOU WILL HAVE FOR THIS COMMITTEE.

WE ARE AN INCREDIBLY DIVERSE GROUP. WE HAVE AN INCREDIBLE BREADTH OF EXPERIENCE AND EXPERTISE, AND WE ALL HAVE THE SAME PASSION TO DO WHATEVER IS NECESSARY AND SAFE TO ADVANCE THIS FIELD.

TODAY IS KIND OF A MILESTONE DAY. WE HAD OUR FIRST COMMITTEE MEETING JANUARY 31ST IN 2005, SO THIS IS ACTUALLY OUR TENTH ANNIVERSARY. AND WE'VE ACTUALLY HAD 28 MEETINGS OF THE WORKING GROUP. WHEN WE FORMED THIS WORKING GROUP, WE SAID THAT WE WERE A CONTINUAL WORK IN PROGRESS, THAT THE FIELD OF

SCIENCE WAS MOVING VERY QUICKLY, AND WE WERE GOING TO ADJUST TO IT. WE WERE GOING TO ALWAYS BE ON TOP OF WHAT WAS GOING ON, AND WE WERE GOING TO ADJUST THE STANDARDS COMMITTEE AS THE SCIENCE PROGRESSED.

AND ACTUALLY THAT IS WHAT WE HAVE DONE. WE HAVE CONTINUALLY REDEFINED WHAT THIS COMMITTEE'S RULES WERE. BUT I'D LIKE TO REFLECT BACK FOR A SECOND AND REMIND YOU THAT WE ARE THE GROUP THAT WAS A PIONEER. WE HAD THE FIRST COMPREHENSIVE SET OF STANDARDS GOVERNING STEM CELL RESEARCH, THE VERY FIRST. AND AS I'VE SAID OVER THE YEARS, WE HAVE MODIFIED AND REDEFINED THOSE RULES TO ADJUST TO THE NEW ADVANCES IN SCIENCE. WE ACTUALLY HAVE BEEN AN INTERNATIONAL LEADER IN THIS AREA. AND SO AS OTHER GROUPS INTERNATIONALLY BEGIN THE FUNDING OF STEM CELL RESEARCH, THEY LOOK TO US FOR ADVICE. THEY LOOK TO US TO CONSULT WITH THEM.

AND SO I'M REALLY GRATEFUL AS A PATIENT ADVOCATE, AND I THINK I SPEAK FOR ANYBODY WHO IS A PATIENT ADVOCATE OR ANYBODY WHO'S BEEN TOUCHED BY A DISEASE AND HAS THE HOPE OF STEM CELL RESEARCH HELPING THEM, THAT WE HAVE BEEN ABLE TO RESPOND SO QUICKLY TO THE NEEDS TO SERVE THE PATIENTS, WHICH IS REALLY WHAT OUR PRIMARY MISSION IS.

AND THAT BRINGS ME TO HOW GRATEFUL WE ARE

TO HAVE A NEW LEADER, RANDY MILLS, WHO IS THE NEW PRESIDENT AND CEO OF CIRM. AND, RANDY, YOU'VE BEEN SERVING JUST ABOUT A YEAR, AND I WAS FORTUNATE ENOUGH TO BE ON THE SEARCH COMMITTEE. I HAVE TO TELL YOU THAT WE HAD A WORLDWIDE SEARCH. WE HAD PEOPLE FROM ALL OVER THE WORLD, NOT JUST THE UNITED STATES, APPLY FOR THIS POSITION. AND WE WERE EXTRAORDINARILY EXCITED WHEN WE GOT RANDY AS OUR LEADER.

SO, RANDY, AS YOU KNOW, OR MAYBE SOME OF YOU DON'T, IS THE FORMER PRESIDENT AND CEO OF OSIRIS THERAPEUTICS. AND SINCE HE'S BEEN HERE, HE'S REALLY CHANGED THE CULTURE. HE'S GIVEN ALL OF US A SENSE OF URGENCY. HE'S GIVEN ALL OF US A SENSE OF URGENCY TO HELP THE PATIENTS. THERE'S ACTUALLY BEEN A REMARKABLE TRANSFORMATION AT CIRM, AND WE REFER TO IT AS CIRM 2.0. AND RANDY'S FOCUS ON SERVING THE PATIENTS HAS AFFECTED ALL AREAS OF CIRM, NOT JUST THE ORGANIZATION, BUT ACTUALLY WHAT WE ARE FUNDING.

AND SO TODAY'S MEETING IS REALLY GOING TO ADDRESS THAT. IT'S GOING TO ADDRESS HOW WE ALIGN THE MEDICAL AND ETHICAL RULES THAT WE HAVE TO ADJUST TO THE NEW CIRM. AND OUR GOAL REMAINS ALWAYS TO ACCELERATE STEM CELL TREATMENTS FOR THE PATIENTS, TO FUND THE GREATEST RESEARCH, BUT ALWAYS TO BE MINDFUL

OF SAFETY. SO WITH THAT, WITH GREAT ENTHUSIASM, GREAT RESPECT, AND GREAT ADMIRATION, I'D LIKE TO TURN IT OVER TO RANDY.

DR. MILLS: CAN I STAND OVER THERE? IS THAT OKAY? MARIA MILLAN IS ALWAYS HERE TO LAUGH AT ME, WHICH IS A WONDERFUL THING. AND THANK YOU FOR THAT WONDERFUL INTRODUCTION.

AND THE SENSE OF URGENCY, SHERRY, THAT YOU REFER TO, I DON'T KNOW ALL OF YOU ALL THAT WELL. JOHN WAGNER, THOUGH, RIGHT, TAKES CARE OF LITTLE, ITTY-BITTY CHILDREN THAT ARE GOING THROUGH BONE MARROW TRANSPLANTATION FOR SOME OF THEM WHO HAVE DEVELOPED GRAFT VERSUS HOST DISEASE. AND THAT'S THE ROLE THAT I CAME FROM. SO I SPENT TEN YEARS TAKING CARE OF CHILDREN WITH A LIFE-THREATENING CONDITION WHO WITHOUT SUCCESSFUL INTERVENTION UNIFORMLY DIE. AND OUT OF THAT YOU DEVELOP AN INNATE SENSE OF URGENCY, AND YOU LOOK TOWARDS WHAT CAN WE DO. AND, THEN ONCE WE FIGURE OUT EXACTLY WHAT IT IS WE WANT TO DO, WE'LL WORK THROUGH THE STEPS OF HOW WE GET THERE. BUT ONCE YOU'VE LOOKED INTO THAT SORT OF PARADIGM WHERE PEOPLE'S LIVES AND PARTICULARLY CHILDREN'S LIVES ARE ON THE LINE, I DON'T THINK IT'S A PLACE YOU CAN GO BACK FROM. AND JOHN AND I HAVE TALKED ABOUT THIS. AND WHEN YOU FIND PEOPLE WITH

THAT SAME SENSE OF URGENCY, IT'S A GREAT THING BECAUSE IT WILL HELP ADVANCE THIS ENTIRE FIELD TOGETHER.

OKAY. AS SHERRY SAID, OUR MISSION IS REALLY QUITE CLEAR. WE'RE TRYING TO ACCELERATE STEM CELL TREATMENTS TO PATIENTS WITH UNMET MEDICAL NEEDS. I AM HERE TO MAKE SURE WE ALWAYS FOCUS ON THIS AND NEVER LOSE SIGHT OF THIS AND WE NEVER GET LOST IN SORT OF POLITICAL ISSUES OR WHATEVER THE HOT TOPIC OF THE DAY MIGHT BE. WE'RE HERE TO MAKE SURE WE ALWAYS FOCUS ON THE PATIENT BEFORE ANYTHING ELSE.

SO A LITTLE BIT ABOUT CIRM. AND I THINK WHAT I LOVE ABOUT CIRM IS HOW WE WERE CREATED. WE WERE CREATED BY THE PEOPLE OF CALIFORNIA TO CREATE STEM CELL TREATMENTS TO PATIENTS WITH UNMET MEDICAL NEEDS, NOT BY SOME OVERSIGHT BOARD OR BY BEING DICTATED TO. ACTUALLY THE PEOPLE OF CALIFORNIA SAID THIS THING IS TOO IMPORTANT FOR US TO LOSE SIGHT OF, AND SO WE ARE GOING TO PLACE AS A PRIORITY OURSELVES THE IDEA OF STEM CELL THERAPIES FOR PATIENTS WITH UNMET MEDICAL NEEDS ABOVE ALL ELSE.

AND SO AT CIRM, AS SHERRY POINTED OUT QUITE CORRECTLY, WE TRY TO ACT WITH A SENSE OF URGENCY THAT'S COMMENSURATE WITH THAT. WE LIKE TO SAY THAT WE HAVE A JOB -- WE SHOULD ACT LIKE WE HAVE

A JOB THAT PEOPLE'S LIVES DEPEND ON BECAUSE PEOPLE'S LIVES DEPEND ON OUR JOB. THAT'S ACTUALLY QUITE TRUE. THAT'S NOT AN EXAGGERATION AT THIS EXTENT.

WE HAVE A GREAT TEAM OF PROFESSIONALS HERE. WE'VE CHANGED THE ORGANIZATION AROUND SOMEWHAT SINCE I'VE COME. MARIA MILLAN IS NOW HEAD OF OUR INFRASTRUCTURE GROUP, WHICH INCLUDES WHERE GEOFF LOMAX WORKS AS WELL, BUT THE UNIFYING ASPECT OF CIRM IS TO MAKE SURE THAT WE ARE PARTNERING WITH PROFESSIONALS EXTERNAL TO CIRM TO TRY TO ACCELERATE STEM CELL THERAPIES TO PATIENTS WITH UNMET MEDICAL NEEDS. AND WITH OVER $3 BILLION IN FUNDING AND OVER 300 PROJECTS IN ACTIVE PROGRESSION, WE ARE BY FAR THE WORLD'S LARGEST AT WHAT WE DO.

MY CHILDREN, BY THE WAY, WEAPONIZED SOMETHING AND HAVE GIVEN IT TO ME. SO IF I SOUND AWKWARD, THAT'S WHY.

SO SO FAR WE'VE DEPLOYED ABOUT $2 BILLION IN CAPITAL, AND YOU CAN SEE THE FIVE FUNDAMENTAL AREAS IN WHICH WE DO THAT. SO ACROSS THE BOTTOM HERE, THERE'S DISCOVERY, TRANSLATIONAL, AND CLINICAL. THOSE ARE THE THREE ASPECTS OF DRUG DEVELOPMENT WHICH WE DEPLOY MONEY. WE HAVE TWO OTHER AREAS, THOUGH, EDUCATION AND INFRASTRUCTURE, WHICH ARE ALSO QUITE SIGNIFICANT AS WELL. SO WE

TRAIN EVERYTHING FROM HIGH SCHOOL STUDENTS ALL THE WAY THROUGH POST DOCS IN STEM CELL THERAPIES. WE ALSO CREATE INFRASTRUCTURE. THAT'S SOMETIMES LARGE BUILDINGS THAT WE'LL BUILD OR CO-BUILD WITH OTHER PEOPLE. OTHER THINGS LIKE ALPHA CLINICS, OUR CELL BANK, OUR IPS CELL BANK, AND OUR GENOMIC CENTER. SO WE, BETWEEN THESE FIVE AREAS, HAVE DEPLOYED ABOUT $2 BILLION WITH THE LARGEST NUMBER NOW GOING TO CLINICAL. AND THAT'S CONTINUING TO RISE AS THE FIELD ADVANCES.

THAT'S ALSO, BY THE WAY, THE WAY IT SHOULD BE. SO WHEN WE WERE YOUNG, THERE WEREN'T A LOT OF THINGS READY TO GO INTO HUMAN CLINICAL TRIALS. AND SO WE CLEARLY WEREN'T SPENDING THAT MUCH MONEY IN THAT SECTOR; BUT AS WE GOT OLDER AND THE FIELD ADVANCED, THERE WERE MORE OPPORTUNITIES FOR US TO FUND CLINICAL TRIALS.

SO THIS IS WHAT OUR CLINICAL PORTFOLIO LOOKS LIKE. OUR LARGEST AREA WHERE WE'VE DEPLOYED OUR CAPITAL IS IN THE NEUROLOGICAL DISEASES FOLLOWED BY CANCER AND CARDIOVASCULAR. NOT TOO SURPRISING. THOSE ARE ACTUALLY FAIRLY SIGNIFICANT AREAS WHERE STEM CELL THERAPIES CAN MAKE A DIFFERENCE.

IF YOU'RE WONDERING ABOUT THE COLORS. THE COLORS REFLECT TO HOW WE'VE DECIDED TO ORGANIZE. SO

NEUROLOGIC AND OCULAR ARE TOGETHER, CANCER IS ALIGNED WITH BLOOD AND INFECTIOUS DISEASE, HIV/AIDS, AND THEN WHAT WE CALL ORGAN SYSTEMS. SO BASICALLY GROWING NEW ORGANS, CARDIOVASCULAR, ENDOCRINE, THINGS LIKE PANCREAS, NEW STRUCTURAL TISSUES, ORTHOPEDICS, AND OTHERS.

NOW, AS WE TAKE AN HONEST ASSESSMENT OF WHAT'S GONE ON SO FAR, 91 PERCENT OF WHAT WE'VE DONE HAS GONE TO THE ACADEMICIANS. AND YOU CAN LOOK AT THAT AND SAY IS THAT A GOOD THING OR A BAD THING. YOU HAVE TO PEEL THE ONION A COUPLE MORE LAYERS TO REALLY UNDERSTAND THIS NUMBER. THE FIRST THING IS THERE ARE THINGS ASSOCIATED WITH THIS NUMBER SUCH AS INFRASTRUCTURE. CLEARLY WE WEREN'T GOING TO BUILD COMPANIES NEW BUILDINGS. SO, FOR EXAMPLE, THE INFRASTRUCTURE NUMBER IS ALL IN THE ACADEMIC AND NOT THE INDUSTRY SETTING.

THE OTHER THING ASSOCIATED WITH THIS NUMBER IS EARLIER ON IN THE DEVELOPMENT OF CIRM, MOST OF OUR WORK WAS IN DISCOVERY AND TRANSLATIONAL KIND OF ACTIVITIES. THOSE ARE THINGS HISTORICALLY MORE FREQUENTLY DONE BY ACADEMIA AND NOT BY INDUSTRY. AS WE'VE PROGRESSED, WE'VE GOTTEN TO ISSUES MORE ASSOCIATED WITH INDUSTRY, AND THOSE ARE CLINICAL TRIALS. AND SO WHILE WE HAVE $218 MILLION

SO FAR INVESTED IN INDUSTRY, IT'S THE LION'S SHARE OF WHAT'S COMING IN TERMS OF CLINICAL DEVELOPMENT.

NOW, CIRM 2.0, THIS IS CLEARLY A BIG DEAL. IF YOU LIVE INSIDE CIRM, YOU LIVE CIRM 2.0. AND THE CONCEPT OF CIRM 2.0 IS HOW CAN WE TAKE WHAT WE DO AND MAKE IT JUST BETTER. AND THAT'S NOT SAYING WHAT WE'VE DONE HISTORICALLY HAS BEEN BAD, BUT IT'S JUST AN HONEST ASSESSMENT OF HOW WE CAN MAKE WHATEVER IT IS WE DO BETTER. SO IF YOU HAD A PROGRAM THAT WAS READY TO GO INTO CLINICAL TRIALS AND YOU TOOK IT TO US A FEW MONTHS AGO, IT WOULD TAKE US 22 MONTHS IN ORDER FOR US TO GET YOU A DECISION ON THAT CLINICAL PROGRAM. TODAY IF COME TO US, YOU WILL ACTUALLY GET AN ANSWER IN 81 DAYS AND WE'LL GET AN ULTIMATE FUNDING DECISION IN 120 DAYS. SO CIRM 2.0 IS REVOLUTIONARY IN HOW QUICKLY WE CAN BE RESPONSIVE IN ORDER TO GET YOU A FUNDING DECISION.

BUT THERE ARE OTHER ASPECTS ABOUT CIRM 2.0, I THINK, THAT ARE IMPORTANT TO APPRECIATE. THE FIRST IS THAT NOT ONLY IS THE PROCESS FASTER, BUT THE PROCESS IS ITERATIVE. SO THIS IS A REAL BIG ISSUE WITH CIRM 2.0. WE'RE NOT HERE TO PLAY GETCHA OR WHATEVER THAT CORRECT TERM IS, GOTCHA, IS WITH REGARDS TO APPLICATIONS. WE WANT THE APPLICATIONS THAT COME BEFORE US TO HAVE THE BEST SHOT OF A FAIR

REVIEW. AND SO WE DO THIS PROCESS OF ITERATIVE REVIEW.

SO IF AN APPLICATION COMES BEFORE US AND IT'S NOT PERFECT OR THERE ARE QUESTIONS ABOUT IT, UNDER CIRM 2.0 WE'LL ASK QUESTIONS. HOW CAN WE MAKE THAT BETTER? WHAT MORE INFORMATION WOULD WE LIKE TO KNOW? ARE THERE THINGS WE CAN CHANGE ABOUT THE APPLICATION THAT WOULD ACTUALLY MAKE IT SUCCESSFUL? SO THAT'S A HUGE ASPECT OF CIRM 2.0.

ANOTHER TENET OF CIRM 2.0 IS TRUE PARTNERSHIPS. IF YOU PARTNER WITH CIRM TODAY, WE ARE IN THIS THING TOGETHER. WE'RE NOT JUST HERE TO WRITE YOU A CHECK AND SAY, BOY, I HOPE THAT WORKS OUT WELL. WE ARE IN IT TOGETHER, AND WHAT I MEAN BY THAT IS WE FORM THESE PROGRAMS CALLED CAP'S OR CLINICAL ADVISORY PANELS, THAT HAVE PEOPLE FROM CIRM PARTNERING WITH SUBJECT MATTER EXPERTS PARTNERING WITH PATIENTS THAT ACTUALLY HAVE THE AFFECTED DISEASES ALL COME TOGETHER, AGAIN, NOT TO BE ADJUDICATIVE BODIES, BUT TO BE ACCELERATING BODIES. THE POINT OF THIS IS ONCE WE MAKE A DECISION TO SUPPORT YOUR PROGRAM, WE ARE HERE TO DO WHATEVER WE CAN, PULL, PUSH, DRAG, WHATEVER WE CAN DO TO GET THAT THING ACROSS THE GOAL LINE IN A MORE MEANINGFUL WAY. AND THAT RESULTS, BY THE WAY, IN VERY REAL

PATIENT PARTICIPATION, WHICH, AGAIN, IS A CENTRAL THEME THAT I BELIEVE IS ESSENTIAL TO CIRM BEING IMPORTANT.

SO WE ALSO HAVE THINGS LIKE CELL THERAPY AND NONCELL THERAPY. IT'S ACTUALLY A DECISION THE BOARD MADE, NOT ME, TO MAKE SURE IT WAS CLEAR THAT BOTH CELL THERAPY AND NONCELL THERAPIES WERE OPEN. BOTH CALIFORNIA AND NON-CALIFORNIA ORGANIZATIONS ARE ELIGIBLE TO PARTICIPATE. YOU MIGHT SAY, WELL, HOW COULD THAT BE? HOW COULD A NON-CALIFORNIA ORGANIZATION PARTICIPATE IN CIRM? WELL, WHAT WE'RE TRYING TO DO IS BRING YOU HERE. SO IF YOU'RE HERE, BY FAR THE BEST DEAL YOU'RE GOING TO GET IS IF YOU'RE A CALIFORNIA ORGANIZATION. BUT IF YOU'RE NOT A CALIFORNIA ORGANIZATION, WE'RE GOING TO DO EVERYTHING WE CAN TO GET YOU HERE. SO IF YOU'RE RUNNING A CLINICAL TRIAL AND YOU HAVE TEN CLINICAL SITES, IF YOU PUT FIVE OF THEM IN CALIFORNIA, WE'LL PAY FOR THE FIVE THAT ARE IN CALIFORNIA BECAUSE WE WANT THESE PROGRAMS TO BE ACCELERATED, AND WE WANT THEM TO BE ACCELERATED IN CALIFORNIA.

LASTLY, WE ARE READY WHEN YOU ARE. SO WE USED TO PLAY THIS GAME OF KIND OF WHACK A MOLE WITH REGARD TO WHEN PROGRAMS WERE OPEN AT CIRM. WE WOULD RANDOMLY PUT OUT REQUESTS FOR PROPOSALS, AND YOU

WOULDN'T KNOW WHEN A PROPOSAL IS OPEN, WHEN IT WOULD CLOSE, WHEN A NEW ONE WOULD BE OPEN AGAIN. WHAT WE'RE SAYING NOW IS WE ALWAYS WANT GOOD CLINICAL PROGRAMS. THE DOOR IS ALWAYS OPEN. THE CYCLE IS EVERY MONTH. YOU GET IT IN BY THE END OF THE MONTH, YOU'RE IN THE REVIEW CYCLE. IF YOU DON'T, THAT'S OKAY. THE NEXT MONTH'S REVIEW CYCLE IS THERE. AND THAT GIVES US THE OPPORTUNITY TO GET THE BEST APPLICATION FROM THE APPLICANT AND NOT THE APPLICATION THAT GETS SHOEHORNED INTO A PARTICULAR RFA.

AND THEN THE LAST THING IS THESE HAVE TO BE HIGHLY COMPETITIVE. SO AT THE END OF THE DAY, WE'RE NOT LOOKING TO FUND EVERYTHING. WE'RE LOOKING TO FUND THE BEST THINGS. WE'RE LOOKING TO FUND THE THINGS THAT HAVE THE BEST CHANCE OF ULTIMATELY GOING ON AND IMPACTING PATIENT CARE. SO THAT'S A REALLY, REALLY IMPORTANT POINT. THEY'RE HIGHLY COMPETITIVE. THE PART OF THE ITERATIVE REVIEW COMES BACK INTO THIS. WE DON'T WANT TO LAUNCH THINGS THAT ARE -- THIS IS AN INSIDE TERM -- BUT THAT ARE 75S, MEANING JUST GOOD ENOUGH TO BE ACCEPTABLE. WE WANT TO LAUNCH 95S. AND THEN WE WANT TO TAKE A 95 PROGRAM AND MAKE SURE WE DO WHATEVER WE CAN TO ACCELERATE THAT.

SO THAT'S THE NUANCE OF CIRM 2.0. AND I'VE RAMBLED ON FOR A WHILE NOW AND I WILL STOP TALKING. IF YOU GUYS HAVE ANY QUESTIONS, I'LL BE HAPPY TO ANSWER.

CHAIRMAN LO: ANY QUESTIONS?

CO-CHAIR LANSING: CAN WE GET THOSE SLIDES?

DR. MILLS: YOU CAN HAVE ANYTHING YOU WANT.

DR. PATRICK TAYLOR: HAS YOUR STATEMENT FOR WHAT'S GOOD CHANGED? I UNDERSTAND THERE'S A NEW PROCESS.

DR. MILLS: NO, I HOPE NOT. THIS IS A GREAT QUESTION. HAS OUR STANDARDS OF WHAT'S GOOD CHANGED? NO. BUT OUR PROCESS FOR HOW WE ADJUDICATE GOOD. AND WHEN ULTIMATELY DETERMINING GOOD, I THINK, HAS CHANGED.

BY THE WAY, THIS IS A REALLY IMPORTANT SLIDE. I'M GLAD GEOFF PUT IT UP. THIS SLIDE, I DON'T KNOW WHAT THIS SLIDE REPRESENTS TO YOU. THIS WAS AN IDEA I HAD BECAUSE I TRAVEL ON AIRPLANES A LOT. SO I PUT CIRM 2.0 IN THE BUCKLE-UP. THIS SLIDE TO ME IS TO REPRESENT HUMILITY IN THAT WE ARE REPRESENTING -- WE ARE INTRODUCING A RADICAL CHANGE. I SWEAR I'LL GET BACK TO YOUR QUESTION. BUT WE ARE

INTRODUCING A RADICAL CHANGE IN THE WAY WE BEHAVE AT CIRM AND OUR PROCESS AT CIRM, AND THIS SLIDE IS TO SAY WE KNOW, WE KNOW WE'RE NOT GOING TO GET IT RIGHT OUT OF THE GATE AND THAT THERE'S GOING TO BE ITERATION AND THAT THERE'S GOING TO BE ASPECTS ABOUT IT WHICH NEED TO BE MODIFIED AND WE NEED TO BE RESPONSIVE AND LEARN. SO THAT'S WHAT THIS SLIDE IS ABOUT.

WITH REGARDS TO, THEN, YOUR QUESTION ABOUT HAVE WE CHANGED WHAT GOOD LOOKS LIKE? NO, BUT WHAT I HOPE WE'VE DONE IS WE'VE GIVEN THE TRULY GREAT A BETTER OPPORTUNITY OF DEMONSTRATING ITSELF UNDER CIRM 2.0. AND SO THE POINT OF ITERATIVE REVIEW COMES BACK TO WHAT USED TO BE AT CIRM WE WOULD GIVE THE BOARD, AND JEFF WAS AT THE FRONT LINE OF THIS, REALLY POOR -- WE'D GIVE THE BOARD A REALLY POOR DECISION TO MAKE. AND THAT WAS HERE'S AN APPLICATION, IT'S OF MARGINAL QUALITY, BUT THERE'S A LOT OF PROMISE IN IT, RIGHT. SO THERE ARE THINGS ABOUT IT WE LOVE, BUT THERE ARE ALSO THINGS ABOUT IT WE DON'T LOVE. AND, JEFF, YOUR DECISION IS VOTE IT UP AND TAKE A MARGINAL PROGRAM AND SAY WE'RE GOING GIVE IT $20 MILLION TO FUND EVEN THOUGH WE KNOW IT'S MARGINAL, OR VOTE IT DOWN AND WE HAVE THIS MARGINAL PROGRAM WHICH WE'RE GOING TO KILL. BECAUSE VOTING A

PROGRAM DOWN UNDER THE OLD CIRM MEANT THIS THING PROBABLY WOULDN'T HAVE A CHANCE TO COME AROUND IN 18 TO 24 MONTHS. SO THAT'S ESSENTIALLY KILLING IT.

WHAT WE'VE SAID UNDER CIRM 2.0 IS THERE'S A THIRD CHOICE THERE. AND THAT IS FIX IT. AND IF YOU FIX IT, WE COME BACK AND GIVE YOU SOMETHING THAT YOU CAN FEEL BETTER ABOUT VOTING UP OR VOTING DOWN.

DR. BOTKIN: ETHICAL CONSIDERATION IS, OF COURSE, A BIG PART OF THIS GROUP'S WORK. I'M WONDERING HOW ETHICS AND REGULATORY, LEGAL ISSUES ARE OTHERWISE INCORPORATED INTO THE ORGANIZATION.

DR. MILLS: SO WE HAVE INTEGRATED THROUGHOUT CIRM. FROM GEOFF'S STANDPOINT HE'S BEEN INVOLVED IN DAY ONE SOWING THE SEEDS OF ETHICS THROUGHOUT THIS. SCOTT'S HERE. BUT OUR ENTIRE LEGAL COUNSEL FROM A LEGAL STANDPOINT HAS BEEN THROUGH THIS. I DON'T THINK WE'RE PUSHING THE BOUNDARY IN ANY WAY OF ETHICS OR LEGAL IN A WAY THAT'S FURTHER FROM THEM.

MR. SHEEHY: I THINK THIS INNOVATION OF HAVING PATIENTS ON THESE CLINICAL ADVISORY PANELS ARE A HUGE ADVANCE. I THINK THAT'S AN ETHICAL FACT BECAUSE YOU ACTUALLY HAVE PEOPLE -- THE IDEA IS TO HAVE PEOPLE DIRECTLY IMPACTED BY DISEASE ACTUALLY INVOLVED IN THE MANAGEMENT OF THE PROGRAM, OF THE

PARTICULAR PROJECT. AND THAT TO ME IS HIGHLY SIGNIFICANT BECAUSE YOU ACTUALLY HAVE SOMEONE THERE WHO'S GOING TO UNDERSTAND WHAT IT FEELS LIKE TO BE PARTICIPATING IN THIS TRIAL OR HOPING THAT THIS TRIAL SUCCEEDS. AND USUALLY THAT ALL HAPPENS WITH EXPERTS AND SPECIALISTS, AND THE PATIENT'S VOICE IS LOST UNLESS SOMEONE IN THE PROCESS SCREAMS LOUD ENOUGH.

AND I ACTUALLY THINK THAT SHOULD BE ROUTINE FOR EVERYBODY, BUT THAT'S JUST ME. BUT ACTUALLY HAVING, WITH REAL POWER, A PATIENT AT THE TABLE INVOLVED IN THE PROCESS.

DR. MILLS: AND TO ADD TO JEFF'S POINT, WE'VE PUT THEM IN EVERY PART OF THE PROCESS. I DIDN'T HAVE ENOUGH TIME TO GET INTO ANYTHING IN GREAT DEPTH, BUT THE PATIENT ADVOCATES ON THE BOARD NOW ACTIVELY ACTUALLY REVIEW THE APPLICATIONS. THEY USED TO SIT ON THE BOARD, BUT NOT MUCH DO THINGS. NOW THEY ACTUALLY HAVE TO -- JEFF WAS ACTUALLY OUR FIRST TO DO IT -- ACTUALLY HAVE TO, WHEN THE APPLICATION COMES IN, REVIEW THE APPLICATION AND PROVIDE A CRITIQUE AND ARGUE FOR OR AGAINST THE APPLICATION. THAT'S AT THE FRONT END OF THE PROCESS, AND THEN WE INCLUDE THEM ALL THE WAY THROUGH AS THE PROGRAM IS DEPLOYED WITH THE CAP'S

WITH THE PATIENT REPRESENTATIVES, AS JEFF TALKED ABOUT, BEING ACTIVELY INVOLVED. I THINK IT'S QUITE GOOD.

CHAIRMAN LO: IF I COULD JUST FOLLOW ONTO JEFF'S QUESTION. COULD YOU SAY LITTLE BIT ABOUT YOUR VIEW OF THE STANDARDS WORKING GROUP, WHAT YOU ENVISAGE OUR ROLE TO BE IN CIRM 2.0? PARTICULARLY HOW CAN WE HELP YOU AND CIRM ACHIEVE THE VISION AND THE OBJECTIVES?

DR. MILLS: PERFECT. GREAT. THANK YOU.

SO MY VISION FOR CIRM IS HOW DO WE ULTIMATELY HELP AS MANY PATIENTS AS POSSIBLE. AND MY HOPE IS THAT YOU GUYS TAKE THIS WITH YOUR VERY DIVERSE BACKGROUNDS AND MAKE SURE WE NEVER EVER, EVER GO OFF TRACK ON THAT. AND SO ASK THE QUESTIONS THAT ARE HARD. TELL US YOU GUYS SHOULD BE THINKING ABOUT THIS. ARE YOU SURE THAT'S RIGHT? BECAUSE FROM MY STANDPOINT IT'S EASY TO GET A LITTLE BIT LOST IN OPERATIONAL THINGS. SO I CAN GET LOST IN OPERATIONAL EFFICIENCIES OF CIRM AND HOW DO WE MAKE REVIEW CYCLES SHORTER AND BLAH, BLAH, BLAH, BLAH. FROM YOUR STANDPOINT, HOW DO WE MAKE SURE WE NEVER LOSE WHAT'S IN THE BEST INTEREST OF PATIENTS AND THE GREATER GOOD? I THINK THAT'S INVALUABLE TO ME.

DR. LEE: I HOPE I'M NOT SPEAKING OUT OF

TURN. I THINK THE RESEARCH REVIEW IS EXTRAORDINARILY ENABLING IF YOU WANT TO MOVE FORWARD WITH THERAPIES. AS PART OF ESCRO, IT USED TO BE SO COMPLICATED. AND PERHAPS THE CHARGE OF THE SWG, WHEN TECHNOLOGY ADVANCES SO FAST, IS ALSO TO BE ENABLING FOR THESE APPLICATIONS TO MOVE FORWARD BECAUSE A LOT OF TIMES SOMETIMES A LOT OF COMMITTEES ARE MORE OBSTRUCTIONIST RATHER THAN ENABLING.

IF THE MIND SET -- I'M NOT SURE ABOUT ESCRO'S IN OTHER UNIVERSITIES, BUT THE ONES AT UCLA, I THINK, HAVE BEEN PRETTY ENABLING. THAT'S THE KIND OF PHILOSOPHY WITH THE RIGHT CHECKS AND BALANCES FOR THE PATIENT.

DR. MILLS: WE ARE IN THE TIME BUSINESS.

CO-CHAIR LANSING: I WAS JUST GOING TO ADD SO MUCH OF WHAT WE DID EARLY ON, WE WERE THERE AT THE BEGINNING, AND SO MUCH OF WHAT WE DID WE ALWAYS, ALWAYS WENT TO THE EXTREMELY CONSERVATIVE POINT OF VIEW ALWAYS, THE SLOWEST POSSIBLE, THE MOST CONSERVATIVE, AND THAT WAS GOOD BECAUSE WE WERE JUST BEGINNING. BUT AS THE SCIENCE HAS PROGRESSED, AND WE'VE PROGRESSED TOO, WE'VE LIMITED TIME FRAMES, WE HAVE INFORMED CONSENT, ALL THESE THINGS, BUT NOTHING WOULD BE WORSE THAN TO HAVE A THERAPY READY TO GO AND IT'S GOING TO TAKE US A YEAR TO GET THE PATIENTS

BECAUSE WE'VE MADE SUCH A BUREAUCRACY FOR THEM TO COME INTO IT. I'M NOT SAYING THAT WE'VE DONE THAT, BUT I THINK WE WILL NEVER EVER SACRIFICE PATIENT SAFETY. WE ALL KNOW THAT. WE WILL NEVER SACRIFICE THE NECESSARY INFORMATION THAT A PATIENT NEEDS TO MAKE A DECISION AS TO WHETHER OR NOT THEY WANT TO ENTER A CLINICAL TRIAL.

BUT JUST WITH THOSE THINGS IN MIND, HOW CIRM HAS STREAMLINED THE PROCESS AND STREAMLINED IT SO MUCH DIFFERENT THAN THE NCI BECAUSE LIVES ARE BEING LOST WHILE PEOPLE ARE GOING THROUGH THE BUREAUCRACY. I THINK WE HAVE TO LOOK AT -- AND I DON'T HAVE ANY POINT OF VIEW ON THIS YET UNTIL WE START TO EXPLORE IT. HAVE WE MADE THINGS LONGER THAN NECESSARY? I'M NOT SAYING WE HAVE. WE MAY LOOK AT IT AND SAY IT'S FINE.

DR. MILLS: I THINK THE THING THAT KEEPS THE SHIP POINTED IN THE RIGHT DIRECTION IS IF ALWAYS, ALWAYS, ALWAYS WHAT THE DIRECTION IS IS THE PATIENT, THEN WE'RE OKAY. AND ARE THERE GOING TO BE COURSE CORRECTIONS THAT ARE NEEDED ALONG THE WAY? ABSOLUTELY. ARE WE GOING TO MAKE DECISIONS THAT WE NEED TO FIX? YEAH. BUT IF WE ALWAYS KEEP THE PATIENT FRONT AND FOREMOST. EVERY TIME WE TALK, THE FIRST THING WE TALK ABOUT IS THE PATIENT, AND THE

LAST THING WE TALK ABOUT IS THE PATIENT.

IT'S FUNNY. I SAT IN THIS, HONEST TO GOD, I SAT IN THIS EXACT ROOM WHEN WE WERE GOING THROUGH THE PROCESS, AND I POUNDED ON THE TABLE. AND THEY SAID, OH, YEAH, EVERYBODY TALKS ABOUT PATIENTS. NO, YOU CAN'T TALK ABOUT THE PATIENTS A LITTLE BIT. YOU HAVE TO TALK ABOUT THE PATIENTS ALWAYS, ALWAYS, ALWAYS, ALWAYS. AND IF YOU ALWAYS TALK ABOUT THE PATIENTS AND DO WHAT'S BEST, THEN YOU'RE OKAY. WE'RE NOT GOING TO BE PERFECT, BUT WE'RE GOING PROBABLY MOVE A LOT MORE IN THE DIRECTION OF WHAT CIRM NEEDED TO DO.

CHAIRMAN LO: OKAY. OTHER QUESTIONS FOR RANDY? OKAY. THANKS VERY MUCH FOR SETTING THAT UP FOR US.

(APPLAUSE.)

DR. LOMAX: LET ME JUST JUMP IN FOR A MOMENT JUST TO LET FOLKS KNOW THAT PAT TAYLOR AND TED PETERS HAVE JOINED THE MEETING. AND ART AND FRANCISCO, DO YOU WANT SEE AGAIN IF YOU CAN -- I KNOW YOU CAN HEAR, BUT CAN YOU COMMUNICATE WITH US?

MR. TORRES: YES, I CAN. I WANT TO THANK SHERRY FOR HER REMARKS AT THE BEGINNING. CLEARLY THEY PROVIDE A VERY IMPORTANT SEGUE FOR THOSE OF US WHO WEREN'T ON THE BOARD AT THE BEGINNING TO GIVE US

THAT HISTORICAL FRAME OF REFERENCE. THANK YOU, RANDY, FOR THAT PRESENTATION.

DR. PRIETO: THANK YOU. AND THIS IS FRANCISCO. I HOPE I'M AUDIBLE NOW.

CHAIRMAN LO: YES.

DR. PRIETO: GREAT. THANK YOU VERY MUCH.

CHAIRMAN LO: OKAY. SO WELCOME TO BOTH ART AND FRANCISCO. AND I KNOW IT'S HARD SOMETIMES IF YOU WANT TO MAKE A COMMENT OR ASK A QUESTION, SO DON'T BE SHY ABOUT BREAKING IN, OR SEND GEOFF AN EMAIL AND HE'LL BE YOUR PROXY VOICE IN THE ROOM TO GET YOU IN THE QUEUE.

TED, WE HAVE A SEAT FOR YOU RIGHT HERE.

MR. TORRES: BERNIE, I JUST WANTED TO SAY I'M STILL WAITING FOR OSTEOARTHRITIS (INAUDIBLE) KNEE REPLACEMENT.

DR. LOMAX: WAITING FOR THE STEM CELL TREATMENT.

CHAIRMAN LO: OKAY. SO I THINK SHERRY AND RANDY HAVE REALLY SORT OF SET UP THE MEAT OF OUR MEETING IN TALKING ABOUT CIRM 2.0'S FOCUS ON PATIENTS, THE URGENCY OF TRYING TO GET THE BEST RESEARCH THROUGH THE PIPELINE AT CIRM AS QUICKLY AS POSSIBLE CONSISTENT WITH MAKING IT THE BEST RESEARCH PROJECT POSSIBLE AND MAKING IT SOUND SCIENTIFICALLY.

THERE'S A PARALLEL IN WHAT WE DO, WHICH IS TO LOOK AFRESH AT THE POLICIES WE SET UP AND THE REGULATIONS. AND AS SHERRY SAID, ORIGINALLY WHEN WE WERE BEGINNING, BECAUSE THIS WAS SO NEW AND THERE WERE SO MANY UNANSWERED QUESTIONS, WHERE THERE WAS AN ISSUE, WE CONSISTENTLY TENDED TO GO FOR A MORE CONSERVATIVE APPROACH TO SEE HOW THINGS WOULD WORK OUT. AND WE MADE A COMMITMENT TO BEING WILLING TO READDRESS THINGS LATER AS THE FIELD EVOLVED, PUBLIC SENTIMENT EVOLVED, AND OUR EXPERIENCE WITH THIS RESEARCH EVOLVED.

AND NOW ONE OF THE MAIN TOPICS OF THIS MEETING IS TO LOOK AT SOME OF THE REGULATIONS THAT WE HAVE IN PLACE WHICH WERE MODELED ON THE NATIONAL ACADEMY OF SCIENCES' REGULATIONS, WHICH, AS SHERRY SAID, THESE REGULATIONS WE PROPOSED AND ENACTED WERE REALLY PATHBREAKING, BUT WE NEED TO SORT OF TAKE A FRESH LOOK IN 2015 AND TO LOOK FOR POSSIBLE EXAMPLES OF REGULATIONS WHICH HAD A REAL PURPOSE, PROTECTING PATIENTS AND RESEARCH PARTICIPANTS AND ENSURING THE ETHICAL INTEGRITY OF RESEARCH, THAT NOW MAY NO LONGER BE AS NECESSARY IN THE SENSE THAT THEY'RE NOT REALLY PROVIDING ADDITIONAL ETHICAL PROTECTION, PROTECTION FOR SUBJECTS, BUT MAY INTRODUCE INEFFICIENCIES IN THE SYSTEM.

SO WE'RE REALLY TRYING TO BALANCE ON THE ON HAND RESPECT FOR PATIENTS, RESEARCH PARTICIPANTS, THE ETHICAL INTEGRITY OF RESEARCH, AND ON THE OTHER HAND, NOT WANTING TO IMPOSE REQUIREMENTS, REGULATIONS THAT REALLY DIDN'T SERVE TO ADVANCE THESE OTHER GOALS. AND GEOFF AND STAFF HAVE IDENTIFIED SEVERAL ISSUES WHERE I THINK REVISIONS TO THE REGULATIONS MAY, IN FACT, NOT SACRIFICE ANYTHING IN TERMS OF PROTECTION FOR PARTICIPANTS AND ETHICAL INTEGRITY, BUT MAY ALLOW FOR EFFICIENCIES IN THE REVIEW PROCESS.

THE OTHER THING, AGAIN FOLLOWING ON SOMETHING SHERRY SAID, WITH CIRM 2.0 BEING SORT OF HIGH SPEED, SO TO SPEAK, I THINK WE WOULD LIKE TO BE ANTICIPATING ISSUES THAT MAY COME UP. WE DON'T WANT TO WAIT TILL SOMETHING HAS BECOME A FULL-FLEDGED ETHICAL ISSUE AND THEN SAY, WELL, LET'S STOP AND PAY ATTENTION TO IT. SO ANOTHER THING THAT WE'LL DO TOMORROW REALLY IS TO LOOK AT AN ISSUE THAT HAS BEEN BREAKING, SEE IS IT ROUGH SAILING FOR CIRM, AND TO SEE WHAT WE CAN DO AS A GROUP AS PART OF CIRM TO HELP THINK THROUGH THIS ISSUE OF GERMLINE MODIFICATION WHICH IS ATTRACTING A LOT OF INTEREST AND DISCUSSION.

SO WITH THAT, LET ME TURN IT BACK TO GEOFF

HERE TO SORT OF GIVE US A REPORT ON SORT OF WHERE SWG HAS BEEN AND WHERE IT'S GOING AND WHAT HE WOULD LIKE US TO CONSIDER IN OUR DELIBERATIONS TODAY.

I JUST WANT TO SAY THANK YOU TO GEOFF FOR REALLY, AS YOU KNOW, HE AND THE STAFF ARE REALLY RESPONSIBLE FOR KEEPING SORT OF THIS PART OF THE TRAIN ON THE TRACKS AND ON SCHEDULE. SO, GEOFF, THANKS VERY MUCH.

DR. LOMAX: THANK YOU, BERNIE. WELCOME EVERYONE. THANKS FOR TAKING THE TIME BECAUSE THIS IS A VERY IMPORTANT WORKING GROUP IN TERMS OF CIRM AND OUR OPERATIONS.

WE PASSED AROUND THE SLIDE DECK, AND I APOLOGIZE IT DEVIATES SLIGHTLY FROM THE FINAL SLIDES, AS ALWAYS, BECAUSE LATE YESTERDAY THE PRINTER DECIDED TO GO ON STRIKE, AND SO WE WERE STUCK WITH THE OLD VERSION. IT PRETTY MUCH IS ACCURATE, AND WE CAN CIRCULATE THE MOST CURRENT VERSION OF BOTH THIS PRESENTATION AND RANDY'S LATER TODAY.

IN ADDITION, THERE ARE ADDITIONAL MATERIALS IN YOUR PACKET IN TERMS OF BACKGROUND AND BRIEFING MATERIALS WHICH, AS I GO THROUGH THE PRESENTATION, IF YOU WANT DETAILED REFERENCE MATERIALS, THEY SHOULD REFLECT SOME OF THE COMMENTS

I'M GOING TO MAKE.

I'M GOING TO START WITH A BRIEF, A LITTLE BIT OF BACKGROUND BECAUSE WE DO HAVE A NUMBER OF NEW MEMBERS. AND SO GIVE A LITTLE BIT OF CONTEXT BECAUSE WE'VE KIND OF ASKED THEM TO JUMP STRAIGHT INTO THE WORKING GROUP MEETING. SO YOU GET ABOUT THREE OR FOUR SLIDES OF BACKGROUND, AND THEN WE'LL MOVE ON TO SOME OF THE POLICY CONSIDERATIONS THAT WE'D LIKE YOU ALL TO CONSIDER TODAY.

SO I DID WANT TO REMIND EVERYONE OF THE CHARGE OF THE WORKING GROUP. THIS IS FROM PROPOSITION 71, WHICH IS THE LEGISLATION THAT ENABLED OUR ORGANIZATION. AND THIS WORKING GROUP IS TO RECOMMEND TO OUR GOVERNING BOARD STANDARDS FOR MEDICAL, SOCIOECONOMIC, AND FINANCIAL ASPECTS OF RESEARCH, RECOMMENDATIONS FOR ACCESS TO THERAPIES, AND SAFE AND ETHICAL PROCEDURES FOR OBTAINING MATERIALS. A LITTLE BIT BACKGROUND THERE. FOR EXAMPLE, THERE WAS ACTUALLY VERY EARLY ON A SUBCOMMITTEE THAT WAS FORMED THAT ACTUALLY DEVELOPED A POLICY FOR ACCESS TO THERAPEUTICS. AS THAT PROCESS WAS MOVING ALONG, THAT SUBCOMMITTEE WAS INTERACTING WITH THIS GROUP. AND SO THERE WAS ALL THESE VARIOUS ISSUES THAT COME UP. THEY HAVE BEEN DEVELOPED BOTH IN COMMITTEES AND SUBCOMMITTEES. SO

WE ACTUALLY HAVE A POLICY, FOR EXAMPLE, TO PROMOTE ACCESS TO NEW THERAPIES TO PEOPLE IN CALIFORNIA WHO MIGHT BE UNINSURED OR UNABLE TO OTHERWISE PAY FOR THOSE THERAPIES.

AND THEN THERE'S COMPLIANCE WITH PATIENT PRIVACY LAWS. AND WHAT THE WORKING GROUP DOES IS THEN ADVISE THE ICOC. WE WOULD TAKE ANY -- SO, FOR EXAMPLE, TODAY WE'LL ASK YOU TO CONSIDER A NUMBER OF CHANGES TO OUR FORMAL REGULATIONS. AND FROM THERE WE WILL TAKE THAT RECOMMENDATION TO OUR BOARD WHICH WOULD APPROVE ANY RECOMMENDATION FROM THIS WORKING GROUP.

SO JUST TO AMPLIFY A BIT MORE ON SOMETHING THAT RANDY MENTIONED, SORT OF THE GENESIS OF OUR STANDARDS AND HOW THEY'VE EVOLVED, I THINK IT'S BEEN QUITE ELOQUENT. ORIGINALLY IN 2006 THE PRIMARY GUIDANCE ON STEM CELL POLICY WAS THE RECOMMENDATIONS OF THE NATIONAL ACADEMIES' COMMITTEE ON HUMAN EMBRYONIC STEM CELL RESEARCH. AND THAT WAS A SET OF GUIDELINES WHICH WE WERE ABLE TO ADOPT IN EARLY 2006 BECAUSE WE WANTED TO INITIATE SOME TRAINING PROGRAMS. AND BEFORE WE COULD INITIATE ANY PROGRAMS, WE HAD TO HAVE A SET OF REGULATIONS OR POLICIES IN PLACE. HOWEVER, BECAUSE THEY WERE GUIDELINES, THERE WERE SOME TECHNICAL CONSIDERATIONS

IN TERMS OF HOW GUIDELINES ARE PRESENTED AS OPPOSED TO FORMAL STATE REQUIREMENTS.

SO BETWEEN FEBRUARY OF 2006 AND THE END OF 2006, WE TOOK THAT DOCUMENT AND ADOPTED IT INTO FORMAL STATE REGULATIONS. AND IT WAS IN LATE 2006 THAT WE PRODUCED THE FIRST SET OF FORMAL CIRM REQUIREMENTS, WHICH SHERRY ALLUDED TO AS THE FIRST COMPREHENSIVE SET OF POLICIES ON STEM CELL RESEARCH.

NOW, IN THAT PERIOD THE TYPES OF ISSUES THAT WERE REALLY THE FOCUS OF POLICY DEVELOPMENT FOCUSED ON ISSUES THAT WERE FUNDAMENTALLY ABOUT BASIC RESEARCH. AND A LOT OF THE ISSUES WERE CENTERED AROUND EMBRYOLOGY, EMBRYO ISSUES, USE OF HUMAN EMBRYOS, CONSENT FOR DONATION OF EMBRYOS, GAMETE RESEARCH. FOR EXAMPLE, OUR EARLY SEED GRANT PROGRAM WAS VERY BASIC RESEARCH AROUND HOW ONE WORKS WITH CELLS. IT COULD BE CELL DERIVATION, CELL LINE DERIVATION, BUT THE POINT BEING IT WAS VERY BASIC IN THE EARLY YEARS.

NOW, AS OUR PROGRAMS MOVED FORWARD, AND THIS IS OBVIOUSLY A VERY SORT OF COARSE LOOK AT THINGS, I'M NOT GIVING A COMPLETE DESCRIPTION OF ALL OUR PROGRAMS, BUT THEY CLEARLY MOVED FROM BASIC TO INCLUDE BOTH MORE CLINICALLY ORIENTED PROGRAMS WITH OUR DISEASE TEAMS AND SOME OF THE INFRASTRUCTURE

PROGRAMS, CELL BANKING. SO, AGAIN, ABSENT ANY DETAIL, WHAT THAT NECESSITATED WAS A SERIES OF REVISIONS OF THE STANDARDS IN RESPONSE TO BOTH THE NEEDS OF THE CLINICAL PROGRAMS AND THEN ALSO SOME OF THESE INFRASTRUCTURE PROGRAMS. THEY'RE A BIT DIFFERENT BECAUSE A CELL BANK IS A LITTLE BIT DIFFERENT THAN, SAY, AN INSTITUTION THAT WAS GETTING RESEARCH FUNDING. SO WE CONTINUED TO EVOLVE THESE STANDARDS TO MEET THE NEEDS OF THE PROGRAMS.

AND THE OTHER THING TO KEEP IN MIND IS THAT BEHIND SORT OF THESE REVISION CYCLES WERE INTERACTIONS WITH, SAY, GRANTEE INSTITUTIONS. WE WOULD HOLD MEETINGS WHERE WE WOULD HAVE STRUCTURED DISCUSSION TO EVALUATE THE STANDARDS. WE ACTUALLY HAD A PROGRAM OF WHERE WE'D GO OUT IN THE FIELD AND EVALUATE OPERATIONS OF THE OVERSIGHT COMMITTEES. SO WE TRIED TO THROUGHOUT THIS PERIOD LOOK BOTH FROM THE STANDPOINT OF WHAT'S THE NEEDS TECHNICALLY FOR THE STANDARDS, BUT ALSO WHAT'S THE EXPERIENCE OF THE INSTITUTIONS, AND HOW CAN WE STRIVE FOR BOTH EFFICIENCY AND QUALITY. AND SO THIS CONCEPT, I THINK, OF EFFICIENCIES HAS BEEN ONGOING AND BUILT INTO THIS PROCESS.

AND, AGAIN, AT THIS POINT NOW I THINK WE SORT OF HAVE CIRM 2.0 HERE. IT'S SORT OF A NEW

MILESTONE IN THE SENSE THAT, WITH PARTICULARLY THE TIMELINES THAT RANDY DESCRIBED, WE'RE LOOKING, ONCE AGAIN, TO SAY ARE THERE THINGS -- FIRST OF ALL, THERE ARE THINGS WE'VE DONE IN THE OTHER POLICIES WITHIN CIRM TO ADAPT TO CIRM 2.0, AND ARE THERE THINGS THAT WE NEED TO DO WITH THE MEDICAL AND ETHICAL STANDARDS TO ADAPT AS WELL?

SO ANY QUESTIONS AT THIS POINT? THERE WAS A LOT OF CONTENT. JUST WANT TO MAKE SURE.

SO, AGAIN, RANDY DID THIS MUCH BETTER AND IN MUCH MORE ANIMATED FASHION THAN I CAN, BUT, AGAIN, CIRM 2.0, IT'S DESIGNED TO BOTH ACCELERATE AND REDUCE CYCLE TIME. AND THE OTHER ASPECT, AGAIN, TO GET VERY HIGH QUALITY APPLICATIONS IN AND GET THEM IN IN REAL-TIME. SO THE IDEA THERE IS PARTICULARLY, FOR EXAMPLE, IF SOMEONE WAS -- IN ONE OF MY OTHER LIVES AT CIRM, I FACILITATE SOME OF OUR INTERNATIONAL PROGRAMS. AND WITH THE ADVENT OF CIRM 2.0, WE'RE GETTING A LOT OF INTEREST INTERNATIONALLY FOR ORGANIZATIONS THAT ARE REALLY CONSIDERING BRINGING TRIALS TO CALIFORNIA. SO THEY'RE STARTING TO ASK QUESTIONS ABOUT HOW THEY COULD TAKE ADVANTAGE OF CIRM 2.0 OPPORTUNITIES TO DEVELOP A CLINICAL TRIAL SITE IN CALIFORNIA. SO IT'S A TREMENDOUSLY EXCITING TIME.

THESE ARE THE PROCESS OBJECTIVES, AND OUR EXPERIENCE TO DATE IS IT'S BEEN QUITE A BIT OF INTEREST.

WHAT RANDY DIDN'T MENTION, BUT THIS IS A LITTLE BIT MORE IN THE WEEDS, IS AT THE MOMENT WE HAVE ACTUALLY THREE RFA'S THAT WENT OUT AT THE END OF THE YEAR, SO JANUARY 1ST THEY WERE AVAILABLE. THIS IS A PROGRAM ANNOUNCEMENT THAT DEALS PRIMARILY WITH PRECLINICAL RESEARCH, SO IT ACTUALLY HAS QUITE A BIT OF RELEVANCE TO SOME OF THE ISSUES WE'RE GOING TO BE TALKING ABOUT TODAY IN TERMS OF THE OVERSIGHT OF DOING PRECLINICAL STUDIES, PARTICULARLY THE ANIMAL STUDIES. THERE'S A PROGRAM ANNOUNCEMENT BASICALLY FOR FOUR CLINICAL TRIALS. AND, MARIA, HELP ME WITH THE THIRD ONE.

DR. MILLAN: SO THAT'S RELATED TO THOSE THAT ARE ALREADY IN THE CLINIC OR IN CLINICAL TRIALS AND THEY'RE ACCELERATING ACTIVITIES ADDITIONAL TO WHAT'S ALREADY FUNDED. SO IF THERE WERE SOME ADDITIONAL RECOMMENDATIONS THAT WOULD FACILITATE THE CLINICAL DEVELOPMENT OF THAT PROGRAM, FOR INSTANCE, BUT IT'S A SEPARATE TYPE OF TRIAL OR IF THERE WERE SOME CRITICAL ACTIVITIES THAT WOULD BRING THE PRODUCT DEVELOPMENT FORWARD.

DR. ROBERT TAYLOR: THAT'S A SUPPLEMENT TO

AN ONGOING CIRM AWARD OR ANY AWARD?

DR. MILLAN: ONGOING CIRM AWARD.

DR. LOMAX: I KNOW AT THIS STAGE WE'VE HAD --

DR. MILLAN: I THINK FOUR HAVE COME IN. ONE WAS JUST REVIEWED AND ONE IS UPCOMING FOR A REVIEW.

DR. LOMAX: AGAIN, WHAT I THINK IS EXCITING ABOUT THIS IS WE ARE REALLY DEALING WITH THIS PROCESS IN REAL-TIME. IT'S KIND OF -- I THINK IT'S KIND OF AMAZING BECAUSE OFTEN THE TENDENCY IS YOU SET UP A PROCESS AND YOU CAN'T DO ANYTHING TILL ALL THE I'S ARE DOTTED AND T'S ARE CROSSED, BUT WE'RE REALLY OPERATING IN REAL-TIME HERE. I THINK THAT'S REALLY COOL.

SO I'M GOING TO SORT OF CHANGE TOPICS SLIGHTLY BECAUSE, AGAIN, WE TRY TO BRING ISSUES TO THE WORKING GROUP, AS I ALLUDED TO EARLIER, IN RESPONSE TO SORT OF FEEDBACK, EVALUATION, EXPERIENCE, AND OBSERVATIONS. THESE ARE WHAT FOLKS REPORT. I WOULDN'T SAY THIS IS SCIENTIFIC. THIS IS SORT OF MORE ANECDOTAL IN TERMS OF WHAT FOLKS ARE SAYING.

ONE OF THE ISSUES THAT FOLKS, WHEN YOU ASK THEM ABOUT HOW'S IT GOING IN TERMS OF YOUR OVERSIGHT

PROGRAMS, THE REGULATIONS, COMPLIANCE, ONE THEME THAT DOES COME BACK, AND THIS WAS IN THE CONTEXT OF A SURVEY WE DID ABOUT SIX MONTHS AGO, IS THAT LENGTHY REGULATIONS CAN BE HARD TO FOLLOW AND IT'S DIFFICULT TO UNDERSTAND HOW CIRM REQUIREMENTS DIFFER FROM FEDERAL POLICY. I DON'T KNOW ACTUALLY IF YOU CAN REALLY CONQUER THAT ONE. I ALWAYS REMIND PEOPLE THIS IS MY PHONE NUMBER, THIS IS MY EMAIL ADDRESS. AND IF YOU FIND YOURSELF IN THAT SITUATION, I TRY TO GET BACK TO YOU WITHIN 24 HOURS UNLESS IT'S A QUESTION ABOUT MY PAY GRADE, AND THEN I'LL GET BACK TO YOU AS SOON AS THE NEXT PERSON. STEVE'S IN THE BACK OF THE ROOM NODDING HIS HEAD.

DR. PECKMAN: I'LL JUST SAY THAT GEOFF IS AN AMAZING RESOURCE. AND THE STAFF AT CIRM HAVE BEEN INCREDIBLE FOR ALL THE PARTICIPATING INSTITUTIONS THAT ARE REQUIRED TO FOLLOW CIRM REGULATIONS. HE'S CALLED ME FROM TRAIN STATIONS AND AIRPORTS AND THINGS, ESPECIALLY WHEN WE HAVE ESCRO MEETINGS COMING UP WHERE THINGS NEED TO BE DELIBERATED UPON. SO IT'S BEEN A TREMENDOUS RELATIONSHIP.

DR. LOMAX: THANKS FOR THAT.

DR. PECKMAN: I WASN'T PAID FOR THAT.

DR. LOMAX: ONE OTHER THING THAT COMES UP,

AND, AGAIN, IT'S SOMETHING WE WILL TRY TO WORK ON, BUT CALIFORNIA IS ACTUALLY QUITE UNIQUE BECAUSE WHILE WE SORT OF MAY BE VIEWED AS LIKE THE LAND OF OPPORTUNITY FOR STEM CELL RESEARCH, IT'S ACTUALLY GOT QUITE A BIT OF LAYERS OF REGULATORY POLICY. THERE'S AN ADDITIONAL LAYER. SO BESIDES THE CIRM REGULATIONS, THE MAJORITY OF OUR GRANTEES ARE ALSO AWARE OF A SET OF STATE GUIDELINES THAT MORE OR LESS MIRROR OUR REGULATIONS, BUT THEY DON'T EXACTLY. AND IT'S ALWAYS THOSE AREAS OF DISCREPANCY WHICH ARE A CHALLENGE FOR PEOPLE. PEOPLE LIKE TO SAY, GOSH, WE'VE GOT FEDERAL REQUIREMENTS, WE'VE GOT CIRM REQUIREMENTS, WE'VE GOT CALIFORNIA REQUIREMENTS. THAT'S A LOT OF TRIANGULATION. IF WE COULD STREAMLINE THOSE SORT OF THINGS, THAT'S GOOD.

SO, AGAIN, WHAT I TRY TO DO IN THAT ROLE IS I PARTICIPATE -- THERE IS A COMMITTEE THAT'S MANAGED BY THE STATE DEPARTMENT OF PUBLIC HEALTH. I INFORMED THEM OF THIS MEETING AND SOME OF THE ISSUES WE'RE WORKING ON. I KIND OF REMINDED THEM OF AREAS -- I ASK PEOPLE WHAT ARE THE SPECIFIC DISCREPANCIES THAT ARE CAUSING FRICTION. I TRY TO GIVE THEM THOSE EXAMPLES, AND THEY'VE EXPRESSED A WILLINGNESS TO SORT OF ONCE WE DECIDE, TO SORT OF THEN GO AND REEVALUATE THEIR GUIDELINES. SO

HOPEFULLY WE CAN ALSO PLAY A ROLE THERE IN TERMS OF BRINGING TO THEM SORT OF THE THOUGHTS OF THIS GROUP AND HOW WE CAN CALIBRATE AS BEST POSSIBLE.

BECAUSE THE THING I'M MOST IMPRESSED ABOUT IS I HAD A CALL FROM A COMPANY ABOUT FIVE OR SIX WEEKS AGO, AND THE DEGREE TO WHICH THEY HAD READ EVERY DETAIL AND WERE COMMITTED TO FOLLOWING THEM WAS TRULY IMPRESSIVE. SO YOU REALLY SEE FIRSTHAND HOW ALL THESE VARIOUS REQUIREMENTS CREATE A LOT OF -- CONSUME A LOT OF BANDWIDTH WITHIN ORGANIZATIONS. TO THE EXTENT WE CAN MAKE SURE THAT THAT BANDWIDTH IS WELL USED, I THINK --

CO-CHAIR LANSING: ARE YOU SAYING -- I KNOW YOU CAN'T PREDICT THIS, BUT ARE YOU SAYING -- OBVIOUSLY IT WOULD BE NICE IF THERE WAS ONE SET OF RULES. BUT THE FEDERAL, CAN WE AFFECT THAT AS WELL? WE DON'T KNOW, DO WE? THAT'S A MUCH MORE DIFFICULT PROCESS.

DR. LOMAX: THAT'S RIGHT.

CO-CHAIR LANSING: SO WHAT YOU'RE SAYING IS HOPEFULLY IF WE ADOPT SOMETHING, WE'LL BE ABLE TO CONVINCE THE STATE TO DO SO AS WELL?

DR. LOMAX: THAT'S RIGHT. THAT'S BEEN OUR EXPERIENCE. IT HASN'T BEEN AN ARM-TWISTING EXERCISE. IT'S GENERALLY BEEN WHAT WAS THE THINKING

HERE? OH, THAT'S VERY GOOD THINKING. THANK YOU. WE'LL FOLLOW ALONG.

DR. PECKMAN: STEVE PECKMAN FROM UCLA. I'M NOT A MEMBER OF CIRM OR ON THIS BOARD. BUT I HAVE TO SAY THAT CIRM AND THE STATE DEPARTMENT OF PUBLIC HEALTH HAVE ALSO DONE AN AMAZING JOB AT HARMONIZING TWO DISTINCT SETS OF REGULATIONS THAT ARE SOMETIMES IN CONFLICT. AND SO FROM A USER POINT OF VIEW, AGAIN, IT'S VERY HELPFUL. AND IT'S MUCH MORE IN HARMONY THAN THE FDA, NIH FEDERAL REQUIREMENTS, WHICH ARE CONSTANTLY IN CONFLICT.

SO WE VERY MUCH IN THE FIELD APPRECIATED THE FACT THAT THE DEPARTMENT OF PUBLIC HEALTH AND CIRM ARE ABLE TO ACCOMPLISH THOSE GOALS. IT STREAMLINED THINGS TREMENDOUSLY.

DR. LOMAX: THEN, AGAIN, THIS FITS KIND OF THE THEME OF THIS MEETING. AS WE MOVE TOWARDS THE CLINICAL TRIALS AND CLINICAL PROGRAMS, A LOT OF THE FEEDBACK IS WE'RE REALLY FOCUSED ON MEETING FDA AND THOSE TYPES OF REQUIREMENTS, AND WE BELIEVE THAT'S AN EFFECTIVE FRAMEWORK. SO I DON'T KNOW IF THAT MEANS THAT -- I DON'T KNOW IF THAT'S A CRITIQUE OR NOT, BUT IT'S SOMETHING THAT COMES UP QUITE FREQUENTLY.

DR. BOTKIN: GEOFF, I WONDER IF YOU COULD

GIVE ANY SORT OF SPECIFIC EXAMPLES THAT COME TO MIND OF THE SORT OF INCONSISTENCIES THAT YOU'RE DEALING WITH HERE.

DR. LOMAX: ON THE CALIFORNIA?

DR. BOTKIN: ON THE CALIFORNIA VERSUS FEDERAL SORT OF LANDSCAPE.

DR. LOMAX: WELL, THE ONE THAT WE DEALT WITH PREVIOUSLY, AND THIS WILL BE HOPEFULLY A REMINDER FOR THE MEMBERS WHO HAVE BEEN AROUND LONGER AND THE NEWER MEMBERS, IF YOU REMEMBER AT ONE STAGE WE ASKED YOU TO CONSIDER REMOVING THE REQUIREMENT THAT A STEM CELL RESEARCH OVERSIGHT COMMITTEE OPINE OVER A CLINICAL TRIAL PROTOCOL AND BASICALLY DELEGATE THAT TO THE IRB. BECAUSE THAT WAS AN AREA WHERE WE WERE IN CONFLICT, AND THE QUESTION BECAME, IF YOU HAVE AN IRB REVIEW OF A CLINICAL PROTOCOL, WHAT DOES THE STEM CELL OVERSIGHT COMMITTEE ADD TO THAT? AND IS IT BEST TO HAVE THAT BE A FOCUSED REVIEW AT THE IRB LEVEL, WHICH IT WOULD HAVE BEEN AT THE FEDERAL LEVEL? SO THAT'S THE MAJOR ONE THAT WE DISPENSED WITH PREVIOUSLY.

AND THANKS TO SCOTT, I THINK THAT'S NOW CLEARED ALL THE ADMINISTRATIVE PROCEDURES.

MR. TOCHER: IT HAS.

DR. ROBERT TAYLOR: GEOFF, IF I COULD ASK,

BASED ON SORT OF STEVE'S COMMENT ABOUT THE CALIFORNIA STATE. DO YOU GET THE SENSE THAT THERE'S KIND OF FLEXIBILITY ON BOTH SIDES IN TERMS OF THE HARMONIZATION, OR HAS THE STATE DEPARTMENT OF PUBLIC HEALTH BEEN PARTICULARLY RECEPTIVE TO THE INPUT YOU GUYS HAVE HAD?

DR. LOMAX: I THINK IT'S ONE OF THEY OFTEN COME TO US BECAUSE WE'RE SO OBVIOUSLY JUST CONSTANTLY INTERACTING WITH THE FIELD. THE STATE DEPARTMENT OF HEALTH, THE PROGRAM IS ACTUALLY NESTED WITHIN A MATERNAL CHILD HEALTH PROGRAM. THEY CLEARLY HAVE A WHOLE OTHER SET OF PRIORITIES THAT THEIR PROGRAM IS FOCUSED ON, BUT THEY'VE ALSO BEEN ASKED TO ADMINISTER THIS PROGRAM. BUT I THINK IT'S REALLY AN EXPERTISE AND CAPACITY ISSUE. IT'S REALLY NOT THEIR BAILIWICK. WE'VE ALWAYS HAD A VERY CORDIAL AND PRODUCTIVE RELATIONSHIP. I DON'T MEAN TO IN ANY WAY DISPARAGE THEIR WORK, BUT IT'S JUST WE DO THE STEM CELL STUFF. WE'RE ON THE FRONT LINES AND THEY'RE NOT.

DR. ROBERT TAYLOR: THE LULLABY.

CHAIRMAN LO: OTHER QUESTIONS FOR GEOFF?

DR. BOTKIN: I HOPE I'M NOT TAKING YOU OFF TASK HERE.

DR. LOMAX: THE NEXT PHASE WOULD BE THE

POLICY MINUTIAE, SO THIS IS A GOOD PLACE TO HAVE GIVE-AND-TAKE.

DR. BOTKIN: I SKIPPED AHEAD, AND IT DOESN'T LOOK LIKE YOU'RE GOING TO ANSWER MY QUESTION, SO I'M GOING TO ASK IT. GETTING INTO A LOT OF CLINICAL TRIALS AT THIS POINT, WHAT'S BEEN YOUR EXPERIENCE WITH THE IRB REALM? HAS THAT BEEN ONE OF THE CHALLENGES TO GETTING TECHNOLOGIES, CELL THERAPIES FROM BENCH TO CLINICAL BEDSIDE RESEARCH? OR WHAT'S BEEN YOUR EXPERIENCE IN GENERAL WITH THE IRB SYSTEM?

DR. LOMAX: WELL, WE'VE HAD -- I MIGHT DEFER TO SOME OF THE OTHER MEMBERS TO CHIME IN. BUT WE OFTEN GET QUESTIONS FROM IT COULD BE INDIVIDUALS SITTING ON IRB'S OR CHAIRS. I THINK THE EXPERIENCE HAS REALLY BEEN THEY'RE LOOKING TO DO THE MOST COMPLETE AND THOROUGH EVALUATION NECESSARY SO THAT THEY KNOW THEY'RE APPROVING THE TRIAL IN A WAY THAT'S APPROPRIATE FROM THE RISK, SAFETY, AND VARIOUS ISSUES THEY'RE TRYING TO ADDRESS. SO IN THAT LIGHT, MY EXPERIENCE HAS BEEN IRB MEMBERS, PARTICULARLY CHAIRS, ASKING VERY THOUGHTFUL QUESTIONS. AND THE REASON THEY'RE ASKING THE QUESTION IS NOT THAT I HAVE ANY ABILITY TO ANSWER THEM, BUT CAN YOU GIVE US A REDIRECT? WHO COULD WE

GO TO?

SO WE GET THAT SORT OF THING. SO OBVIOUSLY YOU HAVE NO DENOMINATOR, AND IT'S JUST KIND OF WHAT COMES IN. BUT FROM MY PERSPECTIVE, IT SEEMS LIKE PEOPLE ARE CERTAINLY ASKING THE RIGHT TYPES OF QUESTIONS.

DR. BOTKIN: YOU HAVEN'T TRIED TO MOVE TO A CENTRAL IRB SYSTEM? AND DOES CIRM TAKE ANY ACTIVE ROLE IN HELPING SUPPORT INVESTIGATORS WITH THE IRB, OR IS THAT MOSTLY THEIR SORT OF JOB?

DR. LOMAX: MARIA, DO YOU WANT TO SORT OF TOUCH BRIEFLY?

DR. MILLAN: I ACTUALLY ASKED STEVE BECAUSE THEY HAVE THE PRACTICAL EXPERIENCE FROM THEIR INSTITUTION WHAT THE LENGTH OF THAT IRB APPROVAL, BUT ALSO TEMPERED WITH THE FACT THAT UCLA HAS ACTUALLY BEEN INVOLVED IN THE UC BRAID, AND I DON'T THINK THAT'S INTRODUCED EFFICIENCIES REGARDING IRB'S AND TRYING TO MOVE TOWARD, NOT NECESSARILY CENTRAL IRB'S, BUT CENTRALIZING PROCESSES AND RECIPROCAL IRBS' APPROVALS.

BUT I THINK WHY GEOFF DIRECTED THE QUESTION TO ME IS CIRM HAS FUNDED THIS ALPHA STEM CELL CLINICS NETWORK. AND CURRENTLY WE'RE STARTING OFF WITH THREE MAJOR PROGRAMS: UCSD, UC SAN DIEGO,

UCLA WITH UC IRVINE AS A CONSORTIUM, AND CITY OF HOPE. AND THESE THREE WHAT'S CALLED ALPHA CLINICS ARE SETTING UP A NETWORK TO INTRODUCE EFFICIENCIES. AND ONE OF THE FOCUSES IS AROUND IRB AND PULLING RESOURCES TO MAKE SURE THAT WE CAN FACILITATE A MORE EFFICIENT IRB SUBMISSION, REVIEW, AND INFORMED DISCUSSIONS.

SO GETTING THE EXPERTISE FROM THE VARIOUS INSTITUTIONS AND OUTSIDE TO COME IN ON THE DISCUSSION SO THAT IT DOESN'T HOLD UP THE PROCESS. AND SO THAT NETWORK IS JUST BEING LAUNCHED NOW. SO TWO OF THE CLINICS HAVE JUST NEGOTIATED, WE JUST LAUNCHED THOSE TWO, AND UCLA IS THE NEXT ONE UP. SO IN ADDITION TO OTHER EFFICIENCIES AND OPERATIONAL-TYPE RESOURCES THAT THE NETWORK SEEKS TO PUT IN PLACE, THINGS RELATED TO CAPTURING AE'S OR MAJOR INFORMATION THAT WOULD BE HELPFUL ACROSS THE VARIOUS INSTITUTIONS AS WELL AS PARTICIPATING -- UTILIZING SOME OF THE CENTRALIZED IRB EFFICIENCIES AND EXPANDING ON THAT, BEING INFORMED BY THE DATASET IN TERMS OF THE EXPERIENCE WITH STEM CELL CLINICAL TRIALS ACROSS THE TECHNOLOGY PLATFORMS. SO WHEN THINGS LIKE INFORMED CONSENT OR CONTINUOUS CONSENT PROCESSES ARE IN PLACE, THEY'RE INFORMED BY SOME DATASETS IN TERMS OF THIS IS OUR EXPERIENCE SO FAR

WITH X NUMBER OF TRIALS WITH THESE PARTICULAR PLATFORMS.

SO THERE'S NOT A HUGE BODY OF LITERATURE OUT YET WITH STEM CELL THERAPIES IN CLINICAL TRIALS. SO I THINK THAT THIS TYPE OF INTERIM EXPERIENCE, PULLING BACK AND BEING ABLE TO HAVE A CONVERSATION WITH THE PATIENTS SO THEY'RE MORE AWARE OF SOME OF THE POTENTIAL -- GOOD AND BAD POTENTIAL SIDE EFFECTS THAT THEY MAY ENCOUNTER AS WELL AS SOME ACTUALLY UPSIDES TO PARTICIPATION IN THE TRIAL THAT MAY NOT BE THAT TANGIBLE.

I'LL TURN IT OVER TO STEVE BECAUSE I DON'T KNOW WHAT THE TYPICAL TIMELINE IS NOW FROM SUBMISSION OF A PROTOCOL TO --

DR. PECKMAN: AGAIN, I'M STEVE PECKMAN FROM UCLA. I SPENT 11 YEARS RUNNING THE IRB PROGRAM AT UCLA AND THEN MOVED OVER TO STEM CELLS. IT SEEMED A LOT MORE INTERESTING AT THE TIME.

SO UCLA IS RUNNING TWO OF THE ONLY HUMAN EMBRYONIC STEM CELL-BASED CLINICAL TRIALS, BOTH FOR BLINDNESS, SCAR HEART DISEASE, AND MACULAR DEGENERATION. AND THE TIMELINE, FOR US THE PRINCIPLE HERE IS IS THE EXPERTISE AVAILABLE TO REVIEW THE WORK. AND AT PLACES LIKE UCLA, UC SAN FRANCISCO, SAN DIEGO, WE HAVE DECADES OF EXPERIENCE

REVIEWING CELL-BASED THERAPEUTIC TRIALS. AT UCLA WE'VE BEEN REVIEWING THEM IN THE IRB FOR MORE THAN 25 YEARS, 30 YEARS.

SO THE ISSUES AREN'T REALLY THAT DIFFERENT FROM OTHER CELL-BASED PRODUCTS AS THEY WOULD BE FROM A HUMAN EMBRYONIC OR IPS-BASED CLINICAL TRIAL.

SO FOR OUR TWO BLINDNESS TRIALS, WHAT WE DO IS WE PREPARE THEM WELL. SO IF YOU WORK WITH THE INVESTIGATORS BEFORE IT GOES TO THE BOARD, THEN YOU HAVE A MUCH EASIER TIME. A PLACE LIKE UCLA, IT'S A BIG UNIVERSITY AS THE OTHER UC'S AND STANFORD. YOU CAN'T DO THAT WITH EVERY PROJECT THAT YOU GET; BUT BECAUSE THESE ARE EXPLORING NOVEL PATHWAYS, IT'S FOUND THAT IT'S WORTH THE ADDITIONAL EFFORT TO MAKE SURE THAT THE INVESTIGATOR IS WELL PREPARED TO PRESENT THE PROJECT TO THE BOARD, EITHER THE ESCRO OR THE IRB.

SO TIMELINES ARE TYPICALLY, SUBMIT THE PROJECT AND MAYBE SOME MINOR MODIFICATIONS REQUESTED, WE SEE APPROVALS WITHIN 45 DAYS. SO IT'S NOT REALLY AN ISSUE SO LONG AS THE PROJECTS ARE PREPARED PROPERLY AND THE INVESTIGATOR IS SENSITIVE TO THE ISSUES THAT ARE GOING TO BE RAISED.

OUR QUESTION HAS BEEN THE PARALLEL OR DUPLICATIVE REVIEW OF MULTIPLE COMPLIANCE

COMMITTEES. WHAT ROLE, IN ESSENCE, DOES THE ESCRO PLAY IN THIS PROCESS ANYMORE? TEN YEARS AGO WE DIDN'T REALLY FORESEE CLINICAL TRIALS HAPPENING ANY TIME SOON ANYWAY, AND WE THOUGHT ABOUT WHAT COULD POSSIBLY BE AN ESCRO ROLE. BUT AS IT TURNS OUT, FROM AT LEAST OUR PERSPECTIVE, THERE'S NOT A GREAT ROLE FOR THE ESCRO TO PLAY. ALTHOUGH IT CAN SERVE AS A WONDERFUL RESOURCE FOR CONSULTATION, WHICH I THINK IS WHAT GEOFF WAS ALLUDING TO IN TERMS OF THE CALLS HE GETS. SO FOR IRB'S THAT ARE NOT WELL VERSED IN CELL THERAPEUTICS OR INSTITUTIONS THAT HAVEN'T DONE A LOT OF WORK IN THAT AREA, AND SO THEIR ESCRO'S WON'T HAVE MEMBERSHIP NECESSARILY THAT'S INVOLVED IN THAT AREA, IS ENSURING THAT THERE'S EXPERTISE AVAILABLE TO IRB'S TO HELP THEM EVALUATE THE RISKS AND BENEFITS OF PARTICIPATION AND DO THOSE KINDS OF THING.

THAT'S WHERE I THINK THE ALPHA STEM CELL CLINIC NETWORK CAN ALSO PLAY A CRUCIAL ROLE. IF YOU HAVE THREE INSTITUTIONS, ESSENTIALLY CITY OF HOPE, UC SAN DIEGO, UCLA WITH UCI, WE'VE BEEN IN THIS AREA FOR DECADES, AND THEN WE'LL CREATE A RESOURCE OF EXPERTS THAT ARE AVAILABLE TO OTHER INSTITUTIONS TO HELP THEM THROUGH THESE PROCESSES. I THINK THERE'S A LOT OF WAYS TO LOOK AT THIS AT WHICH THE TIMELINE

TO REVIEW MAY BE THE LEAST SIGNIFICANT; WHEREAS, THE MOST IMPORTANT IS MAKING SURE THAT THE REVIEW BOARDS THAT ARE REVIEWING THEM HAVE THE EXPERTISE AND THE KNOWLEDGE BASE TO ADEQUATELY ASSESS THEM. THAT'S WHAT'S GOING TO SLOW THE PROCESS DOWN BECAUSE WHEN YOU HAVE PEOPLE ON BOARDS WHO DON'T UNDERSTAND THE SCIENCE, WHO ARE NOT FAMILIAR WITH THE MEDICINE, WHO ARE GOING GET INVOLVED IN ISSUES AND START TO ASK QUESTIONS THAT ARE NOT ACTUALLY RELEVANT TO THE PROJECT, NO. 1.

NO. 2 IS MAKING SURE THAT THE INVESTIGATORS SUBMITTING THE PROJECT ARE WELL PREPARED TO SUBMIT THE PROJECTS.

AND, 3, MAKING SURE THAT YOU HAVE A SYSTEM IN PLACE THAT CAN MOVE THEM FORWARD IN THE BEST POSSIBLE WAY, ENSURING THE RIGHTS AND WELFARE OF THE SUBJECTS WHILE ALSO UNDERSTANDING THAT THESE PROJECTS HAVE A LIFE SPAN, AND THEY NEED TO BE MOVED FORWARD WHEN POSSIBLE AND WHEN APPROPRIATE.

CHAIRMAN LO: I'M GOING TO INTERVENE HERE TO TRY AND KEEP US ON TIME, AND TO THE EXTENT THAT EFFICIENCY IS A WATCH WORD. I'M GOING TO GIVE GEOFF LOMAX A CHANCE TO FINISH HIS PRESENTATION AND WE HAVE MORE TIME FOR DISCUSSION.

JUST TO BRACKET THE ISSUES JEFF BOTKIN

RAISED, IF CIRM'S ORGANIZATION IS DEDICATED TO GETTING WELL-DESIGNED CLINICAL TRIALS THAT ARE ETHICALLY SOUND FROM THE PROTOCOL INTO THE FIELD AS QUICKLY AS POSSIBLE, IRB'S ARE NOT NORMALLY TALKED ABOUT AS BEING ENGINES OF EFFICIENCY AND URGENCY. AND JEFF BOTKIN SORT OF UNDERLINED TWO ISSUES. ONE IS MULTISITE CLINICAL TRIALS GETTING TO THE STAGE WHERE WE AVOID DUPLICATIVE REVIEW.

I THINK A NUMBER OF PEOPLE ALSO RAISED THE QUESTION OF HOW DO YOU DO THE SCIENTIFIC PART OF THE VIEW, MAKING EXPERTISE AVAILABLE, FOR EXAMPLE. I WOULD JUST SAY THAT, GEOFF, THIS MAY BE SOMETHING YOU AS STAFF WANT TO KEEP AN EYE ON. AND AS A POSSIBLE POTENTIAL ROADBLOCK TO GETTING TRIALS INTO THE FIELD, YOU MAY WANT TO MONITOR THE CHALLENGES INVESTIGATORS ARE FACING WITH IRB'S AND BE PREPARED TO ADDRESS THOSE PROBLEMS, AND THEN COME BACK TO US AS WE NEED IT. BUT I THINK CLEARLY THIS IS AT LEAST A POTENTIAL ROADBLOCK THAT NEEDS TO BE LOOKED AT.

AND THERE ARE THINGS THAT YOU CAN DO, SUGGESTIONS ABOUT IDENTIFYING EXPERTS WHO COULD BE CONSULTANTS TO AN IRB THAT DOESN'T HAVE THE STEM CELL EXPERTISE, SORT OF INTRODUCING THEM TO SORT OF AN IRB NETWORK THAT THEY CAN DEFER THE LEAD AND THE REVIEW TO. THESE ARE ALL OPTIONS THAT PEOPLE HAVE

WORKED ON. THEY'RE NOT EASY TO PULL OFF. AND YOU CAN BUILD ON EXISTING COLLABORATIONS BETTER. IT'S SOMETHING YOU MAY WANT TO FLAG.

DR. MILLAN: I WON'T BELABOR. SO NOW WITH THE NETWORK IN PLACE, WE'RE ACTUALLY GOING TO BE -- THAT IS ONE OF THE GOALS, AND WE'LL BE ABLE TO TRACK IT. AND WE'LL BE TRACKING METRICS AND COMPARING IT TO WHAT THE TRADITIONAL ROUTE HAS BEEN FOR GETTING THESE TO REVIEW. AND WHEREVER THERE ARE STILL SOME ROADBLOCKS, ABSOLUTELY, TAKE YOUR POINT, THAT'S REALLY IMPORTANT FOR US TO CONTINUE TO KEEP TRACK OF AND ADAPT TO THAT.

CHAIRMAN LO: PROBLEM SOLVING. GEOFF.

DR. LOMAX: ONE LAST COMMENT THERE IS WE WERE DEBATING WHETHER TO PRESENT THE ALPHA CLINIC NETWORK TO YOU. WE FELT IT WAS A LITTLE BIT PREMATURE BECAUSE WE HAVEN'T REALLY COMPLETELY STARTED EVERYTHING, BUT WE LOOK FORWARD TO REALLY BEING ABLE TO BRING THAT BACK TO YOU. WE MAY ACTUALLY HAVE ISSUES TO DISCUSS WITH YOU BASED ON THAT EXPERIENCE.

I'M GOING TO MOVE ON. BETH, ARE YOU OKAY.

THE REPORTER: I'M FINE.

CHAIRMAN LO: SOME OF YOU ON THE PHONE, I THINK WE'RE PICKING UP SOME PAPER RUSTLING OR

SOMETHING. SO IF YOU CAN MUTE YOUR PHONES IF YOU'RE NOT SPEAKING, WE WON'T GET BACKGROUND NOISE.

I'M GOING TO ASK GEOFF TO GO AHEAD AND REALLY FOCUS ON ISSUES THAT HE THINKS ARE RIPE FOR US AS A GROUP TO CONSIDER TODAY AND PERHAPS WE REACH AGREEMENT AS JUSTIFYING SOME MODIFICATIONS TO THE CURRENT REGULATIONS.

DR. LOMAX: SO IN YOUR PACKET AND IN THE BRIEFING MATERIALS, YOU HAD THIS MEMO WHICH I HOPE WAS EFFECTIVE IN KIND OF LAYING OUT THREE LEVELS OF ISSUES WE'D LIKE YOU TO CONSIDER. AND SO THE IDEA IS WE CAN KIND OF GO THROUGH THEM STEPWISE ONE, TWO, THREE AND KIND OF DECIDE THEM IN THAT ORDER, WITH PERHAPS THREE NEEDING THE MOST DISCUSSION, AND HOPEFULLY ONE AND TWO NEEDING LESS DISCUSSION.

SO ONE OF THE FIRST THINGS WE WANTED TO DESCRIBE TO YOU ARE AMENDMENTS INTENDED TO ALIGN OUR MEDICAL AND ETHICAL STANDARDS REGULATION WITH OUR GRANTS ADMINISTRATION POLICY. I JUST WANT TO DEFER MY COLLEAGUE SCOTT TOCHER FOR A MINUTE TO GIVE YOU A QUICK DESCRIPTION OF WHAT OUR GRANTS ADMINISTRATION POLICY DOES AND HOW WE'RE CHANGING IT. GIVE A QUICK.

MR. TOCHER: YOU KNOW, OUR GRANTS ADMINISTRATION POLICY IS JUST AS IT SOUNDS. IT'S

THE ADMINISTRATIVE POLICY THAT GOVERNS OUR GRANT RECIPIENTS IN THE EXECUTION OF THEIR AWARDS AND THE PERMISSIBLE CONDUCT AND ACTIVITIES.

LARGELY, I THINK THAT IT IS, WITH RESPECT TO THE MEDICAL AND ETHICAL STANDARDS, A NONSUBSTANTIVE DOCUMENT. THE SUBSTANCE OF THE MEDICAL AND ETHICAL STANDARDS ARE INCORPORATED INTO THE REGULATIONS THEMSELVES. THE GAP HELPS IMPLEMENT THEM IN THE INTERFACE BETWEEN CIRM AND OUR GRANTEES. SO WE LARGELY USE THAT AS A WAY TO ALERT THE GRANTEE OF THEIR OBLIGATIONS AND PROVIDE ADMINISTRATIVE STEPS AS TO HOW THEY CAN SHOW CIRM THAT THEY ARE IN COMPLIANCE.

AS PART OF RANDY'S CIRM 2.0, ONE OF THE GOALS OF THE PROGRAM IS TO VASTLY SHORTEN THE AMOUNT OF TIME THAT IT TAKES ONCE A GRANTEE IS GIVEN AN AWARD BY THE ICOC TO THE DATE THAT ALL THE NECESSARY DOCUMENTATION IS SIGNED AND OUR NOTICE OF GRANT AWARD IS EXECUTED AND THE RESEARCH CAN BEGIN. THAT CAN TAKE AS LONG AS SIX AND EVEN NINE MONTHS IN SOME CASES. SO WE'D LIKE TO SHORTEN THAT TO ABOUT 45 DAYS.

SO PART OF THE ADMINISTRATIVE REVISIONS WILL BE IN SHORTENING THE TIME THAT IT TAKES FOR OUR GRANTEES TO SHOW THEIR COMPLIANCE WITH THESE MEDICAL

AND ETHICAL STANDARDS. SO THAT PROCESS IS IN PARALLEL WITH YOUR WORK HERE ON THE MEDICAL AND ETHICAL STANDARDS. SO ANY SUBSTANTIVE REVISIONS THAT YOU MAKE WE WILL HAVE OUR ADMINISTRATIVE PROCESS ALREADY BEGUN SO THAT WE CAN FOLD YOUR RECOMMENDATIONS INTO AN ONGOING PROCESS AND GET THEM EXECUTED QUICKLY.

CO-CHAIR LANSING: SO WE ALREADY HAVE THIS. SO WHAT IS IT, IF WE CAN JUST BE REALLY SPECIFIC BECAUSE I'VE READ THIS AND I'M A LITTLE CONFUSED. IN OTHER WORDS, ARE YOU ASKING US TO CHANGE THE REQUIREMENTS, OR ARE YOU ASKING US TO JUST DO IT SHORTER?

MR. TOCHER: WELL, GEOFF, YOUR COMMITTEE WILL ADDRESS THE REQUIREMENTS THEMSELVES, THE SUBSTANTIVE REQUIREMENTS. PARALLEL WE IN THE GAP, THAT'S NOT THE PURVIEW OF THIS COMMITTEE, WE IN THE GAP WILL BE LOOKING AT HOW CAN WE QUICKLY ENSURE THAT WE HAVE THE NECESSARY ASSURANCES THAT YOU HAVE REQUIRED.

CHAIRMAN LO: LET'S ASK GEOFF TO PICK THAT UP BECAUSE YOU ARE PROPOSING SOME MODIFICATIONS TO THE REGULATIONS.

DR. LOMAX: LET ME TRY TO TACKLE THAT BECAUSE PROCESS IS ALWAYS TRICKY. SO LET ME START

BY SAYING THE FIRST THING WE'RE ASKING YOU TO CONSIDER ARE THINGS -- SO LET ME GIVE YOU A CONCRETE JUST BY WAY OF EXAMPLE BECAUSE I THINK IT'S EASIER. SO IN THE MARKED-UP DOCUMENT WE CIRCULATED AS THE BRIEFING MATERIAL FOR THIS MEETING, ONE OF THE THINGS THEY'VE DONE IN THE GRANTS ADMINISTRATION POLICY IS CHANGED THE DEFINITION. WE USED TO SAY RESEARCH INSTITUTIONS. AND THEY'VE COME UP WITH A SHORTHAND. THEY HAVE A TERM "AWARDEE."

CHAIRMAN LO: THIS IS PAGE 2, LINE 41 IN THE GREEN HIGHLIGHTED.

DR. LOMAX: SO IN THE CASE OF THE SET OF CHANGES WE'RE PROPOSING THAT ARE ABOUT MAKING SURE THAT THE GRANTS ADMINISTRATION POLICY AND THE MEDICAL AND ETHICAL STANDARDS MATCH UP IS GETTING THE SAME WORDS ON PAPER. OTHERWISE WE DON'T GET PHONE CALLS, WELL, WHY DOES IT SAY THIS HERE AND THAT HERE?

CO-CHAIR LANSING: DO YOU WANT US TO CHANGE THE WORD FROM "GRANT INSTITUTIONS" TO "AWARDEES."

DR. LOMAX: WE'VE GIVEN YOU A SET OF EXAMPLES. I'LL ADD ANOTHER SLIDE ON THIS PARTICULAR TOPIC SO I CAN EXPAND ON SOME EXAMPLES. JUST FOCUSING ON THE FIRST LEVEL, IT'S THINGS THAT ARE

REALLY ABOUT MAKING THE TWO DOCUMENTS AS TIGHTLY COUPLED AS POSSIBLE.

DR. ROBERTS: BUT JUST IN TERMS OF THINGS LIKE WORDING, NOTHING SUBSTANTIVE IN TERMS OF NO. 1. IF GAP INCORPORATES THE MEDICAL AND ETHICAL STANDARDS, IT WOULDN'T MAKE SENSE TO SAY THAT THE MEDICAL AND ETHICAL STANDARDS SHOULD BE CHANGED TO FIT GAP. GAP FITS THE MEDICAL AND ETHICAL STANDARDS. AND THE CHANGES ARE JUST FOR NO. 1 IS JUST WORDING. NOTHING SUBSTANTIVE.

DR. LOMAX: CORRECT.

CO-CHAIR LANSING: THAT WAS WHAT I WAS ASKING. I'M NOT TRYING TO -- I'M JUST TRYING TO GET TO THE MEAT. I THINK WE ALL ARE UNITED IN WANTING TO, WHAT WE SAID IN THE BEGINNING, HAVE THE HIGHEST ETHICAL STANDARDS, BUT WE'RE NOT TRYING TO IN ANY WAY HAVE LANGUAGE IMPEDE US. I CAN ONLY SPEAK FOR MYSELF. I SEE THESE THREE THINGS ON PAGE 1 AND PAGE 2. THEY'RE A CHOICE OF WORDS, BUT THEY DON'T CHANGE ANYTHING THAT WE'VE DONE. I'M SURE WE'RE GOING TO GET TO SOMETHING THAT MAYBE WE SHOULD CONSIDER CHANGING; BUT IN ORDER TO GET THROUGH THIS, I CAN'T SEE ANY PROBLEM WITH SUBSTITUTING THE WORD "AWARDEE" FOR "INSTITUTION." IT SEEMS TO ME FINE. IT SEEMS TO ME A BROADER THING. I CAN'T SEE ADDING THE TERM

"HUMAN SUBJECTS RESEARCH" DOESN'T SEEM TO ME, IT SEEMS AGAIN BROADER, SO I DON'T KNOW.

AND THEN THE OTHER ONE IS JUST CONTINUING THAT. SO IF THAT'S WHAT YOU'RE ASKING FROM ONE, I THINK WE SHOULD MAKE SURE EVERYBODY ELSE IS COMFORTABLE, BUT IT DOESN'T SEEM LIKE A PROBLEM.

DR. LOMAX: AGAIN, PART OF THE REASON WE KIND OF GO THROUGH, I WOULD HOPE THEY ARE STRAIGHTFORWARD, AND I APPRECIATE THAT COMMENT.

CO-CHAIR LANSING: YOU'VE DONE ALL THE WORK FOR US, SO I'M VERY GRATEFUL.

DR. LOMAX: PART OF THE THINGS WE WANT TO DO IS HAVE A CLEAR RECORD FOR THE ADMINISTRATIVE PROCESS SO IF SOMEONE LOOKS BACK AT WHAT WE DID, IT WAS JUST CRYSTAL CLEAR.

CO-CHAIR LANSING: IT DOESN'T SAY THAT WE IN A WAY -- WHAT I'M VERY GRATEFUL TO YOU, AS ALWAYS, FOR YOU IS THAT YOU SEEM TO HAVE DONE THE WORK. YOU'RE BASICALLY SAYING THESE ARE THE THINGS THAT WE VIEW, AT LEAST IN ITEM ONE, AS A DISCONNECT AND ADDS TO CONFUSION FOR PEOPLE WHO ARE APPLYING. WHY IS IT HERE AND WHY ARE YOU SAYING THIS HERE AND WHY ARE YOU SAYING THAT HERE, AND IT SEEMS TO BE LANGUAGE. AND ACTUALLY I THINK YOUR LANGUAGE IS BROADER AND BETTER, BUT THAT'S JUST MY INITIAL

REACTION. IF YOU WANT TO KEEP GOING AND THEN WE COULD ACTUALLY TAKE A VOTE ON IT.

CHAIRMAN LO: SO I'D ACTUALLY SECOND SHERRY'S PERSPECTIVE. LET'S TRY AND LINK THE ACTUAL CHANGES TO THE BROAD NO. 1 YOU SKETCHED OUT IN YOUR SLIDE. SO SHERRY'S CALLED ATTENTION TO THE FIRST TWO BULLETS ON PAGE 1, BY ADDING THE TERM "HUMAN SUBJECTS RESEARCH" RATHER THAN REFERENCING THE COMMON RULE, SAYING AWARDEE.

COULD YOU JUST CLARIFY FOR ME ON PAGE 2 ALL THE THINGS IN THE GREEN ARE WHAT YOU'RE PROPOSING TO CHANGE UNDER THIS FIRST NO. 1? IS THAT THE COLOR CODED?

DR. LOMAX: I BELIEVE SO. LET ME JUST CHECK THAT ACTUALLY.

CHAIRMAN LO: SOME ARE JUST WORDS, BUT NO. 4 ON LINE 73 WAS DELETED ABOUT CONSCIENTIOUS OBJECTION.

DR. ROBERT TAYLOR: IT'S BEEN MOVED UP.

DR. LOMAX: SO LET ME SAY WHAT WE DID THERE. SO ORIGINALLY THE WAY THESE STANDARDS WERE WRITTEN, AND THESE ARE LITTLE THINGS THAT ACTUALLY ARE IMPORTANT, SO ORIGINALLY, IF YOU LOOK AT HOW IT'S BEEN MARKED UP, WE ORIGINALLY SAID THAT ANYONE WHO RECEIVES A CIRM GRANT NEEDS TO HAVE BASICALLY A

STEM CELL OVERSIGHT COMMITTEE. THAT'S NOW RESTRUCTURED TO ACKNOWLEDGE THE FACT THAT SOME OF OUR AWARDEES ACTUALLY AREN'T DOING ANYTHING THAT REQUIRES REVIEW AND APPROVAL BY A STEM CELL RESEARCH OVERSIGHT COMMITTEE. SO WHAT WE'VE ENDED UP DOING THERE IS BREAKING IT UP TO SAY EVERYONE IS RESPONSIBLE FOR ONE AND TWO. AND IN THE EVENT YOU'RE DOING SOME TYPE OF ACTIVITY THAT REQUIRES ADDITIONAL OVERSIGHT, PART B, YOU'RE THEN REQUIRED TO DO THOSE OTHER THINGS. SO THAT WAS, AGAIN, NONSUBSTANTIVE. WE JUST MOVED THE PARTS AROUND.

CHAIRMAN LO: SOMETHING VERY LITERAL, CONSISTENT WITH SHERRY. SO LINES 73 TO 80, WHICH IS THE DELETION MARKED IN GREEN, COULD YOU EXPLAIN?

DR. LOMAX: WE JUST MOVED IT UP TO LINE 54 TO 61.

CHAIRMAN LO: AND THEN, AGAIN, A VERY SIMPLISTIC QUESTION ABOUT LINES 82 TO 85. YOU DELETED THAT SECTION, SAYING IT'S NOW IN THE GRANTS ADMINISTRATION POLICY.

DR. LOMAX: THAT'S ACTUALLY KIND OF A NO. 2 ITEM, BUT I CAN HANDLE IT NOW IF YOU WANT.

CHAIRMAN LO: WHY DON'T YOU GO THROUGH NO. 2 BECAUSE I HAVE A QUESTION ON THAT.

MR. TOCHER: MAYBE IF YOU SKIPPED FORWARD

TWO SLIDES, YOU SORT OF HAVE A ROAD MAP OF WHAT YOU SEE AS YOUR CATEGORY ONE CHANGES, YOUR CATEGORY TWO CHANGES, AND YOUR CATEGORY THREE.

DR. LOMAX: ROB, DO YOU HAVE A QUESTION.

DR. ROBERT TAYLOR: I DO. I APOLOGIZE BECAUSE THIS IS EXTANT LANGUAGE THAT WAS IN THIS, BUT I JUST WANT TO POINT OUT A LITTLE BIT OF A SLIPPERY SLOPE IN THAT NEW PART 54 TO 61. I'VE BECOME SORT OF SENSITIZED TO THIS, I THINK, HAVING MOVED FROM MAYBE THE BAY AREA TO THE SOUTHEAST. BUT THIS CONSCIENTIOUS OBJECTION ISSUE CAN HAVE SOME PRETTY IMPORTANT IMPACTS ON HOW PATIENTS ACTUALLY LEARN ABOUT SOME OF THE OPPORTUNITIES THAT EXIST.

AND JUST TO GIVE YOU A SPECIFIC EXAMPLE THAT I'VE SEEN MUCH MORE OF NOW THAT I'M LIVING PERHAPS IN THE PART OF THE WORLD WHERE I AM IS THE CLINICAL PROVIDERS WHO DON'T GIVE VERY MUCH INFORMATION ABOUT FETAL ANOMALIES TO WOMEN IN WHICH THEY'RE DETECTED UNTIL AFTER THE TIME THAT THEY COULD LEGALLY ABORT THEIR PREGNANCIES. AND SO THE DELAY OR THE CONSCIENTIOUS OBJECTION THINGS CAN REALLY HAVE AN IMPACT ON THE OPTIONS THAT THOSE INDIVIDUALS HAVE.

AND I'M SORT OF SENSITIZED TO THIS. I DON'T KNOW. THIS IS PROBABLY GOVERNMENTAL FEDERAL

LANGUAGE THAT WE'RE NEVER GOING TO BE ABLE TO CHANGE, BUT I JUST WANT TO KIND OF POINT OUT THAT THIS IS THE KIND OF THING THAT --

DR. LOMAX: THIS IS WHY WE HAVE A COMMITTEE AND WHY WE BRING IN OUTSIDE PERSPECTIVES THAT WE DON'T HAVE. THAT'S NOT COME UP. IT'S CERTAINLY BEEN THE PURVIEW OF THIS WORKING GROUP TO RECOMMEND CHANGES. WE DIDN'T BRING THAT RECOMMENDATION TO YOU BECAUSE WE WEREN'T AWARE -- WE DIDN'T SEE THE NEED FOR IT. BUT CERTAINLY IF THAT IS SOMETHING THE WORKING GROUP CHOOSES TO TAKE UP, THAT'S WELL WITHIN YOUR PURVIEW, BUT I DEFER TO THE CHAIR.

DR. ROBERT TAYLOR: THAT'S A THREE-DAY DISCUSSION.

MS. ROBERTS: MAYBE WE SHOULD PUT IT ON THE AGENDA.

DR. ROBERT TAYLOR: I'M A BIG BELIEVER IN CONSCIENTIOUS OBJECTION, BUT I HAVE SORT OF SEEN KIND OF THE DARK SIDE OF THIS.

CHAIRMAN LO: WE'VE SEEN JUST RECENTLY SPLASHED IN THE HEADLINE NEWS STATES PASSING LEGISLATION OR PROPOSING LEGISLATION TO TRY AND STRIKE SOME SORT OF BALANCE BETWEEN CONSCIENTIOUS OBJECTION AND ANTI-DISCRIMINATION. AND AS I READ

IT, DOROTHY, I'LL DEFER TO YOU, THIS IS YOUR FIELD, NO. 4 THAT'S BEEN MOVED TO LINES 73 TO 80, WHICH ROB CALLED ATTENTION TO, AS I READ IT, THAT SAYS THAT CONSCIENTIOUS OBJECTION ONLY APPLIES TO THE DONATION OF GAMETES AND EMBRYOS FOR RESEARCH. AND AS I READ THAT, BUT HELP ME OUT, IT DOESN'T EXTEND TO THE CARE OF THE DONOR AND RECIPIENT FOR DONATION FOR RESEARCH, BUT IT DOESN'T SAY ANYTHING ABOUT CONSCIENTIOUS OBJECTION TO INFORM A POTENTIAL PARTICIPANT IN A CLINICAL TRIAL THE RIGHT OF HEALTHCARE PROVIDER TO OPT OUT OF MENTIONING IT OR WHATEVER.

AND DOES THAT SILENCE SOMETHING WE WANT TO JUST MAINTAIN THERE? AGAIN, IT'S A QUESTION OF YOU WANT TO RESPECT CONSCIENTIOUS OBJECTION, BUT ALSO SAY YOU DON'T WANT TO NECESSARILY DEPRIVE A PATIENT OF INFORMATION ABOUT A CLINICAL TRIAL THEY MAY INTERESTED IN. SO THIS SEEMS TO ME IN THIS YEAR AND THIS MONTH IN PARTICULAR TO RAISE THE WHOLE SET OF ISSUES. I JUST WANT TO -- I KNOW GEOFF HAD JUST WANTED TO SORT OF MOVE IT UP, BUT IT SEEMS LIKE THIS MAY ACTUALLY RAISE A HOST OF OTHER ISSUES.

DR. ROBERTS: I THINK IT POSSIBLY COULD. IT DEPENDS ON HOW THAT LANGUAGE IS READ, WHETHER IT'S READ AS ONLY APPLYING TO THAT PARTICULAR

INSTANCE THAT'S MENTIONED AND, THEREFORE, NOT ANY OTHER, OR WHETHER IT'S IMPORTANT TO AFFIRMATIVELY SAY THIS WOULD NOT -- THIS DOES NOT ALLOW FOR FAILING TO. WE CAN PROBABLY COME UP WITH BETTER LANGUAGE, BUT THE IDEA THAT WE'D NOT ALLOW FAILING TO INFORM PATIENTS.

DR. PETERS: WITHHOLDING.

DR. ROBERTS: WITHHOLDING THE INFORMATION. IT MAY BE SOMETHING WE WANT TO CONSIDER IN MORE DEPTH.

CHAIRMAN LO: WE COULD FLAG THIS AS SOMETHING TO COME BACK TO.

DR. ROBERTS: THAT'S WHAT I WOULD RECOMMEND. I THINK TO THINK ABOUT NOW THE IMPLICATIONS OF IT AND WHAT THIS LANGUAGE MEANS, HOW IY MIGHT BE INTERPRETED IN FIVE MINUTES MAY NOT BE ENOUGH TIME TO DO IT.

CHAIRMAN LO: AGAIN, THIS IS SOMETHING THAT MEANS SOMETHING A LITTLE DIFFERENT IN 2015.

DR. ROBERTS: I AGREE.

CHAIRMAN LO: GEOFF JUST WANTS TO MOVE IT FROM LINE 73 UP TO 54.

DR. ROBERTS: THAT'S OKAY FOR NOW.

DR. ROBERT TAYLOR: JUST SORT OF BROUGHT ATTENTION.

DR. LOMAX: AS A REMINDER, THE GENESIS OF THIS STATEMENT IS THE NATIONAL ACADEMIES' GUIDELINES, AND THAT COMMITTEE HAS NOT -- THAT COMMITTEE DISBANDED IN 2010. SO I THINK WE ARE IN A UNIQUE POSITION OF BEING ONE OF THE ONLY GROUPS THAT'S CONTINUING TO REEVALUATE THAT DOCUMENT AND THAT SET OF RECOMMENDATIONS THAT HAS NATIONAL IMPLICATIONS. EVERYONE IN THE STEM CELL SPACE MORE OR LESS ADOPTS THOSE GUIDELINES. SO IT'S AN IMPORTANT ISSUE. AND WHAT YOU ALL THINK ON THESE ISSUES IS -- YOU'RE THE ONLY GROUP THAT I'M AWARE OF THAT'S REALLY HAVING THESE KINDS OF DELIBERATIONS. IF YOU THINK IT'S IMPORTANT, THEN PERHAPS IT'S IMPORTANT, AND WE CAN DEFINITELY COME BACK TO IT.

CHAIRMAN LO: MY SENSE OF THE COMMITTEE, TELL ME IF I'M WRONG, IS THAT TODAY WE'D LIKE TO JUST ADDRESS THE TECHNICALLY NO. 1, AND THIS WILL ASTERISK AS SOMETHING WE DON'T WANT TO TRY AND DECIDE IN FIVE MINUTES TODAY.

SO LET ME JUST, AGAIN, FOR THE SAKE OF EFFICIENCY, IF YOU COULD PUT THE SLIDE UP THAT SCOTT REFERRED US TO THAT HIGHLIGHTS, NOT THIS ONE, THE NEXT TWO, THAT HIGHLIGHTS WHAT GOES WITH THE FIRST BULLET.

DR. LOMAX: THIS IS THE --

CHAIRMAN LO: WE'VE GONE THROUGH THE THREE GREENLINE CHANGES THAT FALL UNDER THE FIRST BULLET. AND I GUESS I JUST WANT TO MAKE SURE IS THERE ANY FURTHER QUESTION OR DISCUSSION BY THE COMMITTEE OF THOSE THREE BULLET CHANGES, WHICH ARE JUST TO ALIGN THE REGULATIONS WITH CIRM'S 2.0 GRANTS ADMINISTRATION POLICY?

DR. BOTKIN: COULD YOU STATE THE FUNCTION OF MOVING THAT PARAGRAPH FROM THE CURRENT LOCATION TO THE NEW LOCATION? WHAT'S THE EFFECT OF THAT MOVE?

DR. LOMAX: SO WHAT WE WERE -- ORIGINALLY IT WAS A GENERAL REQUIREMENT THAT THE NATIONAL ACADEMIES THOUGHT SHOULD APPLY TO ANYONE WORKING IN THIS FIELD. SO THE EFFECT OF MOVING IT UP, AGAIN, THE FIRST TWO, SO (A)(1) AND (A)(2) ARE PROVISIONS THAT WOULD APPLY TO ANY AWARDEE, ANY CIRM AWARDEE, IRREGARDLESS OF WHETHER THEY'RE DOING HUMAN SUBJECTS RESEARCH OR RESEARCH THAT REQUIRED REVIEW BY AN OVERSIGHT COMMITTEE. WHAT WE'RE DOING IS WE'RE SEPARATING THE SET OF REQUIREMENTS THAT ARE GENERAL TO EVERYONE TO THOSE SET OF REQUIREMENTS THAT ARE SPECIFIC TO INSTITUTIONS WHERE YOU NEED IRB OR SCRO REVIEW.

DR. BOTKIN: SO IT ORIGINALLY WAS INTENDED

TO BE UNIVERSAL, BUT PERHAPS THIS MOVE MAKES IT CLEAR THAT IT'S UNIVERSAL FOR ALL AWARDEES.

DR. LOMAX: IT'S THE OPPOSITE ACTUALLY. INITIALLY EVERYTHING WAS UNIVERSAL EVEN IF YOU DIDN'T FALL INTO THAT CATEGORY, SPECIFICALLY DOING HUMAN SUBJECTS RESEARCH OR SOMETHING THAT REQUIRED SCRO REVIEW. SO THAT COULD BE A PROBLEM IF YOU DIDN'T HAVE AN IRB OR A SCRO, BUT YOU WEREN'T DOING ANYTHING.

CHAIRMAN LO: AT THE RISK OF FOULING UP EVERYTHING, GEOFF, IT SEEMS TO ME IF YOU'RE HAVING A PROJECT WHERE YOU'RE PROVIDING DONORS INFORMATION OR GETTING THEIR CONSENT FOR RESEARCH USE OF GAMETES OR EMBRYOS, DOESN'T THAT PUT YOU ONTO HUMAN SUBJECTS RESEARCH? IF YOU'RE NOT DOING THAT, YOU'RE NOT DOING HUMAN SUBJECTS RESEARCH, I'M NOT SURE WHY IT'S NO LONGER REQUIRED TO HAVE A POLICY ON CONSCIENTIOUS OBJECTION OR CONSENT IF YOU'RE NOT DOING CONSENT AND JUST USING A CIRM-APPROVED STEM CELL LINE. AGAIN, I JUST MAY BE VERY DENSE.

DR. LOMAX: POINT WELL TAKEN. BECAUSE THEY'RE NESTED REQUIREMENTS, YOU DON'T GET OUT OF IT. SO IT'S SORT OF -- IN THE END (A)(1) AND (A)(2) APPLY TO EVERYONE. AND THEN IF YOU FALL INTO THAT B CATEGORY, YOU STILL GET IT LATER.

CHAIRMAN LO: NO. NO. I'M SAYING THE OTHER WAY AROUND. I'M NOT GETTING INVOLVED WITH DONATION OF EMBRYOS OR GAMETES. WHY SHOULD NO. 2, LINE 54 APPLY TO ME?

DR. LOMAX: IT ACTUALLY GOES BACK TO DOROTHY'S POINT. WE'RE TRYING TO AVOID CHANGING AND MAKING ANY SUBSTANTIVE CHANGE TO POLICY. IN MY VIEW THAT WAS THE BEST WAY TO AVOID CHANGING ANYTHING. WE'RE ONLY TRYING TO CHANGE --

DR. ROBERT TAYLOR: ORIGINALLY IT WAS DOWN BELOW. I'M KIND OF FOLLOWING BERNIE'S LOGIC HERE, I THINK.

CHAIRMAN LO: THAT CLAUSE WE'RE MOVING AROUND SEEMS TO ME ONLY APPLIES IF YOU'RE DOING HUMAN SUBJECTS RESEARCH. THE FACT THAT YOU'RE GETTING CONSENT FOR DONATIONS MAKES IT HUMAN SUBJECTS RESEARCH. AND I CAN IMAGINE INSTITUTIONS THAT DON'T GET INVOLVED IN CONSENT, AND THEN YOU MAY BE SLIPPING UP INTO LINE 54 A REQUIREMENT ON THEM THAT THEY'LL SAY, HEY, THAT JUST DOES NOT APPLY TO ME.

DR. LOMAX: OKAY. IF THE SENSE IS THAT'S THE BEST PLACE FOR IT TO BE, I THINK THAT'S A FAIR POINT. WE CAN MOVE IT BACK DOWN.

CHAIRMAN LO: I'M IN THE FIELD OF PAT

TAYLOR AND DOROTHY ROBERTS. I SEE YOUR INTENT. I'M JUST WONDERING.

DR. LOMAX: I THINK IT'S FINE EITHER WAY. AND IF IT APPEARS MORE INTERNALLY CONSISTENT TO HAVE IT UNDER B, WE CAN MOVE IT BACK. THE POINT BEING IS THAT CLAUSE WOULDN'T -- IS STILL GOING TO BE PART OF THE REQUIREMENT SOMEPLACE.

DR. ROBERTS: I HEAR BERNIE'S POINT, THOUGH, THAT WHERE IT IS NOW IT'S CLEAR IT ONLY APPLIES TO AWARDEES CONDUCTING HUMAN SUBJECTS RESEARCH. OTHERWISE, THEY WOULDN'T NEED TO HAVE THIS. AND SO NOW IT SEEMS AS IF YOU'RE REQUIRING RESEARCHERS WHO AREN'T ENGAGED IN HUMAN SUBJECTS RESEARCH TO HAVE A POLICY ABOUT CONSCIENTIOUS OBJECTION THAT WOULDN'T APPLY TO THEM. SO IT'S LIKE AN UNNECESSARY ADDED REQUIREMENT. IS THAT RIGHT, BERNIE?

DR. BOTKIN: WHAT I'M HEARING IS PERHAPS EVEN A LITTLE BIT MORE BROADLY A PROBLEM. IF YOU'RE AN AWARDEE BY VIRTUE OF BEING A CLINICAL SITE FOR A NEW CELL THERAPY FUNDED BY CIRM, DOESN'T HAVE ANYTHING TO DO WITH DONORS AT ALL, AND SO SHOULD YOU HAVE TO HAVE AN INSTITUTIONAL POLICY ABOUT CONSCIENTIOUS OBJECTION OR NOT? IF YOU DON'T HAVE ONE, DOES THAT PRECLUDE YOUR ACCEPTING CIRM FUNDING

FOR YOUR CLINICAL TRIAL?

DR. ROBERT TAYLOR: I SEE THAT.

DR. LOMAX: SO WE LEAVE IT WHERE IT IS. THIS IS WHY WE HAVE A SMART COMMITTEE.

DR. ROBERTS: I'M JUST TRYING TO THINK WAS THERE ANY REASON FOR MOVING IT THAT NOW WE STILL WANT TO TAKE INTO ACCOUNT DESPITE THIS PROBLEM.

DR. BOTKIN: IT SEEMS YOU WANT A DIFFERENT CATEGORY THAT SAYS FUNDED INSTITUTIONS THAT ARE ACQUIRING EMBRYONIC STEM CELLS, THEY OUGHT TO HAVE A -- OF COURSE, WE CAN TALK ABOUT THAT AS A SEPARATE ISSUE, BUT CONSISTENT WITH THIS DOCUMENT, THAT WOULD BE THE SUBSET OF INSTITUTIONS YOU'D REALLY BE WORRIED ABOUT.

CHAIRMAN LO: JEFF BOTKIN'S POINTS UNDER B, IF I'M DOING HUMAN SUBJECTS RESEARCH BUT NOT OBTAINING CONSENT FOR DONATION OF GAMETES OR EMBRYOS, DO I REALLY NEED TO HAVE A POLICY ABOUT CONSCIENTIOUS OBJECTION, THAT TYPE OF RESEARCH I'M NOT DOING?

IN THE SPIRIT OF DON'T PUT IN REQUIREMENTS THAT DON'T SEEM TO APPLY TO THE WORK AN INSTITUTION IS DOING, WE MAY WANT TO SORT OF NARROW DOWN THE SCOPE OF INSTITUTIONS TO PEOPLE DOING THE TYPE OF RESEARCH WHERE THE CLAUSE REALLY PERTAINS TO WHAT

THEY'RE DOING.

DR. ROBERTS: THAT WOULD BE A C.

DR. BLEDSOE: IT MIGHT BE CLEANER THAT WAY, I THINK.

CHAIRMAN LO: PAT, LET ME GET YOU ON THE RECORD HERE BECAUSE THIS IS YOUR BREAD AND BUTTER.

DR. PATRICK TAYLOR: C IS FINE.

DR. LOMAX: SO IF I UNDERSTAND THE COMMENT, THAT'S RIGHT, C IS FINE. SO IT WOULD BE HUMAN SUBJECTS RESEARCH AND PROCUREMENT OF GAMETES AND EMBRYOS.

CHAIRMAN LO: SORRY I DIDN'T CATCH THAT BEFORE.

DR. LOMAX: THANK YOU. THIS IS WHY WE LIKE TO GET PEOPLE'S BRAINS AROUND THIS.

CHAIRMAN LO: NO. 2, AMENDMENTS INTENDED TO MAKE THE REGULATION SHORTER AND CLEARER AND EASIER TO IMPLEMENT. LET'S ASK GEOFF TO MOVE ON TO THOSE.

DR. LOMAX: SO THE FIRST ONE IS ON PAGE 2, IT WAS BERNIE'S QUESTION EARLIER, LINES 82 TO 107. SO THIS SECTION IS IDENTICAL TO THE COMPLIANCE REQUIREMENTS IN THE GRANTS ADMINISTRATION POLICY. SO WHAT WE CAN SIMPLY DO IS JUST CITE OUR GRANTS ADMINISTRATION POLICY.

CO-CHAIR: THAT MAKES SENSE.

DR. BLEDSOE: IT SEEMS THIS IS MORE ABOUT IMPLEMENTATION.

DR. LOMAX: IT'S IMPLEMENTATION. SO THAT ONE HOPEFULLY IS FAIRLY STRAIGHTFORWARD.

AND THE SECOND ONE ON PAGE 7, THE SECOND MAJOR CHANGE IN THIS CATEGORY, COMPLIANCE. FETAL TISSUE. SO WHAT WE ENDED UP DOING WHEN WE ADOPTED OUR POLICY ON FETAL TISSUE USE IS WE RESTATED A FEDERAL REQUIREMENT. AND, AGAIN, HERE WHAT WE WOULD PROPOSE DOING IS, RATHER THAN RESTATING IT, IS TO, AGAIN, JUST REFERENCE IT. AND THAT'S THE PUBLIC LAW WE'RE CITING. SO, AGAIN, I DON'T KNOW IF THERE'S ANY QUESTIONS THERE.

CO-CHAIR LANSING: NONE OF THESE ARE CHANGING WHAT WE AGREED TO. THEY'RE REALLY JUST MAKING IT CLEARER IN THEIR LANGUAGE.

DR. LOMAX: I THINK THE CATEGORY 2 -- THE CATEGORY 1, IT WAS USEFUL TO HAVE THE DISCUSSION.

CO-CHAIR LANSING: ABSOLUTELY. I'M NOT TRYING TO SHORTEN IT. I'M JUST TRYING TO CLARIFY.

DR. PATRICK TAYLOR: THERE'S ONE THING THAT'S IN HERE THAT'S GOING ON IN THE FIRST ONE THAT NEEDS TO BE CLEAR. IN ORDER TO AMEND YOUR REGULATION, YOU WANT US TO GIVE SOME COMMENTS TODAY.

SO INFORMAL. (INAUDIBLE.)

DR. LOMAX: WHY DON'T I JUST QUICKLY SHOW YOU BECAUSE YOUR QUESTION IS WHAT'S THE AMENDMENT PROCESS. BOTH THIS DOCUMENT AND THE GRANTS ADMINISTRATION POLICY ARE GOING THROUGH A PROCESS. AND LIKE ANYTHING, IT'S A PROCESS. SO YOU'RE CONSIDERING SOME CHANGES. AND THEN WE WOULD TAKE THOSE CHANGES TO OUR BOARD, SO THERE'S OPPORTUNITY THERE FOR FURTHER DISCUSSION AND COMMENT. AND THEN THEY GO TO THE OFFICE OF ADMINISTRATIVE LAW, WHICH IS THE AGENCY THAT REGULATES THE PRODUCTION OF REGULATIONS. AND THEY MANDATE A PROCESS WHERE WE HAVE TO RECEIVE PUBLIC COMMENT, PUBLIC REVIEW.

NOW, BASED ON WHAT WE GET BACK, WE COULD COME BACK TO YOU AND SAY, OKAY, HERE'S WHAT WE HEARD, HERE ARE THE ISSUES, AND THEY'RE SUBSTANTIVE, AND SO HELP US OUT HERE. SO, FOR EXAMPLE, THE LAST SET OF AMENDMENTS, WE RECEIVED NO SUBSTANTIVE PUBLIC COMMENT. SO WE STILL HAD TO TAKE THEM BACK TO THE BOARD FOR APPROVAL. AND THEN THE OFFICE OF ADMINISTRATIVE LAW WILL AGAIN LOOK AT THAT FINAL PACKAGE, WHICH SCOTT PUTS TOGETHER, AND SAY, OKAY, THIS IS OKAY.

DR. PATRICK TAYLOR: SO MY BASIC QUESTON IS QUESTION IS WHETHER OR NOT THE AMENDMENT TO THIS

GRANTS POLICY, THE MANUAL THING, REQUIRES A LITTLE BIT OF A RULE CHANGE. THE ANSWER SEEMS TO BE IT DEPENDS ON THE ANSWER GIVEN BY THE OFFICE ABOUT THIS. IT'S SORT OF A HYPOTHETICAL. SO SUPPOSE THAT YOU DECIDED TO ACTUALLY TO SEE SOMEONE'S FIRST-BORN CHILD. I'VE BEEN THINKING ABOUT THIS FOR A LONG TIME. YOU SAID YOU CAN DO THAT. IT'S IN THE MANUAL. IF IT'S DONE THE NIH WAY, IT'S IN THE MANUAL. (INAUDIBLE.) COMMENTS RETURNED, NOTHING. (INAUDIBLE), IT'S OBVIOUSLY A VERY DIFFERENT AND FORMAL PROCESS, ACCOUNTABILITY.

DR. LOMAX: I THINK IF I UNDERSTAND THE QUESTION, IT'S DOES THE OAL EVALUATE THE PROPOSED CHANGES ON A SUBSTANTIVE LEVEL?

DR. PATRICK TAYLOR: PROCESS LEVEL.

DR. LOMAX: THEY'RE CONCERNED WITH PROCESS. THEY'RE ALL ABOUT PROCESS.

MR. TOCHER: CORRECT. THEY'LL LOOK AT THE SUBSTANCE OF IT JUST FOR INTERNAL CLARITY TO MAKE SURE THERE AREN'T SOME SORT OF ERRORS AND INCONSISTENCIES, BUT THEY DON'T EXAMINE FOR THE SUBSTANCE OF THE RULES THEMSELVES.

DR. PATRICK TAYLOR: MAYBE I'M NOT BEING CLEAR. MY REAL QUESTION IS WHETHER OR NOT BY INSERTING THIS TO COMPLY WITH THE MANUAL AS OPPOSED

TO THE SECTIONS THAT DEAL WITH CIRM'S POWER TO DO BAD THINGS, WHETHER OR NOT TO MAKE THAT CHANGE IN THE FUTURE, USE OF THE (INAUDIBLE), AS A RESULT OF THIS PROPOSED CHANGE THAT'S APPROVED, GEOFF, YOU JUST AMEND THE MANUAL AS AN ADMINISTRATIVE MATTER. IT GOES BACK TO THE QUESTION OF WHETHER OR NOT THE PUBLIC REVIEW AND COMMENT IS THE SAME FOR BOTH THE MANUAL AND FOR REGULATIONS. IF IT ISN'T --

MR. TOCHER: I THINK I UNDERSTAND. SO YOUR QUESTION IS SINCE THIS IS GOING TO BE PART OF THE ADMINISTRATIVE MANUAL, ARE THOSE AMENDMENTS AND THOSE CHANGES SUBJECT TO THE SAME PROCESS OF PUBLIC COMMENT AND REVIEW? AND THE ANSWER IS YES.

DR. ROBERTS: YES.

DR. LOMAX: THEY'RE MOVING FROM ICOC APPROVAL TO REVIEW AND COMMENT. SO THEY'RE A LITTLE BET AHEAD OF THIS PROCESS.

CO-CHAIR LANSING: ALL WE'RE DOING IS MAKING RECOMMENDATIONS TO THE BOARD, AND THEN IT HAS TO GO THROUGH THIS WHOLE PROCESS.

DR. ROBERTS: I DON'T KNOW IF THIS IS EXACTLY YOUR POINT, BUT IT REMINDS ME OF THIS POINT, THAT IF THIS SECTION OF THE ETHICS STANDARDS REFERS TO THE GAP, IF THE GAP CHANGES IN THE FUTURE, THIS WILL STILL REFER TO THOSE CHANGES. SO IF IT WOULD

HAVE TAKEN MORE TO CHANGE THE ETHICS STANDARDS THAN IT WOULD TO CHANGE THE GAP, WE ARE EFFECTIVELY GIVING OVER THE REVIEW OF THE ETHICS STANDARDS TO THE PERHAPS LESSER REVIEW OF THE GAP. YOU SEE WHAT I'M SAYING? I DON'T KNOW IF THAT'S TRUE OR NOT. I JUST SAYING THAT'S AN ISSUE. IT'S NOT JUST THE SAME I THINK, SHERRY, AS SAYING WE ARE JUST REFERRING TO THE GAP. IT'S IF THE GAP COULD BE MODIFIED, AND THEN WE WOULD HAVE THIS REFERENCE.

CO-CHAIR LANSING: WE'D HAVE TO SAY THE GAP AS DATED. YOU HAVE TO GIVE A TIME.

DR. ROBERTS: THAT MAY NOT BE A REAL ISSUE. I DON'T KNOW.

CO-CHAIR LANSING: I HEAR WHAT YOU ARE SAYING. I'M SAYING YOU HAVE TO DATE IT. YOU HAVE TO SAY AS OF THE CURRENT GAP AND SUCH AND SUCH A DATE.

MR. TOCHER: HISTORICALLY THIS LANGUAGE, I THINK THE ATTEMPT HAS ALWAYS BEEN WHETHER IT'S THE COMPLIANCE WITH YOUR STANDARDS REGULATIONS OR WHETHER IT'S COMPLIANCE WITH OUR INTELLECTUAL PROPERTY REGULATIONS, WHETHER IT'S COMPLIANCE WITH OTHER ASPECTS OF THE GAP, THE GRANTS ADMINISTRATION POLICY SETS FORTH ALREADY A SET OF CONSEQUENCES THAT MAY FLOW FROM FAILURE TO ABIDE BY ANY OF THOSE

RULES. AND THOSE CONSEQUENCES ARE ALL PART OF THE REVIEW PROCESS, THE PUBLIC COMMENT PROCESS, THE EXAMINATION BY OUR BOARD. SO IT'S REALLY JUST, INSTEAD OF HAVING THE SAME CONSEQUENCES REITERATED IN VARIOUS DIFFERENT PLACES, IT'S JUST TO PUT IT ALL IN ONE PLACE.

DR. ROBERTS: I UNDERSTAND THAT. BUT MY POINT IS WHAT IF THE GAP -- ONE OF THESE CONSEQUENCES IS MODIFIED IN THE GAP? THEN THE MEDICAL AND ETHICAL STANDARDS WILL AUTOMATICALLY BE MODIFIED.

CO-CHAIR LANSING: I UNDERSTAND. THIS IS AN EASY THING TO SOLVE.

DR. ROBERTS: PUT THE DATE, AS OF TODAY.

CO-CHAIR LANSING: YOU JUST HAVE TO SAY WE ARE APPROVING THIS ALIGNMENT, THE GAP IS DATED X, AND WE ARE ALIGNING WITH IT AS OF THAT DATE, AND ANY CHANGES WE WILL HAVE TO EVALUATE. IN OTHER WORDS, YOU JUST MAKE IT FOR THE CURRENT DATE OF THE GAP. I THINK THAT'S FAIR ACTUALLY. I DON'T THINK ANYONE -- RANDY, YOU'RE AGREEING. IF YOU MAKE SOME RADICAL CHANGE, WE HAVE ANOTHER MEETING. WE'RE USED TO THIS.

DR. MILLS: THE POINT IS IF THERE ENDS UP NEEDING TO BE A CHANGE IN THE GAP, THAT WE EXPLAIN

IT TO THIS GROUP TOO AND MAY ADOPT IT AS WELL.

CO-CHAIR LANSING: EXACTLY. AND THEN WE WILL DECIDE WHETHER TO AGREE. THIS IS THE CONSTANT PROCESS. WE NEVER EXPECTED THESE RULES TO LAST FOREVER BECAUSE THE SCIENCE IS CHANGING.

DR. MILLS: BUT IF YOU DON'T DO IT, I THINK THE POINT IS IF YOU DON'T DO IT, THEN YOU'RE ASSIGNING YOUR OVERSIGHT TO THE GAP. AND THEN YOU'RE HOPING LIKE THAT JUST WORKS.

CO-CHAIR LANSING: WE DON'T WANT TO. SO I THINK, SCOTT, WHAT YOU'RE SAYING IS WE'RE HAPPY WITH THIS AS OF THE GAP RULES DATED TODAY AND WE WILL EVALUATE IT LATER. I THINK THAT'S A VERY GOOD POINT THAT BOTH OF YOU BROUGHT UP.

DR. PATRICK TAYLOR: OR YOU COULD JUST NOT CHANGE THE GAP (INAUDIBLE). THAT'S POSSIBLE TOO.

DR. LOMAX: ACTUALLY WHERE THIS IS MORE IMPORTANT IS ON THE FEDERAL, WHEN WE'RE CITING FEDERAL POLICY, WHICH WE DO CITE TO A DATE. EVEN IF THE FEDERAL POLICY CHANGES, WE'RE PEGGING OURSELVES TO A POLICY AT A POINT IN TIME. ON THE SECOND ONE, THAT'S A -- I THINK FROM OUR PERSPECTIVE PERHAPS MOST IMPORTANT IS WE'RE NOT LETTING FEDERAL POLICY TRUMP OUR REQUIREMENTS.

SCOTT, IS THAT WORKABLE PROCEDURALLY?

THAT'S A FINE RECOMMENDATION. THANK YOU FOR THAT.

CHAIRMAN LO: THANK YOU. GOOD CLARIFICATION.

DR. LOMAX: SO THERE ARE A FEW OTHER AREAS WHERE, AGAIN, ON THIS -- AGAIN, I HOPE WE HAVEN'T CHANGED ANYTHING, BUT JUST TO GET YOUR EYES ON IT BECAUSE WE'VE ALREADY FOUND THAT YOU ARE PICKING UP THINGS THAT WE MISSED, IN SOME AREAS WE CHANGED TO HUMAN SUBJECTS RESEARCH AND REFERRED TO THE DEFINITION OF HUMAN SUBJECTS RESEARCH. FOR EXAMPLE, ON PAGE 3, THERE'S LINE 107.

SO WHAT WE'RE TRYING TO DO IN SOME PLACES IS JUST SHORTEN UP, PUT THAT IN AS DEFINITIONS AND KEEP RESTATING OUR REFERENCE TO THE FEDERAL REGULATIONS, AND WE'VE MOVED THAT INTO DEFINITION. AND SO I HOPE --

DR. ROBERT TAYLOR: IF I COULD ASK, LOOKS LIKE YOU'RE KIND OF REMOVING CIRM-FUNDED. IS THIS IN ANTICIPATION THAT THERE WOULD BE OTHER SORT OF ORGANIZATIONS THAT MIGHT BE PARTNERS OR INDEPENDENT PARTNERS THAT THESE RULES WOULD APPLY FOR? I'M JUST KIND OF CURIOUS.

DR. LOMAX: NOT REALLY. IT'S ACTUALLY IF YOU LOOK IN THE SCOPE SECTION, SECTION 1010, IT'S ALREADY PART OF THE SCOPE OF THE REGULATION. EVERY

TIME WE SAY CIRM-FUNDED, AGAIN, WE'RE JUST KIND OF -- I THINK WE ORIGINALLY DID IT BECAUSE WE THOUGHT IT WOULD BE CLEAR, BUT IT DOESN'T ADD UP. SCOPE OF THESE REGULATIONS, THAT CONCEPT IS CAPTURED IN THE SCOPE.

CHAIRMAN LO: LET ME JUST ASK A QUESTION THEN ON PAGE 4, LINE 63 AND 96. UNLIKE THE OTHER A, B, C, D, WE ACTUALLY INSERT EXPLICITLY CIRM-FUNDED HERE WHERE WE'VE TAKEN AWAY FROM D, C, B, AND A. SO I WASN'T CLEAR ON THE REASONS FOR THAT.

DR. LOMAX: SO 63 IS ACTUALLY WHAT WE WANT TO DISCUSS WITH YOU BECAUSE JUST HIGHLIGHTING THAT'S THE BIGGER POLICY DISCUSSION. THAT'S CATEGORY 3.

CHAIRMAN LO: I'M JUST LOOKING AT THE CIRM-FUNDED, THE FIRST TWO WORDS, TO PICK UP ON ROB TAYLOR'S POINT. IF IT'S ALL SUBSUMED --

DR. ROBERT TAYLOR: THIS IS RALPH WALDO EMERSON ACTUALLY.

CHAIRMAN LO: WE SHOULD MAKE THEM ALL CONSISTENT.

DR. LOMAX: YES, WE WILL. THAT'S OUR GOAL. THE ONLY QUESTION I HAVE, IN SOME CASES THERE MAY BE AN ODD TERM HERE OR THERE IN SECTIONS WE HAVEN'T PROPOSED AMENDING. AND SIMPLY TO AMEND -- OPEN UP A WHOLE SECTION OF REGULATIONS JUST TO MAKE

THAT CHANGE, I DON'T KNOW IF IT'S WORTH IT. SO I KIND OF DEFER TO SCOTT ON THAT.

MR. TOCHER: I SEE. I THINK WHAT YOU WERE DOING IS YOU WERE HIGHLIGHTING THOSE SEPARATELY AS IF NONE OF THE CHANGES, NONE OF THE OTHER CHANGES WERE MADE, JUST THESE WERE CONSIDERED, WOULD YOU EVEN WANT TO BOTHER. BUT TRUST THAT WE WILL HARMONIZE THE DOCUMENT SO THAT ANY DUPLICATIVE, REDUNDANT LANGUAGE IS ENTERED.

CHAIRMAN LO: WE'RE REALLY GETTING PICKY, BUT WE'RE PRECISE PEOPLE.

DR. LOMAX: JUST DOING YOUR JOB.

AT THIS POINT, HAVING GONE THROUGH 1 AND 2, I WOULD PROPOSE THAT WE GET A MOTION TO APPROVE THOSE SET OF CHANGES BECAUSE THE THIRD ONE IS REALLY THE SUBSTANTIVE. AND THAT WILL HAVE A DIFFERENT FLAVOR.

CO-CHAIR LANSING: I'LL MOVE IT.

DR. PETERS: SECOND.

CHAIRMAN LO: JUST TO BE CLEAR, WE'RE TALKING ABOUT BOLD 1 AND BOLD 2 ON THIS COVER SHEET. DISCUSSION? PUBLIC COMMENT? IS THERE ANY PUBLIC COMMENT ON THE MOTION TO RECOMMEND ADOPTION OF THE AMENDMENTS PERTAINING TO ALIGN THE MEDICAL AND ETHICAL STANDARDS REGULATIONS WITH THE GAP

REVISIONS, AND, NO. 2, AMENDMENTS THAT TEND TO MAKE REGULATIONS SHORTER, CLEARER, EASIER TO IMPLEMENT? ANY DISCUSSION?

DR. ROBERTS: TO ADD THE MODIFICATION THAT THE DATE OF THE GAP WILL BE ADDED.

CHAIRMAN LO: WITH THE UNDERSTANDING --

CO-CHAIR LANSING: WITH THE MODIFICATIONS WE DISCUSSED.

CHAIRMAN LO: ANY PUBLIC COMMENT, DISCUSSION? ANYONE ON THE PHONE WISH TO COMMENT? UNMUTE YOURSELF AND SPEAK UP LOUD AND CLEAR. NO. CAN I HEAR SOMEONE CALL THE QUESTION?

MR. TOCHER: WE CAN JUST DO A VOICE --

CHAIRMAN LO: LET'S JUST DO VOICE VOTE AS A ROLL CALL VOTE.

MR. TOCHER: IT WILL BE A ROLL CALL FOR THOSE ON THE PHONE. BUT ALL THOSE IN FAVOR SAY AYE. THOSE OPPOSED? ANY ABSTENTIONS?

CHAIRMAN LO: ON THE PHONE, THOSE MEMBERS ON THE PHONE.

MR. TOCHER: SENATOR TORRES.

MR. TORRES: AYE.

MR. TOCHER: DR. PRIETO.

DR. PRIETO: AYE.

MR. TOCHER: THE MOTION CARRIES.

CHAIRMAN LO: MOTION CARRIES. THANK YOU. NOW I'M GOING TO ASK GEOFF TO GO TO NO. 3, AMENDMENTS INTENDED TO MAKE CHANGES -- SORRY.

DR. PRIETO: I DIDN'T HEAR YOU CALL MY NAME, BUT I'LL VOTE AYE AS WELL.

MR. TOCHER: WE THOUGHT WE HEARD YOU BEFORE WE HEARD YOU.

CHAIRMAN LO: THANK YOU FOR THE CLARIFICATION. OKAY.

WITH THAT, I'M GOING TO ASK GEOFF TO MOVE US ON TO NO. 3, THE AMENDMENTS INTENDED TO MAKE CHANGES TO REGULAR REVIEW AND OVERSIGHT POLICY. THIS IS MORE SUBSTANTIVE THAN THE FIRST TWO.

DR. LOMAX: ONE OF THE ISSUES WE'RE DEALING WITH, AND THIS, AGAIN, COMES UP PARTICULARLY IN OUR CIRM 2.0 CONTEXT, IS THAT UNDER OUR CURRENT REQUIREMENTS, CERTAIN STUDIES WHERE YOU'RE PUTTING STEM CELL OR STEM CELL-DERIVED CELLS INTO VERTEBRATE ANIMALS REQUIRE ADDITIONAL REVIEW BY AN OVERSIGHT COMMITTEE. AND WHERE THIS COMES UP, ONE AREA WHERE IT'S COME UP AND HAS CAUSED PROBLEMS IN TERMS OF PEOPLE EITHER BEING ABLE TO APPLY TO CIRM OR MOVE FORWARD WITH THEIR STUDIES IN A TIMELY WAY IS PRECLINICAL STUDIES THAT ARE EFFECTIVELY MANDATED PURSUANT TO WHAT THE FDA WOULD REQUIRE UNDER AN IND.

SO THEY'RE IN PRODUCT DEVELOPMENT, THEY NEED TO DO A SET OF STUDIES, FOR EXAMPLE, PARKINSON'S STUDIES, WHERE CERTAIN CELLS WILL BE GOING INTO THE BRAINS OF ANIMALS. AND IN ONE CASE A GRANTEE MIGHT NOT HAVE ACCESS TO A COMMITTEE THAT WOULD PROVIDE THIS REVIEW.

IN ADDITION, WE ANTICIPATE HAVING APPLICANTS COME IN FROM JURISDICTIONS WHERE THE WHOLE CONCEPT OF A STEM CELL OVERSIGHT COMMITTEE MAY NOT EXIST. SO SUDDENLY THEY'RE TRYING TO NEGOTIATE A REGULATORY REQUIREMENT IN WHICH THEY HAVE NO EXPERIENCE OR CAPACITY.

SO WHAT WE'RE SUGGESTING, AND THEN WHAT I'D LIKE TO DO IS MOVE INTO A PRESENTATION THAT SORT OF DESCRIBES THESE STUDIES IN MORE DETAIL, IS THAT WE CONSIDER WAYS TO MAKE THE REGULATIONS MORE FLEXIBLE PARTICULARLY FOR STUDIES THAT ARE IN THIS PRECLINICAL DEVELOPMENT PHASE AND INVOLVE VERTEBRATE ANIMALS. BEFORE GETTING TOO DEEP INTO THE POLICY DISCUSSION, I DISCUSSED THIS WITH BERNIE, IT THOUGHT IT WOULD BE HELPFUL IF WE HAD SOME BACKGROUND THAT KIND OF ILLUMINATED MORE HOW THESE STUDIES ARE CONDUCTED, WHY THEY'RE BEING DONE, AND WHAT PEOPLE WHO HAVE BEEN INVOLVED IN THIS SPACE ARE LEARNING FROM THIS TYPE OF RESEARCH.

SO I'D LIKE TO INTRODUCE DR. MARTIN MARSALA. HE'S FROM UC SAN DIEGO. AND YOU'RE A PROFESSOR IN THE NEURODEGENERATION LABORATORY AND THE DEPARTMENT OF ANESTHESIOLOGY.

CHAIRMAN LO: HE'S AN ADVOCATE FOR GREEN TRANSPORTATION BECAUSE HE TOOK THE TRAIN, AS I UNDERSTAND IT, RATHER THAN DRIVING.

DR. MARSALA: SO WHAT I WOULD LIKE TO DO TODAY, I WILL GIVE YOU A VERY SHORT VERSION OF THE PRESENTATION, RANDY AND MARIA. WE HAVE AN ALPHA CLINIC INITIATION, BUT THIS WILL BE MORE FOCUSED ON OUR EXPERIENCE IN RUNNING SMALL AND LARGE ANIMAL PRECLINICAL STUDIES WHICH WERE USED IN TWO DIFFERENT IND'S FOR TREATMENT OF ALS PATIENTS AND SPINAL TRAUMA PATIENTS.

JUST ONE BACKGROUND SLIDE FOR SPINAL TRAUMA, BECAUSE THIS IS A TRIAL WHICH WE ARE RUNNING AT UCSD, STATISTICAL DATA SHOW THAT APPARENTLY WE HAVE ABOUT ONE-QUARTER MILLION AMERICANS LIVING WITH CHRONIC SPINAL INJURY. FIFTY-TWO PERCENT OF THESE ARE CONSIDERED PARAPLEGIC, 47 ARE QUADRIPLEGIC. SO IT IS VERY IMPORTANT THAT THERE ARE APPROXIMATELY 11,000 NEW CASES EVERY YEAR, WHICH THE NUMBER IS ADDING TO THOSE ALREADY LIVING WITH CHRONIC SPINAL INJURY. LIFETIME COST TO TAKE CARE OF THESE

PATIENTS IS ABOUT $1.5 MILLION PER PATIENT.

SO IN THE PROCESS OF HAVING IND APPROVAL TO TREAT PATIENTS WITH CHRONIC SPINAL INJURY, SEVERAL HUNDRED RODENTS WERE USED IN OUR TUMORGENICITY AND TOXICITY STUDIES. MAJORITY OF THESE ANIMALS WERE DONE UNDER GLP GUIDELINES, FDA GUIDELINES, AND THEN WERE USED IN SUCCESSFUL IND.

AFTER THAT COMPONENT OF THE STUDIES WHERE WE COVERED TUMORGENICITY, TOXICITY, AND EFFICACY, WE THEN MOVED AND DEVELOPED LARGE ANIMAL MODELS. IN OUR CASE WE USED MINIPIG MODEL, AND WE DID OVER 80 ANIMALS. THIS PARTICULAR MODEL WAS REQUIRED TO ESTABLISH EQUIVALENT HUMAN CELL DOSE AND DEFINE SAFETY AND ALSO TO TEST INJECTION DEVICE WHICH IS CURRENTLY BEING USED IN HUMAN CLINICAL TRIAL. IT WAS EXACTLY THE SAME DEVICE.

JUST TO GIVE YOU A PERSPECTIVE OF WHAT IT INVOLVES, ONCE YOU USE THE RODENT AND YOU DO SPINAL INJECTION, THIS IS THE IMAGE OF EXPOSED LUMBAR SPINAL CORD, THE LOWER PART OF THE SPINAL CORD, WHERE WE REMOVE THE BONE. CELLS ARE LOADED INTO THE GLASS AND THEN INJECTED TO THE SPECIFIC DEPTH OF THE SPINAL CORD. IN THE CASE OF ALS, FOR EXAMPLE, WE TARGET THE VENTRAL HORN SO THE CELLS CAN BE DEPOSITED VERY CLOSE TO (INAUDIBLE). ANIMALS

SURVIVE IN GLP STUDY ABOUT NINE MONTHS. THIS IS THE LONGEST TIME WE CAN KEEP THESE ANIMALS ALIVE EVEN THOUGH THEY ENGRAFT AND THEY START TO DIE. IN THE CASE OF IMMUNOSUPPRESSED OR COMPROMISED ANIMALS, WE CONTINUOUSLY IMMUNOSUPPRESS THESE ANIMALS TO THE END STAGE. AT THE END WE FOLLOW THE -- WE CONFIRM THE PRESENCE OF TRANSPLANTED CELLS BY IMMUNOFLUORESCENT STAINING.

WITH RESPECT TO BEHAVIORAL CHANGES, WHAT WE ARE LOOKING FOR IN THE CASE THAT CELLS ARE TRANSPLANTED INTO THE SPINAL CORD, WE SPECIFICALLY ASSESS SO-CALLED BBB SCORE, WHICH IS A GRADING SCALE TO ASSESS MOTOR FUNCTION. IN ADDITION, WE ALSO ARE LOOKING FOR DEVELOPMENT OF ANY ABNORMAL SENSATION; FOR EXAMPLE, TACTILE ALLODYNIA. TACTILE ALLODYNIA IS DEFINED AS RESPONSE TO NON-NOXIOUS STIMULI WHICH SHOULDN'T BE PRESENT. SO IF THERE'S ANY ADVERSE EFFECT, WE WOULD SEE THAT THESE ANIMALS (INAUDIBLE).

SECOND MODEL, AND THIS IS A LARGE ANIMAL MODEL, WE DEVELOPED IN-HOUSE. AND THIS IS ACTUALLY THE PICTURE OF MINIPIG WHICH IS PLACED IN SPINAL IMMOBILIZATION FRAME WHICH WE DEVELOPED, AND IT'S DESIGNED TO ELIMINATE SPINAL CORD MOVEMENT DURING SPINAL CELL INJECTION.

TO PERMIT LONG-TERM SURVIVAL OF THESE

CELLS, ANIMALS ARE CONTINUOUSLY IMMUNOSUPPRESSED BY USING TACROLIMUS, WHICH IS DELIVERED THROUGH JUGULAR CATHETER. AND THE CATHETER IS INTERCONNECTED TO PUMPS WHICH ARE SECURED IN THIS PIG JACKET, WHICH IS CUSTOM-MADE JACKET, AND CAN ACCOMMODATE TWO PUMPS WHICH CONTINUOUSLY DELIVER THE DRUG FOR UP TO 11 DAYS. THE PUMP CAN BE CHANGED AND BASICALLY YOU CAN KEEP THESE ANIMALS FOR MONTHS WITH CONTINUOUS IMMUNOSUPPRESSION.

SO THESE ARE THE TWO MODELS WHICH WE USED. JUST TO GIVE YOU A PICTURE HOW THE CELL REPLIED AFTER TRANSPLANTATION, THIS IS JUST EXAMPLE FROM ONE OF THE EFFICACY STUDIES WE DID. THIS IS HORIZONTAL SECTION THROUGH THE SPINAL CORD, AND YOU CAN SEE LARGE GREEN AREA HERE. THESE ARE TRANSPLANTED CELLS WHICH RELAY THE GREEN FLUORESCENCE AND WHICH COMPLETELY FILL THE CAVITY WHICH WAS CREATED BY IMPACTS. THIS IS SPINAL TRAUMA INJURY MODEL. IN ADDITION, THESE CELLS DEVELOP VERY WELL-ORGANIZED DENDRITIC ARBOR. THEY ARE ALL GREEN FIBERS HERE WERE DERIVED FROM TRANSPLANTED CELLS.

SO THE CELLS BEHAVE VERY WELL IN RODENT MODEL THAT THEY ENGRAFT. BUT, AGAIN, I WANT TO EMPHASIZE THAT THE TOTAL NUMBER OF CELLS WHICH WE TRANSPLANTED WITH RESPECT TO THE TOTAL NUMBER OF

CELLS PRESENT IN THE SPINAL CORD IS LESS THAN 0.1 PERCENT, VERY SMALL NUMBERS. ALSO, MY LAST SLIDE WHICH IS MORE IMPORTANT IF WE ARE GOING TO DISCUSS THE CELL GRAFTING INTO THE BRAIN.

DR. ROBERT TAYLOR: THIS IS A PIG OR THIS IS THE RODENT?

DR. MARSALA: THIS IS RODENT. THE NEXT SLIDE IS THE PIG WHERE WE DEFINED THE OPTIMAL DOSING. PICTURE IS VERY SIMILAR. HUMAN CELLS ARE IDENTIFIED BY STAINING WITH HUMAN-SPECIFIC ANTIBODIES. SO ALL THE RED AREA HERE ARE THE TRANSPLANTED HUMAN CELLS IN THE CENTRAL BRAIN MATTER IN THE LUMBAR SPINAL CORD OF A PIG. SO VERY SIMILAR BEHAVIOR. DOESN'T REALLY MATTER WHAT ANIMAL MODEL, BUT THEY ENGRAFT, THEY SPROUT, THEY DEVELOP SYNAPTIC CONNECTIVITY AT THE REGION OF TRANSPLANTATION.

THIS IS JUST ONE VIDEO TO SHOW YOU. THIS WAS A STUDY WHICH WAS REQUIRED BY FDA TO PROVIDE EVIDENCE THAT THERE IS NO DETERIORATION IN FUNCTION IN MODESTLY INJURED PIG WITH CONTUSION IN THE CERVICAL SPINAL CORD. THIS ANIMAL RECEIVED SIX INJECTIONS, ABOUT 600,000 OF HUMAN FETAL TISSUE-DERIVED CELLS INTO THE SPINAL CORD AND SURVIVED FOR SIX WEEKS. AND THEN WE FOLLOWED THE ANIMAL NEUROLOGICALLY, AND THEN WE CONFIRMED THE

SURVIVAL OF TRANSPLANTED CELLS AT THE SPECIFIC REGION.

AS YOU CAN SEE, WE DON'T SEE ANY MAJOR NEUROLOGICAL DYSFUNCTION, NO SPONTANEOUS PAIN. SO THESE ARE THE ATTRIBUTES WHICH YOU WOULD LIKE TO HAVE.

DR. ROBERT TAYLOR: THE LESION YOU INDUCED, WOULD HE BE KIND OF DRAGGING HIS BACK FEET AROUND?

DR. MARSALA: YES. IN THE CASE OF CERVICAL LESION, WE DID ONLY VERY MODERATE INJURY BECAUSE IT WOULD BE VERY DIFFERENT TO MAINTAIN THE ANIMAL WITH PARALYSIS. FOR PARAPLEGIA, THE LOWER EXTREMITIES OR HIND LEGS, YOU CAN DO THIS AND THEY CAN TOLERATE PARAPLEGIC STATE FOR MONTHS AND MONTHS.

SO ALL THESE STUDIES WERE USED IN IND. WE DIDN'T SEE ANY DETECTABLE SIDE EFFECTS WITH RESPECT TO MOTOR FUNCTION OR SENSORY FUNCTION. AND THE TRIAL WHICH WE STARTED IN SEPTEMBER IS BASICALLY -- THIS IS ONE OF THE VIDEO FROM OUR SECOND PATIENT WHICH IS BEING INJECTED WITH HUMAN SPINAL STEM CELLS. DR. CIACCI IS RUNNING THE TRIAL, AND YOU WILL SEE HOW HE'S ADVANCING THE NEEDLE INTO THE SPINAL CORD AT THE INJURY SITE. THIS WAS CHRONIC PATIENT ONE YEAR POST INJURY. AND THIS INJECTOR WAS

EXTENSIVELY TESTED IN PIG MODEL WHICH I SHOWED YOU BEFORE, SO ALL APPROACHES AND DESIGN WAS TESTED IN LARGE ANIMAL MODEL BEFORE WE MOVED TO HUMAN PATIENTS.

SO WE HAVE A THIRD PATIENT IS SCHEDULED FOR NEXT THURSDAY, AND THEN TWO WEEKS LATER THE FOURTH PATIENT, AND HOPEFULLY REMOVE THE CERVICAL SPINAL CORD.

SO THE WHOLE PROCESS FROM STARTING THE FIRST RODENT STUDIES TO PATIENT TOOK ABOUT SEVEN AND A HALF YEARS. I STILL REMEMBER WHEN WE GOT THE FIRST LINE OF CELLS FEDEX'D FROM EAST COAST AND WE DID TRANSPLANTATION IN SAN DIEGO. A LOT STUDIES OF WE LEARN, WE MAKE MISTAKES, AND WE LEARN HOW TO REALLY STREAMLINE THE WHOLE PROCESS.

AND THE DESIGN, JUST FOR YOUR INFORMATION, CELLS ARE BEING SHIPPED OVERNIGHT TO UCSD, THEN WE DRIVE THE CELLS TO HOSPITAL, AND THEY JUST START THE PROCEDURE AND THE CELLS ARE INJECTED ON THE SAME DAY.

SO THIS WAS THE SPINAL CORD, BUT I THINK WITH RESPECT TO WHAT WE WANT TO DISCUSS TODAY IS ETHICAL ISSUES OR CONCERN ABOUT USING NEURAL STEM CELLS AND TRANSPLANTING INTO THE BRAIN IN RODENTS. I WAS SERVING IN ESCRO COMMITTEE FOR MANY YEARS.

AND IT WAS ACTUALLY SERIOUS QUESTION THAT IF YOU TRANSPLANT HIGH NUMBER OF NEUROPROGENITORS INTO THE RODENT, DO THEY CHANGE BEHAVIORALLY? THERE WAS A JOKE: ARE THEY BECOMING SMARTER? I THINK WE CAN EASILY ADDRESS THIS ISSUE BY LOOKING AT THIS SLIDE, WHICH COMPARES THE TOTAL NUMBER OF NEURONS IN DIFFERENT MAMMALS. AS YOU CAN SEE, IN HUMAN BRAIN, THERE'S TOTAL 86 BILLION NEURONS. THE RODENT, RAT, WHICH WE USED, HAS 200 MILLION. MACAQUE, NONHUMAN PRIMATES HAS ABOUT 6 BILLION. BUT IN ALL TRANSPLANTATION STUDIES WHAT WE DID SO FAR, AND WE DID A NUMBER OF PIGS WHERE WE TRANSPLANTED HUMAN NEURONAL PROGENITORS, FETAL TISSUE DERIVED, THE TOTAL NUMBER OF CELLS WHICH WE INJECT NEVER EXCEEDED 50 MILLION, WHICH REPRESENT LESS THAN 0.1 PERCENT OF THE TOTAL NUMBER OF NEURONS IN HUMAN BRAIN.

SO I THINK THAT THIS WILL GIVE US VERY CLEAR ANSWER, THAT TO EXPECT THAT WE CAN RECREATE THE CIRCUITRY WHICH IS REALLY NEEDED FOR FULLY FUNCTIONAL HUMAN BRAIN IS BASICALLY IMPOSSIBLE IN ANY OF THESE STUDIES BECAUSE YOU CANNOT INJECT MORE CELLS THAN, FOR EXAMPLE, 50 MILLION, BECAUSE YOU EXPAND THE TISSUE TOO MUCH. YOU CREATE INJURY.

SO THESE ARE VERY SMALL NUMBERS, AND WE NEVER SAW ANY ADVERSE EFFECT OR SOME ABNORMAL

BEHAVIOR IN PIGS, FOR EXAMPLE, WHEN WE INJECTED UP TO 50 MILLION OF HUMAN NEURONAL PROGENITOR CELLS. SO I THINK THESE ARE SOLID SCIENTIFIC ARGUMENTS WHICH WOULD ARGUE AGAINST THAT DO WE REALLY NEED APPROVAL IN THESE STUDIES ONCE -- IF YOU HAVE AN ESTABLISHED CELL LINE. I DON'T REALLY FEEL THAT IT'S NECESSARY EVEN IF YOU TRANSPLANT THESE CELLS INTO THE BRAIN. OF COURSE, THERE'S DIFFERENT ISSUE IF YOU GO AND YOU DEVELOP CHIMERIC ANIMALS. I DID DISCUSS THIS WITH GEOFF ON THE PHONE. I FEEL THAT FOR WELL-ESTABLISHED CELL LINES WHICH ARE LINEAGE PERMITTED, SO THEY CAN BECOME ONLY NEURONS OF REAL CELLS, I WOULDN'T HAVE ANY CONCERN IF YOU GO AND DO GRAFTING INTO THE BRAIN IN DIFFERENT MAMMALS, DIFFERENT SPECIES, EVEN TO THE HIGHEST DOSE WHICH YOU CAN ACCOMMODATE IN THE BRAIN. I FOUND THAT IMAGE ON THE INTERNET FROM ONE PAPER, AND I THOUGHT IT WAS VERY INTERESTING.

DR. BOTKIN: SO THAT'S ADULT ANIMALS.

DR. MARSALA: ADULT ANIMALS, YES.

SO IN SUMMARY, BASICALLY WE SHOW THAT SPINAL AND BRAIN GRAFTING OF HUMAN FETAL TISSUE DERIVED AND ES-DERIVED NEURAL PROGENITORS IS WELL TOLERATED. WE DON'T SEE ANY SYSTEMIC SIDE EFFECTS UP TO NINE MONTHS POST TRANSPLANTATION. AND THE USE

OF BOTH MODELS, RODENT AND MINIPIG, REPRESENTED WELL-DEFINED PLATFORM WHICH IS FDA APPROVED AND CAN BE EFFECTIVELY USED IN PRECLINICAL IND-ENABLING STUDIES. AND WE USE IT IN OUR -- WE USE IT FOR ALS, SPINAL TRAUMA, AND OTHER GROUPS ARE USING IT FOR DEVELOPMENT OF TREATMENT FOR MULTIPLE SCLEROSIS ALSO.

CHAIRMAN LO: THANK YOU VERY MUCH. QUESTIONS FOR DR. MARSALA?

DR. PETERS: VERY FASCINATING, MARTIN. IS THERE ANY HISTORICAL CONNECTION BETWEEN YOUR WORK IN SAN DIEGO ON SPINAL GRAFTS AND THE GERON-FUNDED WORK AT IRVINE AND IN ATLANTA?

DR. MARSALA: NO. SO THE ORIGINAL SOURCE OF THE CELLS IS DIFFERENT. GERON TRIAL IS THROUGH EMBRYONIC STEM CELLS-DERIVED OLIGO PRECURSORS, SO THESE ARE CELL IN SHEATHING CELLS, SUPPORTING CELLS. WHILE WE USE IN THESE STUDIES HUMAN FETAL TISSUE-DERIVED SPINAL STEM CELLS. SO IT'S DIFFERENT.

BUT THERE ARE SIMILAR STUDIES NOW USING ES-DERIVED NPC'S, NEURAL PROGENITOR CELLS. THAT LINE CAN UTILIZE NEURONS AND OLIGO AND ASTROCYTES. BUT IT WAS DIFFERENT CELL LINE.

DR. ROBERT TAYLOR: THIS IS MAYBE MORE

OF -- GREAT PRESENTATION -- MORE OF A COMMENT PERHAPS THAN A QUESTION. BUT I'M REALLY MORE -- I'M AN ENDOCRINOLOGIST, BUT I THINK THAT THERE'S BEEN KIND OF A SORT OF FALSE DICHOTOMY IN OUR THINKING A LITTLE BIT ABOUT THE BRAIN AS BEING SOMETHING SORT OF ABSOLUTELY SPECIAL. IN FACT, WE'VE GOT THESE RETINAL PROGRAMS THAT ARE ONGOING. THE RETINAL NEURONS ARE DIRECT EXTENSIONS FROM THE BRAIN. THERE'S REALLY NO REASON TO BELIEVE THAT THOSE CELLS ARE NECESSARILY ANY DIFFERENT OR WOULD -- SO I'M KIND OF WONDERING WHY -- WE'RE NOT GOING TO CHANGE THIS OPINION, I GUESS, THAT'S OUT THERE, BUT IT'S A LITTLE BIT OF AN UNSOPHISTICATED VIEW THAT THE BRAIN IS SOME KIND OF UBER SPECIAL PART BECAUSE I THINK WE'RE ALLOWING THESE CELLS TO BE APPLIED IN CERTAIN SETTINGS, AND WE'VE KIND OF DRAWN A LINE AT THE BRAIN, BUT ONE COULD SAY THAT THE RETINA IS PART OF THE BRAIN. AND SO THOSE SHOULD BE SCRUTINIZED MORE. IT'S MORE OF A KIND OF A WHINE, I GUESS.

DR. ROBERTS: I WOULD LIKE TO EXPLORE THAT MORE BECAUSE I AM INTERESTED, AS I'M SURE ALL OF US ARE, IN THE ETHICAL DIMENSIONS OF THIS AND WHERE THERE'S A CONCERN OR WHERE THERE ISN'T AND WHAT THAT CONCERN IS.

SO PART OF THE CONCERN IS CONCERN FOR THE

ANIMAL'S WELFARE. PART OF THE CONCERN IS ABOUT CREATING SOME DIFFERENT TYPE OF ANIMAL, THAT PUTTING THE STEM CELLS IN THE ANIMAL, HUMAN STEM CELLS, WILL CREATE SOMETHING NEW. I THINK THERE'S A SENSE, AND I AGREE FROM WHAT YOU'RE PRESENTATION THAT THIS IS A FALSE SENSE, THAT PUTTING HUMAN STEM CELLS IN A BRAIN OF AN ANIMAL IS DIFFERENT FROM PUTTING THEM IN ANY OTHER PART OF THE ANIMAL'S BODY BECAUSE THE BRAIN IS WHAT DISTINGUISHES DIFFERENT SPECIES, ESPECIALLY THE HUMAN SPECIES.

SO YOU EVEN ALLUDED TO IT IN YOUR COMMENT, THAT IF YOU PUT HUMAN STEM CELLS IN THE BRAIN OF AN ANIMAL, THAT'S GOING TO MAKE IT MORE LIKE A HUMAN IN A WAY THAT'S NOT TRUE IF YOU PUT IT IN ANY OTHER PART OF THE ANIMAL. AND I'D LOVE TO HEAR MORE COMMENTS ABOUT THAT.

AND THEN YOU ALSO MENTIONED CHIMERAS, WHICH IS NOW ANOTHER ETHICAL BOUNDARY. AND I JUST WONDER IF YOU'D TALK ABOUT THOSE THREE BOUNDARIES AND WHETHER THESE ARE REAL DISTINCTIONS WE SHOULD BE CONCERNED ABOUT BECAUSE PART OF WHAT WE'RE GOING TO HAVE TO DO IS DECIDE IF THERE SHOULD BE EXTRA REVIEW FOR EACH OF THESE TYPES. WE MIGHT DECIDE THIS BRAIN DISTINCTION MAKES NO SENSE. LET'S LEAVE THAT OUT ALTOGETHER, BUT MAYBE THE CHIMERA DISTINCTION IS

IMPORTANT. SO I'D LOVE TO HEAR MORE ABOUT THAT.

DR. MARSALA: THE POINT I TRIED TO MAKE WAS SHOWING THE BRAIN AND THE NUMBER OF NEURONS WAS THAT BY TECHNICAL LIMITATIONS, WE CANNOT INJECT MORE THAN 50 MILLION CELLS, WHICH REPRESENT LESS THAN 0.1 PERCENT OF TOTAL NUMBER OF NEURONS WHICH YOU NEED TO HAVE IN HUMAN BRAIN TO FUNCTION, AS WE KNOW HUMAN BRAIN. INJECTING IN RODENT, THESE ARE ONLY FRACTIONS OF SMALL NUMBERS OF CELLS, HUMAN CELLS, WHICH MOST HIGHLY LIKELY JUST PROVIDE TROPHIC SUPPORT AT THE REGION WHERE WAS THE PREVIOUS INJURY.

SO I DON'T THINK THAT THIS SHOULD HAVE ANY IMPACT ON ANIMAL BEHAVIOR OR CHANGE HOW THE ANIMAL BEHAVE IN THE ENVIRONMENT OR INTERACT WITH OTHER RODENTS WHICH WERE NOT TRANSPLANTED. I DON'T THINK -- I DON'T SEE SCIENTIFIC BASE FOR THAT, BASED ON THAT, WHAT I SHOW.

FOR CHIMERIC EXPERIMENTS, I THINK I WOULD HAVE -- PERSONALLY I WOULD HAVE RESERVATION BECAUSE IF YOU ARE TRYING TO CREATE THE WHOLE ORGAN, FOR EXAMPLE, SO IT'S POSSIBLE THAT WE WOULD HAVE THE WHOLE CNS DEVELOP IN CHIMERIC ANIMAL WHICH IS HUMAN.

I THINK THAT SHOULD BE PROBABLY -- YOU SHOULD CONSIDER THAT CAREFULLY. BUT I DON'T THINK THAT YOU CAN MAKE TECHNICALLY CHIMERIC ANIMALS WITH

HUMAN CELL OR BODY.

DR. PETERS: I THINK IT'S VERY HELPFUL ON THIS ISSUE WHEN YOU DESCRIBE THE TECHNICAL LIMITS OF WHAT ACTUALLY COULD BE DONE WITH BRAIN. BUT I'M TRYING TO RECALL SOMETHING, AND, BERNIE, MAYBE YOU REMEMBER, WE HAD A MEMBER ON THIS COMMITTEE A HALF DOZEN YEARS AGO WHO WAS A PRIMATOLOGIST OR PRIMATE RESEARCHER IN CHICAGO. AT ANY RATE, AT THAT TIME STANFORD ETHICS STATEMENT CAME OUT IN WHICH THIS ISSUE WAS RAISED. AND THEY THOUGHT THAT PUTTING NEURONAL CELLS IN THE BRAINS OF PRIMATES WOULD MAKE THEM MORE HUMAN; AND, THEREFORE, YOU'VE GOT AN ETHICAL PROBLEM.

SO I CALLED UP THIS MEMBER OF THE COMMITTEE, AND I GOT HIM ON THE PHONE IN THE LABORATORY. AND I SAID, "YOU ARE PUTTING NEURONAL CELLS IN THE BRAINS OF MONKEYS, RIGHT?" HE SAID, "YEP." I SAID, "DOES THAT MAKE THEM BEHAVE LIKE HUMANS?" HE SAYS, "NO, OF COURSE NOT. WHY DO YOU ASK ME THIS?"

SO IT APPEARS TO ME THAT MAYBE IT'S A NONISSUE FOR TECHNICAL REASONS EVEN THOUGH, AND I THINK YOU SAID IT KIND OF NICELY, THE CULTURE WOULD SUGGEST THAT THIS SHOULD BE AN EMOTIVE ISSUE, BUT MAYBE IT'S JUST NOT GOING TO BE FROM THE SCIENTIST'S

POINT OF VIEW. I DON'T KNOW.

DR. MARSALA: I CAN TELL YOU THAT THERE'S A LOT OF INTENT IN THE FIELD NOW TO USE NEURAL PRECURSORS FOR STROKE TREATMENT WHERE THE NUMBERS ARE ABOUT 20 MILLION. DEPENDS ON THE SIZE OF THE STROKE. AND SO THERE ARE SEVERAL STUDIES IN PROGRESS WHICH THEY USE THOSE NUMBERS. BUT SO FAR I HAVEN'T HEARD ANY SIDE EFFECT OR CHANGE IN BEHAVIOR IN NAIEVE ANIMALS. SO I THINK -- BUT BASED ON THAT SCIENTIFIC EVIDENCE AND ANATOMICAL STUDIES, IT'S SHOWING A CLEAR DIFFERENCE. AND WE WENT THROUGH THESE STUDIES MANY TIMES; AND IF YOU LOOK AT THIS BRAIN AND WE INJECT FEW INJECTION OF THESE CELLS, IT'S ALMOST LIKE SMALL DROP IN THE OCEAN. AND THEN, AGAIN, EVEN IF YOU DO, LET'S SAY, THOUSANDS OF INJECTIONS OF THESE CELLS, THEY NEED TO FIND THE PROPER CONNECTION. THEY NEED TO FIND THE PROPER TARGET FROM LEFT AND RIGHT SIDE. SO IT'S VERY COMPLEX. I THINK THAT THE GOAL FOR TRYING TO ACHIEVE IS LIKE TROPHIC SUPPORT AND TO SUPPORT EXISTING SYSTEM WHICH IS LEFT AFTER INJURY.

DR. LEE: THIS ISSUE IS PROBABLY -- IT DEPENDS UPON WHO YOU'RE REVISING YOUR REGULATIONS FOR. IT'S SLIGHTLY MORE COMPLICATED THAN THE EXTREMES THAT HAVE JUST BEEN PROVIDED BECAUSE LATER

STUDIES HAVE PEOPLE, THE BELGIAN GROUP, PUTTING EMBRYONIC OR IPS CELLS INTO NEONATAL MICE. AND THEY FORMED SYNAPTIC CONNECTIONS THROUGHOUT INTRACRANIAL NEURONS THAT CAN FORM. BUT IT'S ALSO WE HAVE TO BE CAREFUL ABOUT USING THE LANGUAGE BECOMING HUMAN BECAUSE AS SCIENTISTS WHEN WE SAY THAT, WE MOCK IT BECAUSE, YOU KNOW, WE'RE HUMAN, NOT MYSTICS HERE, RIGHT. BUT THEN THAT BELITTLES THE COMPLEXITIVE ISSUE BECAUSE DO WE REALLY KNOW WHAT MAKES US HUMAN? WHAT ARE WE AFRAID OF? AND AS A PUBLICLY FUNDED INSTITUTION, WHAT WOULD THE PUBLIC PERCEIVE AS WHAT WE CONSIDER SOMETHING THAT SHOULD OR SHOULD NOT BE DONE, AND IS THERE A DIFFERENCE BETWEEN PRIMATES OR A DIFFERENCE BETWEEN MAN?

IT'S ILLUSTRATIVE TO LOOK AT EXTREME ACTIONS. I MEAN THERE HAVE BEEN PROPOSALS, WAS IT FROM STANFORD, YOU PUT EMBRYONIC STEM CELLS. YES, IT'S A SMALL PERCENTAGE COMPARED TO IN HUMANS, BUT AS PERCENTAGE OF THE MICE IF YOU ENGRAFT. WE'RE ASKED ON OUR ESCRO COMMITTEE TO SAY AT WHAT THRESHOLD DOES IT CONTRIBUTE SIGNIFICANTLY TO THE BRAIN DEVELOPMENT? AND IT ALWAYS COMES UP WE CAN'T GET AN ANSWER WHAT PERCENT YOU CONSIDER. AND USUALLY WE ASK THEM IT'S NOT WHAT PERCENT BECAUSE FOR THOSE -- I'M NOT A NEUROSCIENTIST. I JUST READ

ABOUT IT. FRANCIS CRICK BELIEVED THAT'S THE SEAT OF HUMAN CONSCIOUSNESS. THAT'S A BIT MORE FRIGHTENING IN TERMS OF WHERE AND WHAT YOU WANT TO PUT IN.

SO THE STANFORD PEOPLE WERE SAYING THAT TO PUT HUMAN NEURONS INTO MICE WHICH HAVE DEGENERATIVE DISEASE SO THAT ENDOGENOUS MICE NEURONS ALL DIE OUT UPON CERTAIN AGE. SO EVENTUALLY ALL BECOMES HUMAN NEURONS BECAUSE THE ONES ARE MORE SUBJECT TO DISEASE. ARE WE COMFORTABLE WITH THOSE KINDS OF EXPERIMENTS?

I DON'T THINK THE COMPANIES THAT WANT TO DO THESE EXPERIMENTS WILL DO IT, BUT WE ARE GOING TO WRITE REGULATIONS TO PERHAPS ILLUSTRATE TO THE STATE WHAT -- WE CAN'T PREDICT THE FUTURE, BUT ILLUSTRATE TO THE STATE WHAT WE ARE CONCERNED ABOUT, WHAT WE'RE NOT CONCERNED ABOUT. SAYING THINGS LIKE MAKING HUMANS DOESN'T INFORM, I THINK, OR DOESN'T TAKE INTO ACCOUNT THE COMPLEXITIES OF THE ISSUES INVOLVED.

JUST ONE LAST POINT. THEY'RE SEQUENCING NEANDERTHAL GENOMES AND ALL THE PRIMATE GENOMES AND THE SINGLE MUTATION AND FOXP2 TRANSCRIPTION FACTOR. THE RESULTS, THEY THINK, IS ASSOCIATE DEVELOPMENT OF HUMAN LANGUAGE. SO PEOPLE HAVE GONE IN AND PUT IN THAT MUTATION INTO MICE. AND CLEARLY THE SYNAPTIC CONNECTIONS ARE DIFFERENT. THEY SQUEAK DIFFERENTLY,

NOT THAT THEY SPEAK, AND THIS IS ONE SINGLE MUTATION IN A MOUSE. SO IF TECHNOLOGY BECOMES INVOLVED ENOUGH WHERE YOU LOOK AT IT FROM THE OTHER POINT OF VIEW, WE DON'T USE STEM CELLS TRANSPLANTATION, BUT WE USE GENETIC EDITING TO MAKE ENDOGENOUS MOUSE MORE LIKE HUMAN GENES. WHERE IS OUR COMFORT LEVEL WITH THAT?

THAT'S JUST SORT OF SOME POINTS WE SHOULD PERHAPS FACE. I'M NOT A MYSTIC, BUT IT'S HELPFUL TO --

CHAIRMAN LO: I THINK THIS IS A VERY HELPFUL DISCUSSION. JEFF AND JOHN WAGNER HAD COMMENTS.

DR. BOTKIN: I HAD SORT OF A SCIENCE QUESTION AND THEN A COMMENT TOO. SO YOU'RE TRYING TO ESTABLISH SAFETY AND EFFICACY AND PROOF OF PRINCIPLE IN THESE EXPERIMENTS. SO IT SEEMS TO ME A BIT ANOMALOUS TO BE TRANSPLANTING HUMAN CELLS INTO ANIMALS TO BEGIN WITH. WHY AREN'T YOU USING RAT NEURAL STEM CELLS OR PIG STEM CELLS? WOULDN'T THAT BE A BETTER?

DR. MARSALA: THIS IS VERY GOOD POINT. SCIENTIFICALLY WHAT WE WOULD LIKE TO DO TO ESTABLISH EFFICACY WITH ALLOGENEIC RAT, RAT CELLS TO RAT, PIG CELLS TO PIG. BUT THERE IS A CLEAR REQUIREMENT BY

FDA THAT WE NEED TO ESTABLISH ALSO IN VIVO SAFETY OF YOUR CELL LINE, WHICH IS IN THIS CASE A HUMAN CELL LINE. SO WE NEED TO DO ANIMAL STUDIES ALSO FOR SAFETY BECAUSE YOU DON'T KNOW HOW THIS CELL LINE IS GOING TO BEHAVE AFTER TRANSPLANTATION. ONE, TRANSPLANTED INTO MICE SPINAL CORD, BUT THE SECOND INTO THE INJURED CORD WHERE IS HUGE INFLAMMATION. SO THESE CELLS CAN RESPOND TO TROPHIC FACTORS, THEY CAN CONTINUE TO PROLIFERATE FOR A LONG TIME, AND THEY CAN CREATE TUMOR IN THEORY. SO THIS IS WHY THEY REQUIRED THE IN VIVO STUDIES ALSO. I AGREE WITH THAT POINT.

DR. ROBERT TAYLOR: YOU SAID CELL LINE. IS THIS A CELL LINE OR ARE THESE PRIMARY?

DR. MARSALA: THIS WAS CELL LINE, ESTABLISHED CELL LINES. SO BASICALLY WAS ESTABLISHED FROM FIRST TRIMESTER SPINAL CORD, AND THEY ESTABLISHED CELL LINE EXPANDED FROM ONE DONOR.

DR. ROBERT TAYLOR: TRANSFORMED?

DR. MARSALA: NO. IT CAME UP IN THE PROTOCOL WHICH ALLOWS YOU TO DO VERY LONG-TERM EXPANSION OF CELLS WITHOUT CHANGING KARYOTYPE AND NO MUTATION.

DR. BOTKIN: QUICK COMMENT. I THINK WHAT WE'RE GOING TO BE DEALING WITH IN THIS DOMAIN IS THE

SCIENCE. AND I THINK YOU MAKE A PRETTY COMPELLING ARGUMENT THAT WE'RE NOT LIKELY TO SEE SMARTER RATS WITH THIS KIND OF THING, BUT THERE'S ALSO THE PUBLIC PERCEPTION PIECE. AND WE HAVE MUCH LESS CONTROL OVER HOW THE PUBLIC PERCEIVES THIS SORT OF THING. AND SO WOULDN'T NECESSARILY REGULATE THE SCIENCE DEPENDING ENTIRELY ON PUBLIC PERCEPTION, BUT WE HAVE TO BE SENSITIVE TO IT.

BUT I WOULD SAY ONE OF THE THINGS HERE IS THAT WE MAY BE -- WE HAVE TO BE CONCERNED ABOUT THE POSSIBILITY OF A MIXED MESSAGE. IN OTHER WORDS, YOU'RE PUTTING THOSE CELLS IN THERE BECAUSE YOU WANT TO SEE A SIGNIFICANT EFFECT. IF YOU WEREN'T LOOKING FOR A SIGNIFICANT EFFECT, WHAT'S THE POINT? BUT THEN YOU'RE GOING TO TURN AROUND AND SAY, WELL, IT'S ONLY A FEW CELLS. SO WHAT POSSIBLE EFFECT COULD THAT HAVE? THAT'S NOT A CONSISTENT MESSAGE. IT HAS TO BE A FAIRLY SOPHISTICATED WAY OF ARTICULATING THE FACT THAT YOU WANT A THERAPEUTIC EFFECT WHICH IS REAL; BUT ON THE OTHER HAND, YOU'RE NOT GOING TO CREATE ALGERNON, FLOWERS FOR ALGERNON.

DR. MARSALA: I AGREE.

DR. WAGNER: SO I WAS A MEMBER OF THE NATIONAL ACADEMY WHEN WE HAD THESE DISCUSSIONS, AND MUCH OF WHAT BOTH OF YOU JUST SAID WAS REALLY WHAT

WAS PRIMARY ON OUR MIND. WE HAD A VARIETY OF EXPERTS FROM THE FIELD BOTH BED AND VET MEDICINE AND WHAT THEY DO ABOUT CHANGES AND BEHAVIOR. AND WE HAD PHILOSOPHERS TALKING ABOUT WHAT'S HUMANNESS. SO DISCUSSIONS I THOUGHT I NEVER WOULD HAVE HEARD IN MY LIFE, BUT THEN WE HAD THIS PARTICULAR NATIONAL ACADEMY WORKSHOP. WHAT IT REALLY CAME DOWN TO, IT'S NOT SO MUCH THE SCIENCE. IT WAS ACTUALLY THE PUBLIC REASSURANCE THAT THERE WOULD BE SOME TYPE OF OVERSIGHT, THAT PEOPLE JUST COULDN'T DO THIS BECAUSE THEY HAD A GREAT IDEA.

AND IT JUST SO HAPPENED -- THIS ALL OCCURRED AS A RESULT IN PART OF THE PAPER OUT OF STANFORD SUGGESTING THAT YOU CAN ACTUALLY PUT IN A GENE INTO A MOUSE THAT WOULD BASICALLY ELIMINATE THE ANIMAL'S OWN BRAIN AND REPLACE IT POSSIBLY WITH HUMAN.

NO ONE WAS SAYING THAT, YES, YOU COULD ACTUALLY RECREATE THE HUMAN BRAIN IN A SMALL, LITTLE ENVIRONMENT. BUT ON THE OTHER HAND, WE ALSO BROUGHT IN EXPERTS THAT WERE ABLE TO -- HOW WOULD YOU DOCUMENT CHANGES IN BEHAVIOR? AND THERE'S SO MUCH UNKNOWN ABOUT IT, THAT YOU WOULDN'T BE ABLE TO KNOW NECESSARILY WHAT HAD BEEN CHANGED BECAUSE THERE REALLY WEREN'T THE TOOLS TO ASSESS CHANGES IN

BEHAVIOR. SO AT THE END OF ALL THAT, IT REALLY CAME DOWN TO MUCH OF WHAT THE WHOLE NATIONAL ACADEMIES GUIDELINES WERE FOR WAS TO CONTINUALLY REASSURE THE PUBLIC THAT THERE WAS GOING TO BE SOME TYPE OF MONITORING BEING DONE, THAT IT WAS IMPORTANT THAT THESE STUDIES COLLECT INFORMATION BECAUSE WE MIGHT LEARN SOMETHING OVER TIME ABOUT WHAT IS -- BECAUSE THE SCIENCE WASN'T THERE TO BE ABLE TO ASSESS IT.

SO I THINK IT REALLY COMES DOWN TO REASSURING THE PUBLIC THAT WE'RE NOT JUST DOING ANYTHING BECAUSE WE CAN, BUT THAT SOMEONE IS REALLY WATCHING OVER IT.

CHAIRMAN LO: I HEARD A NUMBER OF IMPORTANT POINTS TO MAKE. ONE IS THAT THERE ARE TECHNICAL CONSIDERATIONS CONCERNING THE NUMBER OF CELLS THAT YOU INJECT INTO A HUMAN ANIMAL AND THE LIMITATIONS OF THAT. A LOT OF COMMENTS HAVING TO DO WITH PUBLIC CONCERNS AND PUBLIC PERCEPTION AND HOW AS A PUBLIC AGENCY WE NEEDED TO PAY ATTENTION TO THAT.

AND THEN JOHN'S COMMENT, THAT THE REAL SUBSTANTIVE ISSUE WAS SOME SORT OF OVERSIGHT OVER THESE KINDS OF EXPERIMENTS. AND I JUST WANT TO UNDERSCORE THIS. HERE WE'RE REALLY TALKING ABOUT A LEVEL, A TYPE OF OVERSIGHT OF THESE EXPERIMENTS.

WE'RE NOT TALKING ABOUT BANNING THEM IN ANY WAY AND NOT FUNDING THEM. WHAT KIND OF OVERSIGHT SHOULD THERE BE? REALLY, AS JEFF CAN TELL US, DO WE NEED A SPECIAL COMMITTEE, A SCRO COMMITTEE, OR IS AN IRB THAT HAS THE OPTION OF ADDING SPECIALISTS IN NEUROSCIENCE AND STEM CELL SCIENCE SUFFICIENT, PARTICULARLY IN INSTITUTIONS THAT DON'T HAVE A SCRO ON-SITE.

DR. LOMAX: DID YOU MEAN TO SAY IACUC?

CHAIRMAN LO: IACUC. SORRY.

BUT, AGAIN, TO GO BACK TO DOROTHY'S COMMENT, THE ANIMAL WELFARE ISSUE IS STRAIGHT IN THE IACUC'S PERMIT. THEY KNOW HOW TO DO THAT. WHETHER THEY ARE REALLY SET UP TO DO -- WHAT DID YOU CALL IT -- MYSTICAL PHILOSOPHICAL QUESTION I THINK ISN'T TRUE.

LET ME JUST TOSS OUT ANOTHER SUGGESTION, GEOFF. GIVEN HOW IMPORTANT THESE PUBLIC PERCEPTIONS ARE AND GIVEN THAT TEN YEARS HAS ELAPSED SINCE THE NAS COMMITTEE THAT JOHN WAS ON GAVE ITS SEMINAL REPORT, IS THERE A ROLE FOR SORT OF A SYMPOSIA ON THE SCIENCE AS WE KNOW IT, SORT OF REALLY GOING THROUGH WHAT MARTIN WAS TALKING ABOUT, BRINGING IN SOME OF THE OTHER SCIENTIFIC CONSIDERATIONS THAT WE WERE JUST TALKING ABOUT, WOULD THAT BE USEFUL? AND

ALSO TO ADDRESS THE PUBLIC PERCEPTION BY BRINGING IN MEMBERS OF THE PUBLIC TO GIVE THEIR PERSPECTIVES. WOULD THAT BE USEFUL FOR CIRM TO DO TO SORT OF HELP TRY TO INFORM PUBLIC OPINION? THIS IS REALLY A HOT BUTTON QUESTION: WHAT IS HUMAN?

CO-CHAIR LANSING: I THINK SO MUCH OF THIS IS BASED ON FEAR BECAUSE -- AND IT'S BASED ON MOVIES THAT HAVE CREATED THAT. PUTTING ALL THESE THINGS IN THE RAT, THEY'RE GOING TO GET SMARTER THAN ME, IT'S *PLANET OF THE APES*. WE'VE DONE THOSE MOVIES.

CHAIRMAN LO: YOU'VE LITERALLY DONE THOSE MOVIES.

CO-CHAIR LANSING: I'VE LITERALLY DONE THEM AND I UNDERSTAND IT. AND THEN THIS SUPER RAT IS GOING TO COME. I THINK THEY EVEN MADE A MOVIE ABOUT THAT. A RAT'S GOING TO COME UP, A SUPER APE IS GOING TO COME UP AND TAKE IT. I ACTUALLY -- I'M AFRAID YOU CAN MAKE IT WORSE BY A PUBLIC FORUM. I NEVER WANT TO STEP AWAY FROM THE PUBLIC. BUT THERE'S SO MUCH. YOU'RE RIGHT. I DON'T KNOW. YOU PUT THAT IN, MAYBE THOSE RATS, YOU CAN'T MEASURE IT, BUT YOU CERTAINLY ARE CHANGING THEIR BRAIN IN SOME WAY. DOESN'T FRIGHTEN ME BECAUSE I THINK THE SCIENCE IS SO IMPORTANT, BUT YOU CAN HAVE SOMEONE SAYING, YOU CAN'T TELL ME THAT THAT BRAIN -- IT

WASN'T BORN WITH THIS. IT SHOULDN'T BE THIS WAY. WE'RE TAMPERING WITH GOD. AND IN ADDITION TO TAMPERING WITH THAT, YOU COULD HAVE THIS SUPER RAT THAT'S GOING TO TAKE OVER THE WORLD.

AND BY THE WAY, ANYTHING THAT WE INJECT INTO AN ANIMAL, IT LEAVES YOU OPEN TO ALL OF THIS. AND GOD KNOWS WE'VE ALL BEEN PICKETED FOR THIS. SO I THINK WHAT'S IMPORTANT FOR US, TO BE AS HUMANE AS POSSIBLE, WHICH I THINK IS TAKEN CARE OF, AND THEN TO EVALUATE THE SCIENTIFIC EVIDENCE, WHICH SEEMS TO BE WHAT YOU'RE SAYING. I BELIEVE YOU. AND TO PROCEED AND MAYBE CONSTANTLY -- I DON'T MIND HAVING SOMEONE THERE TO CONSTANTLY EVALUATE IT. IS THAT RAT SUDDENLY GETTING OUT OF THE CAGE WHEN IT NEVER DID BEFORE? SOMEBODY BETTER TELL US. SOME OF IT. I'M MAKING THIS UP. SOMETHING THAT WE SAY WE'RE GOING TO MAKE SURE THAT REALLY IT HASN'T SUBSTANTIALLY AFFECTED THE BEHAVIOR, THAT WE'RE MONITORING THE SITES WHERE WE'RE DOING THIS. THAT, I THINK, MAKES SENSE.

DR. LEE: JOHN WAS MENTIONING IT'S THE MONITORING ISSUE THAT'S -- YOU DON'T WANT TO BE OBSTRUCTIONIST TO ANYTHING. OF COURSE, THE EXPERIMENTS THAT WE'RE PUTTING STUFF IN SPINAL CORD. BUT THERE'S STUFF THAT MOLECULAR PSYCHIATRISTS ARE

DOING. AGAIN, I'M A SCIENTIST, BUT I'M SENSITIVE TO WHAT PEOPLE MAY THINK. AND THEN THE PROBLEM'S HOW TO DEVELOP A POLICY THAT IS NOT RESTRICTIVE THAT ALSO SHOWS THAT IF WE ARE DOING A CERTAIN KIND OF EXPERIMENTS, WHAT KINDS OF MONITORING DO YOU WANT? DO WE GO EVERY DAY AND SAYS TO THE RAT CAN YOU SAY HELLO? THESE PEOPLE ARE TESTING TRANSPLANTED -- JOKES THAT SAY BEHAVIORAL TESTS, RIGHT. SO LET'S SAY FINDING THE PLATFORM UNDERWATER, AND IT TAKES ON AVERAGE OF SIX SECONDS OR 15 SECONDS. AND YOU DO ENOUGH MICE AND YOU GET A STANDARD DEVIATION. IF YOU DO ENOUGH EXPERIMENTS AND THE MICE FINDS IT IN TWO SECONDS, IS THAT A CAUSE FOR WORRY? I DON'T KNOW, BUT THERE ARE LOT OF GRAY AREAS AROUND.

CHAIRMAN LO: UNDERSCORE THE ISSUE OF MONITORING, BUT ALSO THE ISSUE TO DEAL WITH THIS OVERSIGHT BEFORE THE RESEARCH COMMENCES. WHAT TYPE OF OVERSIGHT BY WHOM?

DR. ROBERTS: I UNDERSTAND SHERRY'S CONCERN, BUT I ALSO THINK ABOUT OPENING IT UP TO THE PUBLIC, BUT I THINK THE QUESTION OF MONITORING BEGS THE QUESTION OF WHAT ARE THE STANDARDS THAT THE MONITORS ARE GOING TO APPLY BECAUSE I'M STILL NOT CLEAR FROM OUR DISCUSSION WHAT IS THE WORRY. I'M NOT SAYING THERE IS NO WORRY, BUT WHAT IS THE

WORRY --

DR. MILLS: HOW DO YOU KNOW WHEN WE CROSS IT?

DR. ROBERTS: HOW DO YOU KNOW IT WHEN YOU CROSS IT? EXACTLY. AND ALSO, IS THERE SOMETHING SPECIAL ABOUT THE BRAIN THAT I WAS ASKING BEFORE? YOUR COMMENTS ABOUT IT'S MORE NUANCED JUST COMPLICATE IT MORE. IT DOESN'T ANSWER THE QUESTION. IT'S SO COMPLICATED ABOUT EXACTLY WHAT ARE WE WORRIED ABOUT WHEN WE INJECT HUMAN STEM CELLS INTO ANIMAL BRAINS?

DR. LEE: THAT'S THE CRUX OF THE QUESTION, ISN'T IT?

DR. ROBERTS: THAT'S THE QUESTION. SO I THINK MAYBE SOME KIND OF WORKSHOP OR SOMETHING WHERE THAT ALLOWS THE SCIENTISTS AND BIOETHICISTS AND SOME MEMBERS OF THE PUBLIC. AGAIN, I DON'T THINK WE WANT THESE -- WE COULD PUT ASIDE THE WORRY ABOUT THE SUPER RAT THAT TAKES OVER THE WORLD, BUT WE DO HAVE WORRIES ABOUT THE RAT WHOSE BEHAVIOR CHANGES, FOR EXAMPLE. BUT WHAT TYPE OF BEHAVIORAL CHANGES? HOW MUCH OF A BEHAVIORAL CHANGE? WHY ARE WE WORRIED ABOUT THOSE BEHAVIORAL CHANGES? THOSE KINDS OF QUESTIONS, I THINK, WOULD BE INTERESTING TO EXPLORE BECAUSE I DON'T THINK THERE'S AN ANSWER TO THEM YET.

CHAIRMAN LO: TED AND THEN JOHN, AND THEN WE SHOULD BE WORKING OUR WAY TOWARDS A BREAK.

DR. PETERS: I HAVE TWO COMMENTS, ONE ABOUT THE SYMPOSIUM AND ONE ABOUT ANIMAL WELFARE. I LIKE THE IDEA OF A SYMPOSIUM LIKE THIS; BUT, AS SHERRY WAS SUGGESTING, THIS IS A BIG TOPIC, NOT A LITTLE ONE. THE REALLY BIG ONE THAT MAKES *TIME MAGAZINE* AS WELL AS ACADEMIA IS IS THE MIND THE BRAIN OR NOT. MOST NEURAL LABORATORY RESEARCHERS DON'T THINK SO, BUT THE NEUROPHILOSOPHERS AND THE NEUROPSYCHOLOGISTS AND MEDIA PEOPLE, THEY ALL LOVE THIS DEBATE. SO IF WE WERE TO TRY TO FOCUS ON JUST THE ISSUE THAT MARTIN RAISED UP, WE'D BE HOLDING UP A ROOM FAN IN LIGHT OF A HURRICANE. FRANKLY, I LIKE THAT IDEA. AND THERE WOULD BE A LITTLE BIT OF PHILOSOPHICAL CONTRIBUTION THAT THIS DISCUSSION WOULD MAKE BECAUSE IT WOULD SUGGEST, NO, THE MIND IS NOT ISOMORPHIC WITH THE BRAIN.

AT ANY RATE, I KIND OF LIKE THAT IDEA, BUT THEN I LIKE SYMPOSIA.

WITH REGARD TO ANIMAL WELFARE, I THINK WE COULD, IN ORDER TO PROTECT THE WELFARE OF THE ANIMAL, COME UP WITH A REG THAT SAYS YOU COULDN'T PUT REPUBLICAN STEM CELLS INTO BRAINS OF AN ANIMAL.

DR. TAYLOR: THEY'RE ALREADY THERE.

CHAIRMAN LO: JOHN, LAST WORD BEFORE WE BREAK.

DR. WAGNER: I DON'T KNOW HOW YOU FOLLOW THAT. TWO THINGS. ONE IS THAT YOUR QUESTION, SORT OF MY FIRST OBSERVATION WAS THAT AFTER A TWO-DAY SYMPOSIUM, I'M NOT SURE THAT WE WERE ANY FURTHER ENLIGHTENED, BUT I THINK THAT IT DID REASSURE THE PUBLIC THAT WE WERE THINKING ABOUT IT. AND IT DIDN'T RESULT IN NEWS REPORTS ALL OVER THE WORLD. SO IT WASN'T AS IF -- WE DIDN'T OPEN PANDORA'S BOX TO THE MEDIA.

ON THE OTHER HAND, THE OTHER QUESTION IS WHAT'S CHANGED IN THE PAST TEN YEARS THAT WE DIDN'T KNOW THEN? AND YOU HAVE TO BE VERY THOUGHTFUL IN WHO YOU WOULD WANT TO BRING TO THIS SYMPOSIUM, BUT I TOO THINK -- IT WAS AN INTERESTING DISCUSSION, AND I THINK THAT WE HAVE TO RECOGNIZE THAT THE IDEA OF CHIMERISM IS THAT CONCERNING YUCK FACTOR THAT THE PUBLIC SEES, AND IT'S REALLY CHIMERISM IN THE BRAIN. I DON'T THINK WE CARE ABOUT ANY OTHER ORGAN BECAUSE I BELIEVE THEY FEEL THIS IS THE SEAT OF THE SOUL, THE SEAT OF HUMANNESS, WHATEVER THE RIGHT TERMINOLOGY IS. WHETHER YOU BELIEVE IT OR NOT, IT'S JUST HOW THE PUBLIC IN GENERAL, AT LEAST A LARGE PROPORTION, THINK ABOUT IT.

CO-CHAIR LANSING: I YIELD TO THE MAJORITY IF YOU WANT TO DO A SYMPOSIUM. IT HAS TO BE OPEN TO THE PUBLIC. SO WE CAN'T RESTRICT WHO COMES AND WHO DOESN'T, WHICH IS FINE.

BUT I THINK ACTUALLY THEY CARE ABOUT EVERYTHING. THE PEOPLE THAT I'VE TALKED TO, THEY CARE. A RAT'S GOING TO HAVE THREE ARMS, AND IS THE RAT GOING TO BE ABLE TO --

DR. WAGNER: THE *LIFE MAGAZINE* WITH THE EAR COMING OUT OF A RAT. THAT DOESN'T HELP THE CONVERSATION.

CO-CHAIR LANSING: IT DOESN'T. THAT'S NOT A MOVIE. I GUESS WHAT I'M SAYING, I'M SAYING THAT IT IS A VERY HOT BUTTON ISSUE. I DON'T MIND HAVING A SYMPOSIUM, AND I DO THINK ASSURING THE PUBLIC THAT WE'RE GOING TO BE -- WHAT WOULD YOU MONITOR FOR? YOU WOULD MONITOR FOR ANY BEHAVIOR THAT APPEARS DANGEROUS IN SOME WAY. I COULD MAKE A CASE -- THIS MAY BE NOT SOMETHING ANYBODY WANTS TO HEAR -- THAT IF YOU PUT THOSE THINGS AND WE GET A BREED OF SMARTER RATS WHO CAN DO SOMETHING QUICKER OR BETTER, AS LONG AS IT DOESN'T HURT ME, IT MIGHT NOT BE THE END OF THE WORLD. SERIOUSLY, IF YOU SAY THAT'S NOT THE END OF THE WORLD. IF YOU INJECT MORE CELLS INTO MY BRAIN AND I BECOME SMARTER, I'D BE VERY HAPPY.

BUT IT'S ALWAYS THE FEAR OF DANGER. IT'S THE FEAR OF BEING HURT BY THIS THING. THAT'S REALLY WHAT IT IS AND TAMPERING WITH THE ORDER, FINANCIAL ORDER.

SO I GUESS WHAT I WOULD WANT TO SAY IS TELL ME EXACTLY WHAT WE'RE LOOKING FOR TODAY THAT YOU'RE LOOKING FOR. THAT'S BECAUSE I WOULDN'T WANT US TO SLOW UP WHAT WE'RE DOING. I WANT TO KNOW EXACTLY WHAT YOU'RE LOOKING FOR TODAY SO THAT WE DON'T SLOW UP THIS EXTRAORDINARY RESEARCH THAT IS HAPPENING AND MAYBE COULD SAVE SOME LIVES. AND I'D LIKE TO KNOW WHAT IT IS YOU'RE LOOKING FOR US, AND THEN WE CAN ADD TO THAT, THAT WE WOULD HAVE A SYMPOSIUM TO MAKE SURE THAT WE MONITOR IT PROPERLY AND KNOW WHAT WE'RE LOOKING FOR.

CHAIRMAN LO: TO FOLLOW UP ON SHERRY, WE'VE HAD A VERY FASCINATING, FAR-REACHING DISCUSSION WHICH WAS CENTRIFUGAL, GOING WAY OUT TO INTERESTING IDEAS. WE DO NEED NOW TO GET CENTRIPETAL AND SAY, GEOFF IS ACTUALLY SUBMITTING FOR OUR CONSIDERATION A VERY SPECIFIC SET OF AMENDMENTS TO THE MEDICAL AND ETHICAL STANDARDS THAT WE SORT OF NEED TO COME BACK TO. THAT'S THE FIRST ORDER OF BUSINESS. THE OTHER ISSUES THAT WE'VE BEEN DISCUSSING, THE SYMPOSIUM, WHATEVER SHAPE IT MIGHT BE, IS SOMETHING SORT OF FOR STAFF AND CIRM

LEADERSHIP TO THINK ABOUT, BUT IT'S NOT SOMETHING WE'RE GOING TO REALLY WANT TO GRAPPLE WITH. OUR JOB IS TO RAISE IT AS AN OPTION, A POSSIBILITY.

SO I'M GOING TO SAY LET'S TAKE A 15-MINUTE BREAK. AND YOU'RE THE OFFICIAL TIMEKEEPER. WHEN DOES THAT MEAN WE COME BACK?

DR. LOMAX: 3:20.

CHAIRMAN LO: WHEN WE COME BACK, WE'RE GOING TO DO WHAT SHERRY SAID, FOCUS ON WHAT WE NEED TO SORT OF MAKE A RECOMMENDATION ON TODAY. GEOFF CAN SET THAT UP, AND WE'LL ASK GEOFF TO START WITH THAT AFTER THE BREAK.

(A RECESS WAS TAKEN.)

CHAIRMAN LO: OKAY. WITH THAT, LET'S MOVE AHEAD WITH WHAT GEOFF HAS FOR US.

DR. LOMAX: SO, AGAIN, IT WAS LAID OUT IN THE BRIEFING DOCUMENT. I HOPE THAT WAS HELPFUL. WHAT WE'VE BEEN LOOKING AT IN PARTICULAR IS A BOTTLENECK THAT WE'RE TRYING TO DEVELOP OPTIONS ON OR THE TYPES OF STUDIES THAT WERE DESCRIBED BY DR. MARSALA. SO IT'S THE INTRODUCTION OF CELLS INTO ANIMALS, AND IT'S GENERALLY DONE IN A REGULATED CONTEXT.

CURRENTLY OUR REGULATIONS WOULD REQUIRE NOT ALL, BUT CERTAIN TYPES OF STUDIES, DEPENDING ON

THE CELL, EITHER THE TYPES OF CELLS BEING USED OR THE TARGET FOR THOSE CELL INJECTIONS, TO UNDERGO REVIEW BY A STEM CELL RESEARCH OVERSIGHT COMMITTEE. AND WHAT WE ARE ASKING YOU ALL IS CAN WE CHANGE THAT TO ALLOW ORGANIZATIONS THAT ARE COMING TO CIRM THAT DON'T HAVE THE SCRO CAPACITY TO CONDUCT THOSE TYPES OF STUDIES.

SO BASED ON CONSULTATION WITH BERNIE AND DIFFERENT STAKEHOLDERS IN THE FIELD, WE SORT OF DECIDED THAT WE'VE KIND OF TRIED TO DEVELOP A MENU OF OPTIONS THAT SORT OF RUNS THE SCOPE. IN TERMS OF THOSE BACKGROUND INTERVIEWS, A NUMBER OF ISSUES THAT CAME UP HERE, AND THAT WAS A TERRIFIC DISCUSSION, BY THE WAY, BECAUSE THOSE ISSUES HAVE COME UP, WE TRIED TO DEVELOP A MENU THAT KIND OF CAPTURES THE CONSIDERATIONS AND THE ISSUES THAT SEEM IMPORTANT FOR THIS TYPE OF WORK. SO THAT DISCUSSION WAS VERY REASSURING. I WOULD HOPE THIS MENU ACTUALLY ALIGNS NICELY WITH HAT A RECOMMENDATION MIGHT BE.

SO I'VE LISTED FOUR OPTIONS HERE IN TERMS OF POLICY OPTIONS. ONE WOULD BE REMOVE THE REQUIREMENT FOR REVIEW OF ANIMAL TRANSPLANTATION STUDIES ENTIRELY, AND ANIMAL RESEARCH WOULD STILL BE SUBJECT TO IACUC REVIEW AND OVERSIGHT, BUT IT WOULDN'T GET THE TYPE OF REGULATORY LANGUAGE AROUND

IT WHICH WE HAVE IN THE REGULATIONS NOW.

SORT OF A MORE NARROW OPTION, AND THESE SORT OF NARROW DOWN TO SOME EXTENT, SO IT'S SORT OF THE WIDEST OPTION AND THEN A GRADUAL NARROWING.

DR. LEE: JUST TO BE SURE, ARE WE TALKING ABOUT TRANSPLANTATION INTO BRAIN?

DR. LOMAX: NO. SO THE CURRENT REQUIREMENT, YOU CAN SEE THE LANGUAGE IN THE STANDARDS AT THE TOP OF THAT SECTION HIGHLIGHTED IN BLUE. LET ME JUST GET THAT FOR YOU.

DR. LEE: I KNOW WHERE IT IS, PAGE 4, LINE 60.

DR. LOMAX: IT'S ON PAGE 4 STARTING AT LINE 63. SO YOU CAN SEE THE SUBSTANCE OF THE REGULATION.

AGAIN, THESE OPTIONS ARE SOMEWHAT INTERACTIVE, SO YOU CAN SORT OF MIX THEM TOO IF YOU FELT IT WAS APPROPRIATE. CONSIDER EXEMPTING RODENT STUDIES OR STUDIES MANDATED PURSUANT TO AN FDA REQUIREMENT. SO THE FDA-MANDATED PRECLINICAL STUDIES. THE IDEA THERE BEING SORT OF ESOTERIC STUDIES THAT ARE KIND OF JUST BEING DONE BECAUSE YOU COULD WOULD STILL BE SUBJECT TO REVIEW; BUT ONCE SOMEONE HAS ENTERED A REGULATORY PATHWAY, YOU COULD SORT OF DO THOSE STUDIES BECAUSE THEY'RE REQUIRED BY

FDA.

ANOTHER WAY OF LOOKING AT THAT OPTION IS THERE ARE CERTAIN STUDIES OF INTEREST WHERE YOU THINK ADDITIONAL REVIEW AND OVERSIGHT IS WARRANTED. AND THAT'S, FOR EXAMPLE, A STUDY THAT WOULD BE DESIGNED TO ENGRAFT HUMAN ORGANS OR FEATURES. THOSE WERE THE SORT OF TWO TOUCHSTONES THAT CAME UP IN TERM OF DOROTHY'S QUESTION, WHAT ARE WE WORRIED ABOUT. IF IT STARTS TO LOOK HUMAN OR SORT OF YOU'RE GROWING HUMAN PARTS IN IT, THAT WAS THE SORT OF FEEDBACK WE GOT THAT COULD SORT OF TRIGGER THAT LEVEL OF CONCERN.

AND THEN THE FOURTH ONE, AND THIS IS REALLY DESIGNED KIND OF WITH ADMINISTRATIVE, SORT OF LOOKING AT THE ADMINISTRATIVE REALITY, IS CONSIDER MAINTAINING THE CURRENT REVIEW REQUIREMENT AND GIVE AWARDEES THE OPTION OF HAVING THEIR IACUC PERFORM THE REVIEW AS SPECIFIED IN OUR REGULATIONS. SO WHAT WE ENVISION THAT INVOLVING WOULD BE THAT -- AND WE SPOKE TO SOME COMPANIES ABOUT THIS, AND THEY SAID THAT WOULD ACTUALLY BE SOMETHING THEY COULD DO -- IS THEY'D LOOK AT OUR REGULATIONS AND THEY WOULD STATE THAT THEIR IACUC IS GOING TO PERFORM THE FUNCTION OF THE ESCRO COMMITTEE WITH REGARD TO ANIMAL STUDIES AS REQUIRED IN OUR REGULATIONS. SO IT'S BOTH SORT OF

DEFERRING TO THE IACUC, BUT NOT JUST SAYING AN IACUC IS GOOD ENOUGH. IT'S SAYING THE IACUC ALSO HAS TO BE SORT OF COMMITTED TO DO THE KIND OF LEVEL OF REVIEW AND MONITORING THAT OUR REGULATIONS REQUIRE.

AND THEN OPERATIONALLY WE WOULD, AGAIN, WANT THEM TO SORT OF SAY, FOR THE PURPOSE OF COMPLIANCE WITH THIS SECTION, OUR IACUC WILL PERFORM THE FUNCTIONS REQUIRED IN THE CIRM REGULATION. SO THAT'S THE MENU, IF YOU WILL.

DR. ROBERT TAYLOR: GEOFF, I HAVE A QUESTION. I COLLABORATE ON ANIMAL MODELS, BUT I DON'T REALLY DO THEM IN MY OWN LAB. IS THERE SOMETHING LIKE A WESTERN IACUC, A CENTRALIZED IACUC THAT PROVIDES THAT SERVICE BROADLY LIKE HAPPENS FOR IRB'S? KIND OF THINKING AHEAD. BECAUSE THAT WOULD BE A GROUP, IF SUCH A THING WERE TO EXIST OR EXISTED, THAT YOU COULD ACTUALLY GET YOUR CRITERIA INTO. I DON'T EVEN KNOW IF SUCH A THING -- I DO BELIEVE THAT FROM THE IRB SIDE, WE'LL SEE MORE AND MORE INSTITUTIONS GOING TO THESE KIND OF CENTRALIZED IRB'S. MAYBE THE SAME TREND WILL OCCUR FOR IACUC WHERE YOU'D HAVE A ONE-STOP SHOP.

DR. LOMAX: MY UNDERSTANDING IS THAT THE EQUIVALENT DOESN'T EXIST IN THE IACUC WORLD BECAUSE THE IACUC, IT'S TIED TO THE PHYSICAL FACILITY AS

OPPOSED TO AN IRB, WHICH CAN EXIST AS A KIND OF EXTERNAL REVIEW BODY. A LOT OF THE IACUC FUNCTIONS ARE ABOUT PHYSICAL HANDLING AND HUSBANDRY OF THE ANIMALS. SO IT TIES TO THE POINT OF INTERACTION, IF YOU WILL. I THINK THAT'S CORRECT.

CHAIRMAN LO: GEOFF, CAN I ASK YOU A QUESTION ABOUT OPTION 2, EXEMPTING STUDIES THAT ARE CARRIED OUT IN ACCORDANCE WITH FDA REQUIREMENTS FOR RESEARCH. SO I'M ASKING A QUESTION ABOUT OPTION NO. 2. EVEN IF THE FDA REQUIRES THAT SUCH A STUDY BE DONE, WOULD THE FDA REVIEW, WHAT'S SUBMITTED TO IT AS A PROPOSED ACTION PLAN, DO THEY ACTUALLY LOOK AT THE ISSUES WE'RE CONCERNED ABOUT AS OPPOSED TO YOU HAVE THE RIGHT NUMBER OF ANIMALS, ARE YOU MAKING THE RIGHT MEASUREMENTS, THOSE SORTS OF MORE TECHNICAL HOW ARE YOU CARRYING OUT THE RESEARCH? AND THEN MY UNDERSTANDING, GEOFF, THE FDA SAYS AND THE IACUC NEEDS TO MAKE SURE, YOU HAVE TO PASS IACUC'S IRREVOCABLE OR YOUR IACUC'S REVIEW FOR ANIMAL WELFARE.

THOSE OF YOU WHO HAVE DONE PRECLINICAL STUDIES, CAN YOU GET THE FDA TO SIGN OFF ON THESE STUDIES WITHOUT HAVING ISSUES THAT WE ARE SORT OF MOVING AROUND ON CONSIDERED BY THE FDA? SO WE'RE DEFERRING TO THE FDA. ARE THEY ACTUALLY REVIEWING

IT BECAUSE IT'S A CONCERN FOR IRB'S, FOR EXAMPLE. THEY DON'T SAY THAT THE FDA MANDATED THE STUDY THAT WOULD EXEMPT IT FROM REVIEW. I DON'T DO THIS TYPE OF RESEARCH.

DR. MARSALA: I THINK THERE ARE TWO SCENARIOS. ONE IS WE WOULD HAVE A GLP FACILITY IN AN ACADEMIC INSTITUTION. SO THIS WOULD BE DIFFERENT THAN IF YOU ARE RUNNING YOUR GLP STUDY IN CRO. IF DONE IN CRO, USUALLY THE PROCESS IS VERY FAST, AND THEY WOULD COMPLY FOR WHATEVER ANIMALS YOU WANT TO DO. AT AN ACADEMIC INSTITUTION, FOR EXAMPLE, FDA WOULD SUGGEST TO YOU TO DO MAYBE 12, 16 ANIMALS PER GROUP FOR SAFETY, LONG-TERM SAFETY. THEN IACUC MAYBE CAN LOOK AT IT. WHY DO YOU REALLY NEED 16 ANIMALS? BUT THEN THIS WILL BE THE DISCUSSION, THAT ONCE YOU HAVE IT, BASICALLY HAVE THE OFFICIAL REQUIREMENT FROM FDA, I THINK IT WILL BE APPROVED EVENTUALLY IN AN ACADEMIC INSTITUTION, BUT IT WILL BE LONGER PROCESS THAN CRO.

MR. SHEEHY: JUST FROM MY PERSPECTIVE, IT DOESN'T SEEM TO REFLECT A SENSE OF URGENCY TO ACTUALLY ADD ANOTHER STEP WHEN THERE'S A REGULATORY REQUIREMENT. YOU'RE TALKING ABOUT SOMETHING THAT YOU'RE HOPING AT THAT POINT WILL MAKE A DIFFERENCE IN PATIENTS.

SO WHEN THE FDA IS ASKING FOR A PRECLINICAL STUDY, YOU'RE ON THE ROAD TO GETTING AN IND AND ACTUALLY TRYING TO ESTABLISH SAFETY IN AN ACTUAL PATIENT AND THE THERAPY YOU THINK WILL SAVE LIVES. SO WHILE WE LOSE SOME ETHICAL OVERSIGHT, IT'S NOT THE ETHICAL PRIORITY ACTUALLY GETTING SOMETHING INTO PATIENTS. AND I WOULD THINK THAT, AT LEAST GIVEN THE MISSION OF CIRM, THAT I WOULD LEAN MORE STRONGLY TOWARDS ACCELERATING TREATMENTS TO PATIENTS THAN I WOULD FOR, AT THIS STAGE OF RESEARCH, WHICH IS PRECLINICAL, WHEN IT'S MANDATED BY A REGULATORY AGENCY, SO IF WE STOP IT, YOU STOP THE THERAPY. AND THERE ARE IRB'S INVOLVED AND IACUC'S. WHY WE WOULD PUT IN ANOTHER LAYER THAT DIDN'T HELP MAKE THE THERAPY AVAILABLE TO PATIENTS IS KIND OF --

CHAIRMAN LO: THE IRB WOULDN'T REVIEW THIS PRECLINICAL RESEARCH.

MR. SHEEHY: THEY WILL REVIEW THE THERAPY BEFORE IT GOES INTO PATIENTS. SO THE FDA NEEDS THIS. THE IACUC WILL REVIEW IT FOR THE ANIMAL STUDIES. THE IRB WILL REVIEW FOR THE THERAPY GOING INTO A PATIENT. SO WHAT IS THE ROLE OF THE SCRO EXCEPT ANOTHER BOX TO CHECK THAT SLOWS DOWN THE REVIEW?

DR. PATRICK TAYLOR: NICE SEGUE. SO I WAS CURIOUS. ONE OF THE FUNCTIONS HERE OF THE ESCRO IS TO ESTABLISH PROVENANCE FOR THE CELL LINES. THIS IS AN ISSUE THAT I WORRY ABOUT. SO THE QUESTION IS IF YOU LOOK AT THE CRITERIA FOR WHAT ESCRO'S ARE SUPPOSED TO ASSURE, YOU ACTUALLY EXCEED THE SCOPE OF A NORMAL IACUC REVIEW IN A COUPLE PARTICULAR RESPECTS. ONE OF THOSE IS PROVENANCE OF THE CELL LINES. WE MAY HAVE CONTROLS FOR THAT, BUT IT'S NO NECESSARY FOR US TO DO THAT. BUT I GUESS THE CONCERN WOULD BE SINCE IACUC IS ALREADY LOOKING AT THAT QUESTION AND IRB'S ARE HERE, WHETHER OR NOT THE DATA WOULD BE STRUNG OUT LATER ON OR YOU GUYS SORT OF LOOK FOR PROBLEMS WITH BAD CELL LINES. THAT'S MY QUESTION.

MR. SHEEHY: WOULDN'T THAT BE ADDRESSED AT SOME EARLIER STAGE? WE'RE TALKING EXCLUSIVELY ABOUT THE FDA COMING IN AND SAYING, OKAY, HERE'S YOUR PRODUCT. IF YOU'RE COMING IN FOR AN IND, I NEED A TOX STUDY INVOLVING X NUMBER OF MICE WITH YOUR LINE. THAT SEEMS LIKE A VERY STRANGE PLACE TO PUT THE BRAKES ON.

DR. PATRICK TAYLOR: I DON'T MEAN TO (INAUDIBLE) PROCEDURAL POINT. BUT IN ANY EVENT, IT PRODUCES BRAKES REALLY IF YOU CARE WHETHER OR NOT --

I ALREADY ASKED THE QUESTION. IS THERE SOME OTHER PLACE OR ELSEWHERE IN THE SYSTEM TO GET THEIR PROVENANCE?

DR. LOMAX: YES. THE PROVENANCE -- THE CELL LINES HAVE TO MEET CERTAIN ACCEPTANCE CRITERIA, AND THOSE ARE WELL DEFINED IN THE REGULATIONS. AND THEY CAN BE -- TYPICALLY, ACTUALLY THE OVERSIGHT COMMITTEE DOESN'T OFTEN NEED TO BE INVOLVED BECAUSE MOST OF THE LINES COMING IN ARE ALREADY WITHIN AN NIH REGISTRY OR COME FROM SOME SAFE HARBOR. BUT THERE IS A REQUIREMENT THAT CARRIES KIND OF THE RULE OF LAW. IF SOMEONE WANTED TO COME IN WITH A CELL LINE, THEY WOULDN'T GET PAST GO IN THE EARLY STAGE. SO IT IS HANDLED IN A SEPARATE, BUT IT'S BY RULE, SO TO SPEAK. DOESN'T NEED A --

DR. PATRICK TAYLOR: SO IT'S ASSURED AT GRANTS REVIEW STAGE?

DR. LOMAX: WE HAVEN'T HAD A CASE IN YEARS WHERE WE'VE HAD AN UNUSUAL -- I MEAN THE CELL LINES THAT ARE BEING APPLIED ARE CELL LINES THAT ARE ALMOST ALL NIH REGISTRY LINES AT THIS POINT.

DR. PATRICK TAYLOR: SO ONE OF THE COOL THINGS ABOUT CIRM IS THEY HAVE SO MANY OTHER PROCESSES IN PLACE THAT CAN TAKE OVER FROM THE ESCRO'S.

DR. LOMAX: CORRECT. IN FACT, WE'VE DONE SOMETHING SIMILAR. A FEW YEARS AGO WE GIVE -- AGAIN, TO ADDRESS THIS EXACT ISSUE, IF SOMEONE IS USING A CELL LINE AND THEY DON'T HAVE AN ESCRO COMMITTEE, IT'S PART OF THEIR COMPLIANCE STATEMENT. IF THEY CERTIFY THAT THEY'RE USING A LINE AND THAT SATISFIES OUR STANDARDS, AND IT'S PART OF THE PRE-AWARD PROCESS.

DR. PATRICK TAYLOR: YOUR STANDARD IS DESIGNATING THE LINES BASICALLY.

DR. LOMAX: YES. CRITERIA FOR ACCEPTING A LINE.

MR. SHEEHY: I JUST WANT TO GO BACK TO THE NARROWNESS OF THE EXEMPTION. IT REALLY IS FDA-MANDATED STUDIES. SO THERE'S A LOT OF WORK THAT'S BEEN DONE IN ANIMALS UP TO THAT POINT. AND PRESUMABLY A LOT OF THESE ISSUES WOULD HAVE BEEN ADDRESSED. HOW DO YOU KNOW YOU EVEN HAVE A PRODUCT THAT HAS ANYTHING THAT'S GOING ON UNTIL YOU'VE BEEN IN ANIMALS QUITE A BIT? IT'S ONLY WHEN YOU'RE ACTUALLY GOING TO FILE AN IND, THE FDA SAYS YOU HAVE TO DO X, Y, AND Z. I JUST THINK THAT THAT'S WAY DOWN THE RIVER FROM WHERE THE SCRO SHOULD BE INTERVENING AND WOULD HAVE INTERVENED ON ALL THE ISSUES YOU JUST IDENTIFIED AT SOME POINT BEFORE

THAT.

DR. PATRICK TAYLOR: I THINK GEOFF ACTUALLY ANSWERED MY QUESTION.

DR. BOTKIN: SO THAT FIRST BULLET IS VERY HELPFUL FOR ME AS APPLIED FROM A FUNCTIONAL STANDPOINT. THE SCRO'S AREN'T CHANGING PROTOCOLS. SO THERE MAY BE STILL BE SOME PUBLIC REASSURANCE SERVICE HERE, BUT WHAT ELSE WOULD WE EXPECT THE SCRO'S TO BE DOING? YOU GUYS ARE DETERMINING THE QUALITY OF THE SCIENCE. SO WE DON'T REALLY NECESSARILY NEED THEM TO REVIEW THE SCIENCE PER SE. IACUC'S LOOKING AFTER ANIMAL WELFARE. ANY OTHER SORT OF INSTITUTION LEVEL ISSUES THAT THE SCRO WOULD BE LOOKING AT, LIKE WHETHER A PARTICULAR INSTITUTION CAN ACTUALLY CONDUCT THE WORK BEING PROPOSED WITH THE TYPE OF OVERSIGHT THAT THE IACUC WOULDN'T KNOW ABOUT? I'M SORT OF LOOKING FOR SOME FUNCTION THAT MIGHT BE THERE. IT SEEMS TO ME ONE OTHER ALTERNATIVE IS TO PERHAPS ENCOURAGE INSTITUTIONS TO ENHANCE THE EXPERTISE ON THEIR IACUC COMMITTEES WITH SOME STEM CELL FOLKS.

DR. WAGNER: THAT'S IT. IT JUST GUARANTEES THE TYPE OF MAKEUP. DEPENDS ON WHAT THE SCRO DOES, BUT THE IACUC MIGHT NOT HAVE THE SAME PROFICIENCIES.

DR. LOMAX: WE HAVE DR. WAGNER IN THE ROOM AND YOU WERE THERE. SO I SORT OF POURED OVER THE NATIONAL ACADEMIES' RECOMMENDATIONS AND NOTES. MY SENSE WAS, PERHAPS YOU HAVE A VIEW ON THIS, IS THAT THE SCRO WAS LARGELY INITIATED TO ADDRESS ISSUES RELATING TO EMBRYO USE BECAUSE THAT WAS THE INITIAL GAP. AND THEN YOU HAVE THE CONCEPT OF BLASTOCYST COMPLEMENTATION OR WORKING WITH EMBRYOS AND MIXING SPECIES INTO SORT OF TRUE CHIMERAS. AND THAT, IF YOU LOOK AT NATIONAL ACADEMIES, THEY MAKE A VERY STRONG STATEMENT THAT THAT'S IN THE PURVIEW OF THE ESCRO COMMITTEE.

BUT THEN WHEN YOU COME OUT THE NEXT STEP TO KIND OF THE ADULT ANIMALS, THE RECOMMENDATION GETS A LOT VAGUER. IT'S A LITTLE BIT MORE, WELL, IT MIGHT BE GOOD TO THINK ABOUT. IT SEEMED LIKE THE CENTER OF GRAVITY, IF YOU WILL, ON THE OVERSIGHT AND WHERE YOU NEED AN EXTRA PAIR OF EYES IS ON THE EMBRYO-SPECIFIC TYPE OF ACTIVITIES.

AGAIN, ON THE ANIMAL SIDE, I TRY TO CITE PARTS OF THE GUIDELINES, AND IT'S JUST NOT AS CLEAR, I THINK. AGAIN, AM I GETTING THAT RIGHT? AM I MISREPRESENTING?

DR. WAGNER: YOU ARE. GETTING BACK TO THE POINT OF THE QUESTION YOU'RE SAYING, THERE'S A

DILEMMA HERE. THAT IS, WHAT IS IT THAT, IF WE STILL WANT AN SCRO INVOLVED, WHAT IS THE INFORMATION THAT THEY'RE GOING TO BE ABLE TO GET BACK FROM THOSE ANIMAL STUDIES THAT MIGHT NOT BE AVAILABLE BY AN IACUC? IT CERTAINLY MAY NOT BE AVAILABLE TO THE FDA IN TERMS OF THE EXPERTISE EVALUATING. THE FDA IS SPECIFICALLY LOOKING FOR DISTRIBUTION, TOXICOLOGY, ABERRANT TISSUE FORMATION. THEY'RE LOOKING FOR VERY SPECIFIC ENDPOINTS, WHICH MIGHT NOT NECESSARILY BE -- THERE COULD BE OTHER ENDPOINTS THAT ARE DISCOVERED IN THIS POTENTIALLY, I GUESS.

BUT THAT'S WHAT I'M TRYING TO WORK THROUGH. WHAT IS IT THAT -- CAN WE COME UP WITH A SCENARIO THAT SOMETHING COULD HAVE OCCURRED THAT, UNLESS YOU HAD AN ESCRO, YOU MIGHT NOT HAVE PICKED UP? I CAN'T THINK OF THAT RIGHT NOW. I CAN'T THINK OF ANYTHING. IF WE CAN'T THINK OF ANYTHING, MAYBE THAT'S THE REASON WHY WE JUST GO BACK TO YOUR ONE BULLET POINT, WHICH SAYS AT LEAST IF IT'S AN FDA TRIAL -- I SHOULD SAY AS LONG AS IT'S DOING THE REQUIREMENTS TO GET AN IND, MAYBE YOU DON'T NEED TO HAVE AN ESCRO.

DR. MARSALA: I WOULD ADD SOMETHING, THAT ONCE YOU'RE AT THE POINT WHERE YOU ARE STARTING YOUR FDA-REQUIRED STUDIES, THERE ARE A NUMBER OF STUDIES

THAT WERE ALREADY COMPLETED. IT'S THE SAME CELL LINES, SO PROBABLY EVERYTHING WENT THROUGH A PROCESS OF ESCRO APPROVAL BECAUSE USUALLY THE FDA-REQUIRED STUDIES COME MUCH LATER, AND YOU HAVE ALREADY EFFICACY ESTABLISHED AND THEN YOU ARE READY TO THINK ABOUT IND.

DR. WAGNER: NO. SPECIFICALLY IT'S GOING TO BE TOXICOLOGY AND DISTRIBUTION IN IMMUNE SUPPRESSED ANIMALS AND DELIVERY. SO YOUR DELIVERY METHODOLOGY. BUT THEY'RE VERY CONCRETE STUDIES.

DR. MARSALA: BUT THE CELL LINE WAS ALREADY ESTABLISHED PROBABLY LONG TIME BEFORE THAT. SO IT WENT THROUGH THE ESCRO APPROVAL, RESEARCH GRADE STUDIES WERE ALREADY APPROVED, AND I THINK IT WOULD BE JUST BASICALLY AMENDMENT TO WHAT WAS ALREADY HAPPENING FOR MAYBE TWO YEARS BEFORE YOU START THE FDA-REQUIRED STUDIES.

DR. WAGNER: YOU'RE ABSOLUTELY RIGHT. THE FOCUS WAS REALLY ON A DIFFERENT ASPECT OF ESCRO. IT WAS A DIFFERENT FOCUS. IT WASN'T SO MUCH ON THIS SORT OF END GAME OF FDA-REQUIRED TRIALS.

DR. LOMAX: THIS IS AN ABBREVIATED LIST OF WHAT THE FDA GUIDELINES STATE ARE THE INTENT OF THESE STUDIES, AND SO WHERE SOME OF THE FOCUS IS IN TERMS OF EVALUATING WHAT THE IMPACT OF CELL

TRANSPLANTATION OR WHAT THE GOALS ARE.

CHAIRMAN LO: SO LET ME ASK A QUESTION TO GO BACK TO PAGE 4, THIS RIGHT-HAND COLUMN, LINE 64 ON DOWN. WE'RE TALKING ABOUT -- THE OPTION WE'RE DISCUSSING IS FOR FDA-MANDATED STUDIES AS PART OF A SUBMISSION PACKAGE, WE'RE TALKING ABOUT WAIVING THE SCRO REQUIREMENT BECAUSE THE ARGUMENT IS THAT THAT'S ALREADY BEEN DONE.

SO HERE FROM LINE 82 TO 95, WE HAVE 1, 2, 3, 4 FUNCTIONS THAT AT LEAST IN THE PAST WE'VE SAID THE SCRO IS GOING TO SORT OF LOOK AT WHETHER THESE HAVE ALL MET THE CHECKED BOXES. AND NO. 1, PROVIDE AN ACCEPTABLE SCIENTIFIC RATIONALE. I'M JUST ASKING SOME QUESTIONS. IT SEEMS TO BE IT COULD BE PLAUSIBLE TO SAY THE FDA REQUIREMENTS IS AN ACCEPTABLE SCIENTIFIC RATIONALE OR THE FDA WOULDN'T REQUIRE YOU.

TWO, PROVIDE ASSURANCE THAT THE STEM CELL LINES HAVE BEEN ACCEPTABLY DERIVED. THE POINTS THAT WE'VE HEARD IS THAT IF THE STEM CELL LINE HAS ALREADY BEEN USED, IT'S ALREADY BEEN CHECKED, OR ALTERNATIVELY THAT'S SOMETHING THAT COULD BE DONE IN THE GRANTS REVIEW PROCESS. YOU DON'T NEED A SPECIAL COMMITTEE TO DO THAT. IT COULD BE AN ADMINISTRATIVE CHECK-OFF.

AND NO. 4, IT SEEMS TO BE DOCUMENTATION OF OTHER REQUIRED REVIEW. AGAIN, YOU DON'T NEED A COMMITTEE. THAT'S AN ADMINISTRATIVE FUNCTION.

SO I WANT TO ASK ABOUT NO. 3, EVALUATE THE PROBABLE PATTERN AND EFFECTS OF DIFFERENTIATION AND INTEGRATION OF THE HUMAN CELLS INTO NONHUMAN TISSUE. QUESTIONS I WANT TO ASK ARE DOES THE FDA PROCESS OF NEGOTIATING WITH THE SPONSOR FOR THE STUDIES TO BE DONE, DOES THE FDA PAY ATTENTION TO THAT IN STEM CELL RESEARCH? AND THEN, SECONDLY, DO WE STILL THINK THAT'S IMPORTANT?

JOHN IS SAYING THAT THE FDA ACTUALLY DOES LOOK AT THAT SPECIFICALLY.

DR. WAGNER: DISTRIBUTION OF THE CELLS.

CO-CHAIR LANSING: WE'RE JUST REPEATING. SO THAT MAKES NO SENSE. SO THAT MAKES NO SENSE.

DR. ROBERT TAYLOR: BASICALLY THE BEST SOLUTION IS TO HAVE A WELL EDUCATED IACUC. I DON'T KNOW THAT WE CAN MANDATE THAT.

CHAIRMAN LO: I THINK THE ARGUMENT IS NOT THAT WE'RE HOLDING UP -- THE ARGUMENT PRIMARILY IS THIS HAS ALREADY BEEN DONE AT THE FDA.

CO-CHAIR LANSING: AND WE'RE JUST REPEATING IT.

CHAIRMAN LO: THERE'S NO ADDED PROTECTION.

CO-CHAIR LANSING: THEN WE ARE HOLDING IT UP BECAUSE WE'RE DOING IT AGAIN. SO WE'RE REPEATING SOMETHING THAT WAS JUST DONE, WHICH IS GOING TO, I'M SURE, TAKE WEEKS, SO WE ARE HOLDING IT UP. I'M RELYING ON YOU'RE ALL TELLING ME. IF IT'S BEEN DONE, I DON'T KNOW WHY I HAVE TO DO IT AGAIN.

DR. ROBERTS: CAN I ASK JUST SOME CLARIFICATION OF THAT? IN THE CIRM STANDARDS WHERE IT SAYS EVALUATE THE PROBABLE PATTERN AND THE EFFECTS OF DIFFERENTIATION. SO IS THE MEANING OF PROBABLE PATTERN AND EFFECT THE SAME HERE AS WHAT THE FDA WOULD BE ASKING? I DON'T KNOW IF THERE'S AN ESTABLISHED MEANING OF THOSE WORDS. THAT'S THE DIFFERENTIATION AND INTEGRATION OF HUMAN CELLS.

DR. ROBERT TAYLOR: I THINK DISTRIBUTION AND SAFETY WOULD KIND OF QUALIFY FOR THIS. THOSE ARE THE TWO CRITERIA THAT THE FDA USES. SO I THINK THAT WOULD COVER THE DISTRIBUTION OF THE CELLS AND THE SAFETY, WHICH I THINK WOULD BE THE MAJOR -- EFFICACY POSSIBLY TOO.

CHAIRMAN LO: I GUESS SEVERAL PEOPLE WHO HAVE BEEN INVOLVED IN THESE SAY THE FDA LOOKS AT THAT. SO I GUESS IS THAT SUFFICIENT FOR US TO SAY IT'S ALREADY BEEN DONE? LET ME ACTUALLY HAVE GEOFF OR SOMEBODY ON LEGAL STAFF LOOK AT WHAT THE FDA SAYS

THEY WILL LOOK AT AND SAY, WELL, THAT'S THE FUNCTIONAL EQUIVALENT OF NO. 3 ON LINE 88. IT SEEMS TO ME IF IT IS SOMETHING FDA HAS REVIEWED, THEN IT'S A DUPLICATIVE REVIEW. IT'S HARD TO IMAGINE ADDITIONAL PROTECTION COMING FROM THAT, BUT IT CERTAINLY IS NOT AN ADDITIONAL TIME BARRIER.

CO-CHAIR LANSING: SO WE CAN ELIMINATE IT BASED ON GEOFF DOUBLE-CHECKING TO MAKE SURE THAT THEY ARE DOING EXACTLY WHAT JOHN THINKS THEY'RE DOING AND MAKE SURE THAT IT'S CLEAR. AND IF IT ISN'T, THEN I WOULD RECOMMEND WE HAVE A CONFERENCE CALL TO DISCUSS IT.

DR. LOMAX: CAN I JUST RESPOND AND GIVE ONE COMMENT ON THAT IS THAT KEEP IN MIND -- AND, DR. MARSALA, YOU'VE BEEN THROUGH THIS PROCESS -- WHAT THE FDA IS ACTUALLY DOING, MY UNDERSTANDING, IS YOU'RE DOCUMENTING. WE SAW YOUR EXAMPLES. YOU'VE GOT HISTOLOGICAL FINDINGS. SO IT'S A DOCUMENTATION OF EXACTLY WHAT HAPPENED IN THAT EXPERIMENT. THE ESCRO COMMITTEE ACTUALLY DOESN'T HAVE THAT ADVANTAGE. IN THE ABSENCE OF DATA, THEY'RE ACTUALLY LOOKING AT IT AT THE FRONT END.

SO IT'S THAT EX-POST EVALUATION WHICH I THINK IN MANY WAYS IS MORE INFORMATIVE BECAUSE IT'S NONSPECULATIVE. YOU'RE EVALUATING THE OUTCOME AS

OPPOSED TO A FRONT-END WHAT-IF.

CHAIRMAN LO: THE CURRENT REGULATION JUST SAYS THE INVESTIGATOR, AS A PART OF THE PROTOCOL, HAS TO SAY WE'RE GOING TO EVALUATE THE PATTERN AND EFFECTS OF DIFFERENTIATION. SO THEY'RE JUST SAYING YOU GOT TO LOOK AT THAT. IF THE FDA HAS ALREADY LOOKED AT IT AND SAID YOU BETTER LOOK AT THAT, THEN IT SEEMS TO ME IT'S DUPLICATIVE.

MR. SHEEHY: I ALSO, BESIDES LOOKING AT WHAT THE FDA REQUIRES, I THINK IT WOULD BE IMPORTANT TO SEE WHAT KINDS OF STUDIES WOULD BE CONDUCTED. LIKE I THINK THESE ISSUES WOULD BE ADDRESSED ACTUALLY BEFORE YOU SUBMIT TO THE FDA. SO IT'S NOT ENOUGH TO SAY -- SO THERE'S TWO CHOKE POINTS, RIGHT. SO YOU'RE SAYING DID THE FDA LOOK AT THE PATTERN, NO. 3. BUT THE OTHER IS -- DR. MARSALA MAY HAVE A POINT ON THIS -- I WOULD EXPECT BEFORE YOU SUBMITTED A PACKAGE TO THE FDA THAT YOU'VE DONE THESE STUDIES IN ANIMALS, AND THAT WOULD HAVE BEEN REVIEWED BY AN ESCRO AT THAT POINT. ONLY IF YOU CAN FIND A GAP WHERE ESCRO REVIEW DIDN'T HAPPEN EARLIER, AT AN EARLIER STAGE OF PRODUCT DEVELOPMENT, OR THE FDA'S ANALYSIS IS NOT ADEQUATE, COULD YOU REALLY -- WOULD IT REALLY MAKE SENSE TO GO AHEAD AND HAVE THE ESCRO INVOLVED, AT LEAST FOR POINT THREE, IN DOING THAT

ANALYSIS?

EVEN IF THE FDA DOESN'T LOOK AT IT, IF IT'S ALREADY SOMETHING THAT WOULD HAVE BEEN DONE AND IS GENERALLY DONE PRIOR TO GOING TO THE IND AND GETTING THE FDA-MANDATED STUDIES, THEN THE FACT THAT FDA DOESN'T DO IT IS KIND OF IRRELEVANT BECAUSE IT'S ALREADY DONE AND REVIEWED BY AN ESCRO AT AN EARLIER STAGE OF PRODUCT DEVELOPMENT. DOES THAT MAKE SENSE?

DR. WAGNER: I DON'T KNOW IF THAT MAKES SENSE, BUT I THINK THAT YOU DO POINT OUT SOMETHING IS THAT THERE'S TWO PROCESSES FOR GETTING YOUR IND. AND YOU CAN EITHER HAVE A PRE-IND MEETING OR YOU CAN MAKE A GUESS WHAT THE FDA WANTS. AND SO THE POINT THAT YOU BROUGHT UP IS IS THAT IT'S THE INVESTIGATOR WHO DECIDES WHAT HE OR SHE WANTS TO DO IN ANTICIPATION OF THE FDA. SO THEY COULD ACTUALLY DO THINGS THAT ARE NOT REQUIRED BY THE FDA.

SO YOU BRING UP THE TIMING, WHICH I WASN'T THINKING OF. SO THE FDA HAS IN ITS MIND WHAT IT WANTS TO SEE, AND BASICALLY THE INVESTIGATOR ACTUALLY HAS TO TRY TO ANTICIPATE THAT. AND SO ONE WAY OF DOING IT IS I WOULD ACTUALLY SAY TO THE FDA, HERE ARE THE 20 THINGS I PLAN ON DOING. AND IS THIS OKAY WITH THE AGENCY? IS THIS SUFFICIENT? I MIGHT HAVE GOTTEN AWAY WITH THREE THINGS. THEY'LL NEVER

TELL YOU TO REDUCE WHAT YOU'RE DOING. THEY JUST WANT TO MAKE SURE YOU ARE DOING THE MINIMUM PLUS WHATEVER ELSE YOU WANT TO DO. DOES THAT MAKE SENSE.

AT A PRE-IND MEETING, I WOULD SUBMIT TO THE AGENCY MY PLAN. AND IF I WAS ABLE TO SAY -- THE WAY I PRESENT THIS IS I WILL SAY IF I DID NOT FIND ECTOPIC TISSUE FORMATION, IF I DID NOT FIND CANCER DEVELOPMENT, AND A VARIETY OF OTHER THINGS, AND I WAS ABLE TO DEMONSTRATE THAT THE CELL DISTRIBUTION WAS LOCATED JUST TO THE HEART WHERE I INJECTED IT, LET'S SAY, WOULD THAT BE SUFFICIENT TO THE AGENCY? AND THEY WILL ANSWER YES OR NO. IF IT'S NO, THEY'LL TELL YOU MORE ABOUT WHAT THEY'RE LOOKING FOR.

SO THAT'S THE PROCESS OF HOW IT REALLY LOOKS. SO THE INVESTIGATOR IN THAT INSTANCE HAS NOT DONE ANY EXPERIMENT BECAUSE IT'S ALL IN ANTICIPATION, BUT I MIGHT HAVE GONE AHEAD AND DONE EVERYTHING THINKING THAT I ALREADY KNOW WHAT'S BEST. AND JUST SO YOU KNOW, THEN I PRESENT IT, I GIVE A WHOLE PACKAGE HAVING ALREADY DONE EVERYTHING LIKE YOU'RE SUGGESTING. AND THEN THEY CAN SAY, WELL, YOU DIDN'T DO THESE FIVE TESTS.

MR. SHEEHY: JUST LOOKING SPECIFICALLY AT NO. 3, YOU THINK IT'S REASONABLE THAT YOU WOULD GO EVEN TO A PRE-IND MEETING NOT KNOWING WHERE THE

CELLS THAT YOU'RE PUTTING INTO -- YOU'RE PROPOSING TO PUT INTO HUMANS, WHERE THEY WENT IN SOME ANIMAL MODEL. THEN WE'RE TALKING ABOUT STEM CELL LINES. SO YOU'RE TALKING ABOUT EMBRYONIC -- YOU WOULD GO TO THE FDA AND SAY, I'VE GOT THESE GREAT CELLS THAT DO THIS COOL STUFF. I PUT THEM INTO ANIMALS. I REALLY DON'T KNOW WHERE THEY GO OR WHAT HAPPENS TO THEM.

DR. WAGNER: THAT'S DONE.

MR. SHEEHY: A CELL DERIVED FROM AN EMBRYONIC SOURCE.

DR. WAGNER: I'M GOING TO SAY IT'S A SMART WAY TO DO IT, BUT THERE'S NOTHING THAT SAYS YOU CAN'T -- THE FDA IS NOT GOING TO TELL YOU IN ADVANCE OF RECEIVING SOMETHING. THEY DON'T KNOW THAT YOU'RE DOING THIS WORK. SO YOU AS THE INVESTIGATOR COULD HAVE SAID I THINK I KNOW WHAT THEY WANT AND JUST DO WHATEVER YOU WANT AND THEN GIVE THE RESULTS. AND THE ANSWER IS THAT THEY'RE PRESENTING THE IND AS THE FIRST DOCUMENT THE FDA RECEIVES. WHAT YOU'RE THINKING, WHICH THE MAJORITY OF PEOPLE WOULD DO, IS THEY WOULD GIVE THE FDA THEIR PROPOSAL. THEY WON'T KNOW THE ANSWERS. THEY'RE TELLING YOU THIS IS WHAT I'M GOING TO DO. IS THIS OKAY? IS THIS SUFFICIENT? SO THERE THEY DON'T KNOW WHAT THE ANSWER IS GOING TO BE.

DR. ROBERT TAYLOR: SO MY EXPERIENCE WITH THE FDA, THEY'RE PRETTY CAGEY. THEY ACTUALLY SAY NO A LOT, BUT THEY DON'T SAY YES VERY OFTEN. WHAT THEY WANT TO DO, AND THIS IS MORE WITH DRUG DEVELOPMENT, THEY WANT TO HEAR WHAT YOU'VE DONE AND WHAT YOU'VE SEEN. THEY ARE PRETTY AGNOSTIC ABOUT WHAT THEY REQUIRE. YOU KIND OF GO BACK. IT'S A VERY ITERATIVE PROCESS.

DR. WAGNER: THAT'S RIGHT. YOU HAVE GUIDELINES, BUT THE GUIDELINES YOU HAVE TO FIT TO THE CELL OF INTEREST. SO YOU HAVE TO GO THERE, AND THEN THE GUIDELINES DO SAY YOU HAVE TO DO THE DISTRIBUTION AND YOU HAVE TO DO THE TOXICOLOGY STUDIES, BUT YOU HAVE TO DECIDE WHAT THAT MEANS WITH EACH CELL THAT YOU'RE INTERESTED IN.

THE POINT I'M TRYING TO MAKE TO YOU OR GET IS THAT I COULD CHOOSE TO DO EVERYTHING I THINK IS GOING TO BE THE RIGHT ANSWER AND THEN JUST SUBMIT THE DATA TO THE FDA AND GET A RESPONSE. IN THAT CASE ALL THE STUDIES HAVE BEEN DONE IN ADVANCE, WHICH MAY BE INCOMPLETE. OR YOU COULD BE, LIKE THE WAY I WOULD LIKE TYPICALLY DO IT, HERE'S THE OUTLINE OF STUDIES I PLAN TO DO. I DON'T KNOW THE ANSWER; BUT IF I GOT THE ANSWER I'M LOOKING FOR, WOULD THAT BE SUFFICIENT?

DR. MARSALA: I CAN ADD TO THIS. I WAS INVOLVED IN DEVELOPMENT FOR THE ALS AND TRAUMA. SO HOW IT WORKED IN THAT CASE, THAT YOU HAVE YOUR CELL LINE, YOUR PRODUCT. INITIAL EFFICACY DATA WERE GENERATED UNDER KNOWN GLP CONDITION. SO YOU KNOW WHERE THEY ARE GETTING SOME EFFECT. AND THEN INITIAL TOXICOLOGY WAS DONE ALSO UNDER KNOWN GLP CONDITION. SO YOU SHOW THEM WE DID THE SHORT-TERM SURVIVAL OF SIX WEEKS. WE DON'T SEE ANY TUMOR FORMATION. THERE IS SOME EFFICACY IN PARTICULAR INJURY MODEL.

THIS WAS THE STARTING POINT. SO WE KNEW THAT THE CELL LINE WAS GOOD, YOU SEE SOME EFFICACY, AND YOU DON'T SEE ANY OBVIOUS TUMORS LIKE IN FIRST SIX WEEKS. BASED ON THAT, I THINK YOU CAN HAVE A PRE-PRE-IND MEETING AND PROPOSE NOW FULL-SCALE GLP TOXICITY STUDY. AND THEY CAN TELL YOU YOU NEED TO GO NOW NINE MONTHS, AND YOU NEED TO DO A HUNDRED ANIMALS WITH THAT PARTICULAR LINE, AND THIS COULD BE SUFFICIENT TO MOVE TO AN IND. I DON'T THINK -- I WOULDN'T GO AND DO THE FULL-SCALE GLP STUDIES BEFORE TALKING TO THEM BECAUSE YOU CAN DO MANY STUDIES WHICH ARE NOT NECESSARY.

DR. WAGNER: SURE. I DON'T DISAGREE WITH YOU EXCEPT THAT THE POINT IS THAT YOU CAN. THERE'S

NOTHING TO PREVENT YOU.

CHAIRMAN LO: LET ME TRY AND COME BACK TO THE PROPOSAL THAT WE'RE TRYING TO MAKE RECOMMENDATIONS. FOR FDA-MANDATED STUDIES, WHICH MEAN THAT THEY'VE REVIEWED IT AND SAID IF YOU DO THIS, THIS WILL BE -- DEPENDING ON THE RESULTS, THIS IS ALL WE'RE GOING WANT TO LOOK AT. WITH THAT CLASS OF STUDIES, I WAS HEARING BEFORE THAT THE WHOLE SECTION E ON PAGE 4 WITH THE 1, 2, 3, 4 WE'RE SAYING DOESN'T NEED TO BE REVIEWED BY A SCRO BECAUSE EITHER THE FDA IS REVIEWING IT IN THEIR PROCESS OF DISCUSSING WITH YOU WHAT YOU NEED TO DO IF YOU CHOOSE TO GO TO AN PRE-IND MEETING OR IT CAN BE DONE IN AN ADMINISTRATIVE WAY BY SOMEONE IN THE CIRM GRANTS REVIEW COMMITTEE.

SO IF WE WERE TO ACCEPT THAT, I THINK WE'VE SAID MAYBE WE SHOULD JUST HAVE GEOFF DO A LITTLE MORE DUE DILIGENCE TO CHECK THAT OUT, ARE WE SAYING THAT FOR THAT CLASS OF STUDIES, FDA-REQUIRED STUDIES THAT WOULD BE ENOUGH TO MEET THEIR REQUIREMENTS, WE WOULD WANT TO WAIVE ANY SCRO REQUIREMENT AS BEING REDUNDANT OR EASY TO DO ADMINISTRATIVELY. THAT'S WHAT I'M SORT OF GETTING A SENSE OF, BUT I JUST WANT TO SEE IF THAT'S -- I DON'T WANT TO GET BOGGED DOWN IN WHAT THE FDA DOES

OR DOESN'T DO. IF THAT'S THE SORT OF APPROACH THAT WE'D EXPECT YOU TO TAKE, THEN IT SEEMS TO ME WE WERE SAYING A LITTLE WHILE AGO WE DON'T NEED TO HAVE A SCRO REVIEW THAT STUDY. IS THAT A FAIR STATEMENT?

DR. WAGNER: I THINK THAT IS A FAIR STATEMENT IS THAT IF THE INVESTIGATOR KNOWS THAT THIS IS AN FDA-REQUIRED STUDY, THEN YOU'RE OKAY.

CHAIRMAN LO: THEY WOULD HAVE TO GO TO THIS PRE-IND MEETING. BUT THAT'S A WHOLE CLASS OF STUDIES THAT ARE ON THE PATH, AS JEFF SHEEHY SAID, TOWARDS CLINICAL TRIALS THAT A SCRO REVIEW FOR THESE CHARACTERISTICS WOULD NOT ADD ANYTHING, BUT WOULD CERTAINLY LENGTHEN.

DR. WAGNER: IT'S AN EXEMPTION.

CHAIRMAN LO: SO IT WOULD BE EXEMPT THEN.

DR. WAGNER: THAT'S RIGHT.

CHAIRMAN LO: SO SECOND CLASS OF STUDIES IS IF YOU'RE DOING BLASTOCYST COMPLEMENTATION STUDIES, IS THAT THE TECHNICAL TERM, ARE WE SAYING WE DEFINITELY WANT THE SCRO TO LOOK AT THOSE BECAUSE OF THE PUBLIC CONCERNS? THAT'S THE CURRENT -- RIGHT NOW WE'RE SAYING THE WHOLE GROUP OF ANIMALS INTO WHICH WE'RE INJECTING HUMAN CELLS INTO ANIMALS HAVE TO GO TO SCRO. WE'RE SAYING, OKAY, NOW ALL THE FDA-REQUIRED STUDIES FOR IND WE'RE EXEMPTING. IS

THERE A CLEAR SENSE THAT THE BLASTOCYST COMPLEMENTATION STUDIES, WE WANT THE SCRO OR ITS EQUIVALENT, FOR EXAMPLE, AN IACUC AUGMENTED WITH STEM CELL EXPERTISE, SOMEBODY TO REVIEW THOSE STUDIES PARTICULARLY, I THINK, FOR NO. 3, SO WE'RE GETTING 1, 2, AND 4 COULD BE DONE. IS THAT SOMETHING WE WANT TO SAY DEFINITELY IS A ROLE FOR THE SCRO? OR DO WE THINK THAT EVEN THOUGH THE SCRO MAY BE UNNECESSARY? AS I UNDERSTAND IT, THAT'S THE SET OF STUDIES WHERE THERE'S THE STRONGEST ARGUMENT OR THE MOST SUPPORT FOR RETAINING THE SCRO.

DR. LOMAX: CAN I JUST MAKE ONE POINT? I'M LOOKING AT IT THROUGH THE LENS OF THE POLICY REQUIREMENTS. THERE WERE SORT OF TWO SEPARATE ISSUES THAT I PARSED OUT THAT CAME TOGETHER THERE. THAT'S FINE. BUT I JUST WANT TO ACKNOWLEDGE THE COMING TOGETHER OF THE TWO ISSUES.

ONE OF THE OPTIONS THAT WE LAID OUT, WHICH WAS, AGAIN, EVALUATED BY PEOPLE OPERATING IN THE FIELD, IS YOU LAID OUT THE ONE, CERTAIN SET OF STUDIES YOU WOULD EXEMPT AND THAT'S FINE. THEN THERE'S THIS OTHER SET OF STUDIES YOU STILL WANT TO UNDERGO SOME LEVEL OF ADDITIONAL REVIEW, BUT YOU ALLOW THE IACUC TO DO IT. AGAIN, DELEGATING SOME RESPONSIBILITY TO THE IACUC, WHICH, AGAIN, GIVES

MORE FLEXIBILITY. SO THAT ADDS FLEXIBILITY. BUT THEN THE CONCEPT, THE BLASTOCYST ISSUE, OR THAT TYPE OF WORK, MY READ OF THE REGULATIONS IS THAT WOULD ALWAYS BE UNDER SCRO BECAUSE THEN WE'RE NOW MOVING INTO A DIFFERENT CLASS OF STUDY. WE'RE NO LONGER DEALING WITH ADULT ANIMALS. WE'RE DEALING WITH HUMAN CELLS TO BLASTOCYSTS. SO YOU'VE BROUGHT THE BLASTOCYST COMPLEMENTATION AND THE IACUC PIECE TOGETHER.

CHAIRMAN LO: SEPARATE THEM BACK OUT.

DR. LOMAX: THE REASON I BRING THAT UP IS BECAUSE AN IACUC WOULDN'T NECESSARILY LOOK AT A BLASTOCYST COMPLEMENTATION STUDY NECESSARILY BECAUSE THEY DEAL WITH VERTEBRATE ANIMALS. IS THAT CLEAR?

CO-CHAIR LANSING: WE CAN CHOOSE TWO THINGS OR JUST ONE OF THE FOUR, RIGHT?

DR. LOMAX: NO. I TRIED TO SORT OF GIVE YOU A RANGE OF OPTIONS. THEY'RE SOMEWHAT MALLEABLE IN A SENSE.

CO-CHAIR LANSING: THE LAST ONE SEEMED, IN A FUNNY WAY -- I DON'T MIND IF WE ELIMINATE, BUT THE LAST ONE IS BASICALLY SAYING THAT YOU ALLOW SOMEONE ELSE -- CAN'T WE COMBINE THEM? YOU ALLOW SOMEONE ELSE TO DO THE REVIEW PROVIDING THAT THEY HAVE TO MEET CIRM REGULATIONS, SO WE WOULD HAVE, IN A SENSE,

THE OVERSIGHT TO MAKE SURE THAT THEY WOULD HAVE TO CHECK THE BOXES UNLESS IT'S ALREADY BEEN DONE BY THE SCRO. WOULDN'T THAT SORT OF -- I'M COMBINING TWO AND FOUR. ISN'T THAT WHAT WE'RE SAYING? I'M NOT AN EXPERT ON THIS, BUT WHAT I'M REALLY SAYING IS WE DON'T WANT TO FORCE ANYONE TO REPEAT SOMETHING THAT'S ALREADY BEEN DONE. SO WE'VE ALL ACCEPTED THAT CONTINGENT ON GEOFF MAKING SURE THAT THE GOVERNMENT IS ALREADY DOING -- THE GOVERNMENT IS DOING WHAT DR. WAGNER THINKS THEY'RE DOING, AND I HOPE THEY ARE.

CHAIRMAN LO: IT'S DR. MARSALA.

CO-CHAIR LANSING: SORRY.

CHAIRMAN LO: IT'S A POLICY.

CO-CHAIR LANSING: THAT IT'S POLICY, AND I TRUST YOU. BUT IF SOMETHING HASN'T BEEN DONE, THEN WE'RE GOING TO LET THE OUTSIDE GROUP DO IT AND WE'RE GOING TO MONITOR IT. THEY HAVE TO MEET OUR CIRM REGULATIONS. THAT SEEMS TO ME THE WAY TO MOVE THE PROCESS FORWARD THE FASTEST TO MAKE SURE WE'RE NOT REPEATING STUFF AND NOT TO BURDEN US WITH THE BUREAUCRACY OF LETTING SOMEONE ELSE DO IT, BUT MAKING SURE THEY MAINTAIN CIRM REGULATIONS.

CHAIRMAN LO: THIS GIVES THE INSTITUTION FLEXIBILITY TO SAY WE'LL HAVE AN AUGMENTED IACUC,

AND WE COULD PUT IN LANGUAGE SAYING THAT INCLUDES APPROPRIATE EXPERTISE IN STEM CELL SCIENCE.

CO-CHAIR LANSING: AND IF IT'S ALREADY BEEN DONE, THEY DON'T HAVE TO REPEAT IT.

CHAIRMAN LO: NOW WE STAY WITH THAT. THAT SEEMS TO BE A PRETTY -- LOT OF QUESTIONS.

MR. SHEEHY: THAT'S VERY REASONABLE BECAUSE YOU'RE NOT CHANGING OUR REQUIREMENTS, WHICH I'M UNCOMFORTABLE ABOUT SAYING, WELL, MAYBE THIS ONE IS IMPORTANT AND THAT ONE IS NOT IMPORTANT. WE'RE MAINTAINING OUR OWN REQUIREMENTS, BUT WE'RE MAKING IT EASIER ON THE GRANTEES BY ALLOWING THEM SOME FLEXIBILITY IN ENFORCING OUR REQUIREMENTS. AND THEN KEEPING THE EXEMPTION FOR FDA-MANDATED PRECLINICAL STUDIES AS AN AMENDMENT TO THAT SEEMS VERY REASONABLE, AND ALSO ALLOWS US TO ACCELERATE INTO THE CLINICAL TRIALS.

CO-CHAIR LANSING: AND IT ACTUALLY DOESN'T EVEN NECESSITATE US HAVING A CONFERENCE CALL BECAUSE IF WE FIND OUT THAT THEY'RE NOT DOING CERTAIN THINGS, THEN NO. 4 WOULD HAVE ADDRESS IT BECAUSE THAT'S PART OF OUR REGULATIONS. SO IT KIND OF COVERS THE BASE.

CHAIRMAN LO: OTHER COMMENTS?

DR. ROBERTS: IF WE DO NO. 4, THOUGH,

ISN'T THAT EFFECTIVELY DOING AWAY WITH THE REQUIREMENT OF ESCRO REVIEW? IT SAYS --

CO-CHAIR LANSING: THEY HAVE TO MAINTAIN OUR REGULATIONS.

DR. ROBERTS: YEAH, BUT IT DOESN'T HAVE TO BE AN ESCRO DOING IT. IT COULD BE SOME OTHER. SO IT WOULD EFFECTIVELY ELIMINATE THE REQUIREMENT THAT'S NOW IN THE REGULATION, THAT IT HAS TO BE ESCRO REVIEW.

DR. LOMAX: THAT'S RIGHT. YES. THAT'S A CORRECT STATEMENT.

CHAIRMAN LO: I THINK WE'RE SAYING LET'S GIVE OR AT LEAST THE PROPOSAL IS TO GIVE THE INSTITUTION FLEXIBILITY IN HOW THEY DO THE REVIEW, THE FUNCTIONS OF THE REVIEW. THEY MAY CHOOSE TO GO TO A SCRO IF THEY WISH, OR THEY MAY CHOOSE TO USE AN ADDITIONAL STRUCTURE SUCH AS AN IACUC AS THE MAIN BODY THAT DOES THAT, ADDING EXPERTISE IF THEY NEED IT.

CO-CHAIR LANSING: THEY HAVE TO PROVE TO US THAT THEY MAINTAIN OUR REGULATIONS.

DR. ROBERT TAYLOR: I GUESS THAT'S THE TRICK.

DR. ROBERTS: HOW DOES THAT HAPPEN?

DR. ROBERT TAYLOR: IDEALLY AS WE MOVE

MORE TOWARD STEM CELL RESEARCH ACROSS THE SPECTRUM, ANIMAL AND HUMAN, THE IRB AND THE IACUC IS GOING TO DEVELOP MORE AND MORE EXPERTISE. AND IT ALMOST MEANS THAT THE SCRO'S ARE GOING TO BE LESS IMPORTANT. BUT UNTIL THAT HAPPENS OR HOW ONE ACTUALLY JUDGES WHEN THAT TRANSITION HAS BEEN MADE IS KIND OF HARD TO CALL.

CHAIRMAN LO: IN A LOT OF REGULATIONS, YOU DO IT, NOT BY SECOND-GUESSING REVIEWS, BUT SAYING THE BODY THAT REVIEWS IT HAS TO HAVE THIS EXPERTISE OR COMPOSITION. AND, AGAIN, THOSE OF YOU WHO ARE SKILLED AT DRAFTING THIS, PAT AND DOROTHY AND JEFF TO SOME EXTENT, PUTTING IN AN IACUC THAT HAS APPROPRIATE STEM CELL SCIENCE EXPERTISE MAKES IT FLEXIBLE AND MAKES IT CLEAR THAT CURRENT IRB'S MAY NOT HAVE THE STEM CELL EXPERTISE, WHICH IS ONE OF THE REASONS INITIALLY WE'RE SAYING DON'T JUST GO TO THE IACUC BECAUSE THEY DON'T REALLY HAVE THE STEM CELL EXPERTISE.

DR. ROBERTS: RIGHT. SO I'M ASSUMING THAT WHEN THIS REQUIREMENT THAT THESE STUDIES BE REVIEWED BY AN ESCRO WAS PLACED IN THE ETHICAL REGULATIONS, THERE WAS A REASON FOR IT. AND I JUST WOULD WANT TO MAKE SURE THAT THAT REASON IS FULFILLED BY NO. 4. IT JUST SEEMS LIKE IT WOULD REQUIRE SOMETHING MORE

TO MAKE SURE THAT THE TYPE OF REVIEW -- I THINK THE ASSUMPTION IS THAT THERE IS A TYPE OF REVIEW THAT ESCRO'S DO THAT IACUC'S DON'T DO, THAT MAYBE THE FDA DOESN'T DO, BUT WE'RE GOING TO LOOK INTO THAT. AND SO I WOULD JUST WANT TO MAKE SURE THAT THAT TYPE OF REVIEW IS DONE, THAT THERE'S A WAY TO ENSURE IT'S DONE. IT CAN BE DONE BY SOMEBODY ELSE, BUT IT SHOULD BE DONE.

CHAIRMAN LO: THE OTHER --

DR. LOMAX: CAN I JUST GIVE A POINT OF -- I DID DO SOME INTERVIEWS WITH PEOPLE. SO THE GENESIS OF THESE REVIEWS, AND I'M SPEAKING GENERALLY, BUT I THINK THIS IS MORE OR LESS CORRECT, IS THAT INITIALLY THERE WAS FAIRLY INTENSIVE REVIEWS, FULL COMMITTEE REVIEWS, OF THESE STUDIES. I THINK PART OF IT IS THE DON'T KNOW WHAT WE DON'T KNOW QUESTION WHEN THE ORIGINAL RECOMMENDATION CAME OUT. AND MY SENSE IS FROM REPEATED EXPERIENCE, AND THAT'S PART OF WHAT DR. MARSALA SHARED WITH US, IS THAT IT BECAME INCREASINGLY -- THE EVIDENCE SUGGESTED THAT THESE TYPES OF EXPERIMENTS WERE BENIGN FROM A KIND OF WHAT ARE WE SCARED OF QUESTION WHICH WAS RAISED EARLIER. A LOT OF THEM HAVE ACTUALLY MOVED TO, AND WE ALLOW THIS, TO MORE ADMINISTRATIVE REVIEW.

SO WE HAVE SEEN A SORT OF EVIDENCE-DRIVEN REDUCTION OF INTENSITY. SO I THINK IT'S SOMEWHAT THE NATURAL EVOLUTION OF THINGS AS WELL. I THINK PART OF IT WAS ORIGINALLY, AGAIN, YOU WERE IN THE ROOM FOR SOME OF THESE DISCUSSIONS, THE DON'T KNOW WHAT WE DON'T KNOW QUESTION, BUT NOW WE HAVE A MORE ESTABLISHED BODY OF EVIDENCE.

CHAIRMAN LO: I THINK THERE WAS A SENSE OF CONSERVATISM AT THE TIME THOSE WERE SET UP. AND THE THOUGHT WAS THAT THESE ISSUES NEEDED SPECIAL ATTENTION, THAT THE IACUC'S WERE ALREADY BUSY DOING ALL THE ANIMAL WELFARE STUFF AND CONCERNS THAT THEY WEREN'T REALLY ABLE TO KEEP UP WITH THEIR NARROW MANDATE. AND SO TO ADD ON A TOTALLY DIFFERENT THING WAS REALLY DIFFERENT THAN WHAT THEY'RE CURRENTLY DOING. SO NOW I GUESS THE ARGUMENT WOULD BE THAT THERE'S MORE EXPERIENCE, THAT A LOT OF THE WORST FEARS HAVEN'T MATERIALIZED. I THINK THERE'S SOME EXPERIENCE NOW FROM SCRO'S AS TO WHAT TO LOOK FOR. AND THE MEMBERS OF SCRO'S PRESUMABLY NOW ARE AVAILABLE TO IACUC'S ON AN AD HOC BASIS TO SAY, WELL, LET ME BE THE LEAD REVIEWER FOR THE SCRO PART OF THE IACUC, KNOWING THAT OTHER PEOPLE DO THE ANIMAL WELFARE PART.

THE QUESTION IS IF WE CAN PROVIDE

EQUIVALENT REVIEW FOR STUDIES THAT DON'T GET IT FROM THE FDA, SO THAT THEY HAVE AN OPTION OF EITHER SCRO OR SOME OTHER BODY THEY'VE CONSTITUTED AS LONG AS THEY HAVE THE APPROPRIATE EXPERTISE AND LOOK AT THE ISSUES OF INTEREST. JEFF, YOU CHAIRED THESE COMMITTEES.

DR. BOTKIN: WELL, NOT I BECAUSE THAT'S A DIFFERENT WORLD FOR ME. I'LL TAKE THE OPPORTUNITY TO MAKE SOME COMMENTS. I'M ACTUALLY LEANING A LITTLE BIT MORE TOWARDS NO. 1 THERE. I THINK HISTORICALLY WE HAVE HEARD EXPLANATIONS ABOUT WHY THE SCRO'S WERE INVOLVED HERE, AND I DON'T THINK THEY'RE PARTICULARLY RELEVANT TO THIS TYPE OF EXPERIMENT. WE'RE TALKING ABOUT ANIMAL RESEARCH AT THIS POINT. I THINK WE HAVE THE DATA TO SUGGEST THAT THEIR REVIEW DOESN'T IMPACT THINGS.

AND I'M LOOKING AT NO. 3. BERNIE, I THINK YOUR POINT IS A GOOD ONE. NO. 3 WOULD BE THE ONE THAT MIGHT BE LEFT OPEN. EVALUATE THE PROBABLE PATTERN AND EFFECTS OF DIFFERENTIATION AND INTEGRATION OF THE HUMAN CELLS INTO THE NONHUMAN ANIMAL TISSUE. ISN'T THAT BREAD AND BUTTER? ISN'T THAT WHAT THE WHOLE SCIENCE IS ABOUT? HOW CAN PEOPLE NOT LOOK AT THAT ISSUE AS PART OF THE OVERSIGHT PROCESS? NO. 3. I'M SORRY. NO. 3. WHAT

ARE SCRO'S SUPPOSED TO DO. AND IT SEEMS TO ME THAT THIS WORK IS ALREADY BEING DONE.

NOW, DO WE WANT THE IACUC'S TO HAVE MORE STEM CELL, THAT WOULD BE NO. 4, BUT I WOULD JUST SAY TO THE EXTENT THAT INSTITUTIONS SAY THEY WANT FLEXIBILITY, THEY DON'T. THEY WANT TO BE TOLD WHAT TO DO. IF YOU ARE GOING TO SAY WE WANT YOUR IACUC TO HAVE STEM CELL EXPERTISE, THEY'RE GOING TO SAY WHAT DOES THAT MEAN? HOW MANY PEOPLE AND WHAT KIND OF EXPERTISE? SO IF WE GO WITH NO. 4, I THINK WE'LL HAVE TO BE FAIRLY EXPLICIT OR CIRM WILL HAVE TO BE FAIRLY EXPLICIT ABOUT WHAT EXPERTISE IS EXPECTED.

CHAIRMAN LO: SO JEFF SORT OF PUT THINGS IN A DIFFERENT PERSPECTIVE BY DEALING WITH NO. 1. SO IF WE ACCEPT NO. 1, AND I GUESS IT WOULD BE FOR STUDIES INTO THE LIVE-BORN ANIMALS. WE WANT TO MAKE SOME MODIFICATION. AND WE REALLY, REALLY MEAN IT IF IT'S FDA MANDATED BECAUSE IT'S TOTALLY REDUNDANT.

BUT THEN I GUESS THERE ARE CERTAIN STUDIES WHERE WE WANT ADDITIONAL REVIEW. AND THE ARGUMENT ORIGINALLY WAS THAT IACUC'S MAY LOOK AT THE PATTERN OF INTEGRATION AND DIFFERENTIATION AND STUFF, BUT THEN THEY MAY NOT WANT TO -- THEY TYPICALLY DO NOT REVIEW, AT LEAST THAT'S WHAT WE WERE TOLD WHEN WE SET UP THE SCRO, DON'T REVIEW THE SORT OF

SIGNIFICANCE OF TRANSPLANTING -- DOING EXPERIMENTS DESIGNED TO INDUCE HUMAN-LIKE FEATURES IN THE ANIMAL AS PROOF OF PRINCIPLE FOR SOME SORT OF TRANSPLANT STUDY. I'M SORT OF MAKING THIS UP. SO THAT I THINK YOU COULD ARGUE THAT FOR STUDIES THEY'RE TRYING TO -- THE PURPOSE OR THE GOAL WHICH IS TO IMPART SOME HUMAN CHARACTERISTICS OR PHENOTYPIC CHARACTERISTIC OR COGNITIVE FUNCTION OR EVEN TRANSPLANTING AN ARTIFICIAL HEART PRODUCED ON SCAFFOLDING BY HUMAN CARDIAC PRECURSOR CELLS, WOULD THAT REQUIRE SOME SORT OF GROUP STEPPING IN AND SAYING, WAIT A MINUTE. DOES THE HEART HAVE SIGNIFICANCE, MAYBE NOT QUITE AS THE BRAIN, BUT DIFFERENT THAN TRANSPLANTING SKIN GRAFTS? AND THIS COMMITTEE, THE SCRO, WAS MEANT TO SAY FOCUS ON THOSE ISSUES.

I COULD SEE AN ARGUMENT FOR SAYING GENERALLY NO ADDITIONAL REVIEW, BUT THERE'S SOME EXCEPTIONS. THIS MIGHT BE ONE. I WOULD ACTUALLY ARGUE THAT BLASTOCYST TRANSFER MIGHT BE ANOTHER BECAUSE THEN IT'S THAT CHIMERA ISSUES.

DR. BOTKIN: LET ME MAKE ONE QUICK OTHER COMMENT THEN. I GUESS I WOULD HOPE THAT CIRM WOULD HAVE OTHER CRITERIA AND NOT RELY ON A SCRO TO STOP THAT KIND OF RESEARCH. SO INVESTIGATOR WANTS TO

CREATE INTELLIGENT RATS, AND THAT'S THE POINT OF THE EXPERIMENT, DO WE REALLY WANT TO RELY ON A SCRO TO SAY THAT'S UNETHICAL TO DO THAT? YOU OUGHT TO HAVE PRIOR CRITERIA WITH CIRM ABOUT THE KINDS OF EXPERIMENTS THAT ARE BEING FUNDED OUT OF THE SYSTEM AND SAY THIS IS NOT WHAT WE'RE ABOUT. WE DON'T DO THIS.

CHAIRMAN LO: I DON'T KNOW. I DON'T KNOW THE SCIENTIFIC AGENDA. BUT IF SOMEONE SAID THIS IS THE FIRST STEP TOWARDS TREATMENT FOR AUTISM SPECTRUM DISORDER, IT SEEMS TO ME THERE'S A FUNDING ISSUE, AND THEN THERE'S A REVIEW OF THE TYPE OF RESEARCH.

DR. PATRICK TAYLOR: THERE'S A CLASS OF TESTS FOR INJECTING STEM CELLS INTO THE BODY TO SEE WHETHER THEY DEVELOP A TERATOMA, TERATOMA TESTS. (INAUDIBLE) OF COURSE. IT CAME TO ESCRO. ESCRO WAS CONCERNED ABOUT WHETHER OR NOT THERE WAS MIGRATION TO THE GERMLINE. THAT'S AN IMPORTANT MATTER, AND NOBODY EVER ASKED THE QUESTION. SO FOR THE PART OF THE ISSUE OF INTENTIONALITY, ASKING THE QUESTIONS FROM A DIFFERENT PERSPECTIVE, CERTAINLY THERE'S A DIFFERENCE.

WHAT I WORRY ABOUT (INAUDIBLE) IS SITTING INSIDE AN ORGANIZATION, NOW IT LOOKS LIKE THEY MIGHT HAVE THREE PATHS. I HAVE MY ORDINARY IACUC, ESCRO,

BUT ESPECIALLY I'VE GOT MY AMPLIFIED IACUC. AM I REALLY GOING TO SET THAT UP? I'M MORE COMFORTABLE --

DR. LOMAX: GOOD POINT. SO THE FEEDBACK -- KEEP IN MIND WHAT'S DRIVING THIS IS IT'S REALLY -- I THINK AS A PRACTICAL MATTER, A LOT OF INSTITUTIONS THAT HAVE ESTABLISHED ESCRO'S AREN'T NECESSARILY GOING TO SUDDENLY CHANGE THEIR POLICIES AND PROCEDURES BECAUSE THEY'RE ESTABLISHED. THE PROBLEM WE'RE TRYING TO SOLVE ARE SOMEBODY WHO'S COMING IN AND REALIZES THAT WE MAY REQUIRE SOMETHING ELSE, BUT WE ABSOLUTELY -- THE ESCRO CLAUSE IS COMPLETELY FOREIGN. IS THERE SOME OTHER WAY WE CAN SATISFY THAT BECAUSE WE DON'T HAVE IT?

SO AS AN IMPLEMENTATION MATTER, THAT'S PROBABLY HOW THINGS WOULD PLAY OUT.

DR. PATRICK TAYLOR: THE BEST WAY IS TO PERMIT IT THAT WAY. JUST SAY PURSUING THE KIND OF STUDIES, YOU'LL CONSIDER IF THE OTHER CRITERIA HAVE BEEN MET. THAT'S WHAT IT MEANS.

CHAIRMAN LO: REMEMBER, IF WE ADOPT 1 AND 2, MOST OF THE TIME WE'LL SAY YOU DON'T NEED SCRO. YOU'VE GOT IT. YOU DON'T HAVE TO GO THERE. BUT I THINK WE ARE SAYING THERE'S SOME STUDIES OF INTEREST, INJECTING HUMAN GERM CELLS INTO AN ANIMAL,

WOULD FALL UNDER HERE. SO THERE MAY BE SOME -- SO RATHER THAN SAYING WE DO EVERYTHING, MAYBE JUST SAYING MOST OF THE TIME YOU DON'T HAVE TO REVIEW, PARTICULARLY NOT IF THE FDA SAYS YOU HAVE TO DO IT FOR AN IND. BUT WE'RE CALLING OUT SOME CLASSES OF STUDIES WHERE WE DO WANT SOME OF SORT OF REVIEW THAT TRADITIONALLY HAS GONE TO A SCRO.

SO WE'RE ALREADY ADDRESSING THE QUESTION THAT'S COME UP TO YOU. WE'RE PRESUMING MOST OF THESE PEOPLE ARE GOING DOWN THE CLINICAL TRIALS PATHWAY. SO THEY SHOULD EITHER HAVE A WAIVER EARLY ON OR JUST GO TO FDA AND SAY, DO I HAVE TO DO THIS? IT SAYS, YEAH, BUT YOU'VE GOT TO DO MORE ANIMALS, DIFFERENT SPECIES OR SOMETHING.

DR. PATRICK TAYLOR: WE HAVE TO ACTUALLY WORRY WHETHER OR NOT THE REGULATION EXEMPTION IS BROAD ENOUGH. I HEARD THE DISCUSSION ABOUT BROADER EXEMPTIONS FOR ESCRO'S, AT LEAST FOR THOSE PEOPLE WHO TRACK, TO BE APPROVED. FOLLOW THAT ROUTE, AND ALL OF A SUDDEN (INAUDIBLE), WHY WAIT?

CHAIRMAN LO: WE MAY BE SAYING THAT FOR MOST STUDIES NOW DOING A SCRO REVIEW, YOU DON'T NEED TO DO IT. FLIPPING THE PRESUMPTION AROUND. YOU ONLY NEED TO DO IT ON CERTAIN SORT OF HIGH CONCERN STUDIES AND OTHERS LIKE WE HAVE IN THIS ONE.

ROUTINE, IT'S GOING TO INJECT THINGS, MAKE SURE THEY'RE DIFFERENTIATING THE CELLS I WANT, THAT THEY DON'T CAUSE HUGE TUMORS IN THE NERVOUS SYSTEM BECAUSE OF WILD DIFFERENTIATION. WE'RE SAYING WE DON'T REALLY THINK YOU NEED TO DO THAT.

DR. PATRICK TAYLOR: THERE'S A LIST OF CLEAR EXEMPTIONS ALL THE WAY THROUGH THE FDA.

DR. WAGNER: I THINK IT MAKES ME VERY UNEASY. I FEEL BETTER ABOUT YOU LEAVE THE RECOMMENDATION AS IT IS AND YOU PUT IN EXEMPTIONS WHERE YOU KNOW OR FEEL MOST COMFORTABLE WITH, LIKE THE FDA REQUIREMENT. WE DON'T KNOW WHAT THE FUTURE OF SCIENCE IS GOING TO BRING. AND AS YOU BROUGHT UP BEFORE, THERE'S UNINTENDED DISCOVERIES, UNINTENDED CONSEQUENCES. SO I MIGHT HAVE BEEN DOING THIS FOR THIS REASON, AND YET I COME UP WITH SOMETHING ELSE LIKE THE GERMLINE ISSUE. AND IT'S HARD FOR ME TO IMAGINE HOW WE'RE GOING TO SAY WHEN THE SCRO IS NEEDED AND WHEN IT'S NOT BECAUSE WE CAN'T ANTICIPATE EVERYTHING.

I'VE ALWAYS BELIEVED THAT THE SCRO HAS A BODY OF KNOWLEDGE AND HAS BEEN THINKING ABOUT IT AS A GROUP, THE BIOETHICISTS AND THE STEM CELL EXPERTS AND A VARIETY OF OTHER PEOPLE. RATHER THAN HAVING AN AD HOC STEM CELL RESEARCHER COME TO AN IACUC

MEETING, THAT'S VERY DIFFERENT THAN HAVING A SCRO WHERE YOU ACTUALLY HAVE A MISSION AND YOU HAVE A CLEAR-CUT REASON FOR BEING. AND BEING CALLED -- I CAN JUST IMAGINE THAT YOU ARE GOING TO BE CALLING A HEMATOPOIETIC STEM CELL PERSON BECAUSE THEY'RE MORE READILY AVAILABLE. AND YOU KNOW THE HEMATOPOIETIC STEM CELL PEOPLE HAVE NEVER EVER THOUGHT ABOUT THESE ISSUES.

DR. PATRICK TAYLOR: SO I GUESS WE MIGHT HAVE A SYMPOSIUM TO GET SOMETHING REALLY DONE. I HEAR WHEN YOU TALK ABOUT THE EXEMPTIONS, REALLY DO SOMETHING REALLY PROACTIVE ESPECIALLY AROUND THIS ISSUE.

MR. TOCHER: LET ME JUST SEE IF I FOLLOWED THIS. I THINK WITH RESPECT TO THE FDA DISCUSSION, IT SEEMS LIKE THE GENERAL CONSENSUS IS THERE'S NOT A PROBLEM WITH THE REQUIREMENTS THAT WE HAVE SO MUCH AS WE DON'T WANT TO CREATE IMPEDIMENT BY LOOKING AS THOUGH WE'RE DUPLICATING WORK THAT MAY HAVE ALREADY TAKEN PLACE. SO MAYBE -- TELL ME IF THIS IS CAPTURING WHAT YOU'RE HEARING, BERNIE, BUT MAYBE THE LANGUAGE WOULD BE SOMETHING ALONG THE LINES OF A COMBINATION OF TWO THAT WE'VE HEARD, WHICH IS WE WOULD EXEMPT RODENT STUDIES FROM SCRO REVIEW FOR STUDIES THAT ARE MANDATED PURSUANT TO FDA-MANDATED

PRECLINICAL STUDIES WHERE THE RESEARCHER CAN CERTIFY THAT THE REQUIREMENTS OF SUBDIVISIONS (E)(1) THROUGH (4) HAVE BEEN MET. FOR ALL OTHER WORK INVOLVING TRANSPLANTATION OF STEM CELLS INTO ADULT ANIMALS, THERE MUST BE A REVIEW BY A SCRO OR IACUC WITH APPROPRIATE EXPERTISE TO ENSURE THAT THE REQUIREMENTS OF (E) SUBDIVISIONS (1) THROUGH (4) ARE MET.

CHAIRMAN LO: FOLLOWING ALONG JEFF'S SUGGESTION THAT WE KEEP THE RULE IN PLACE, BUT ALLOW FOR AN EXCEPTION IF THE INVESTIGATOR CAN DEMONSTRATE THE REVIEW HAS ALREADY BEEN DONE, I THINK WE PROBABLY WANT TO AMEND IT TO SAY NOT JUST RODENTS, BUT ADULT VERTEBRATES OR SOMETHING. AND WE MIGHT ALSO WANT TO SAY IN PARTICULAR IF THE STUDY IS REQUIRED BY THE FDA AS PART OF A PRE-IND DISCUSSION, WE WILL DEEM IT -- PRESUMPTION IS THAT THAT ALREADY MEETS THE CRITERIA 3, I GUESS IT WAS.

DR. ROBERT TAYLOR: IF YOU GO TO VERTEBRATES, THAT MIGHT INCLUDE PRIMATES. JUST AS LONG AS YOU'RE COMFORTABLE WITH THAT.

CHAIRMAN LO: BUT THE STRUCTURE IS TO NOT DO A BLANKET SORT OF YOU DON'T NEED TO GO TO SCRO ANYMORE, BUT TO SAY IF YOU CAN DEMONSTRATE YOU'VE ALREADY HAD SOME REVIEW OF POINTS 1, 2, 3, 4 IN THIS

COLUMN, YOU DON'T NEED TO GO BACK.

DR. PATRICK TAYLOR: TO THE PRIMATE EXAMPLE, TO ELIMINATE SPECIFIC PROHIBITIONS MIGHT BE QUITE --

MR. SHEEHY: FIRST OF ALL, SITTING IN SOME OF OUR CLINICAL REVIEW, I DON'T SEE ANY MANDATES FOR PRIMATE STUDIES ANYWAY. I DON'T THINK THE FDA IS REQUIRING MANDATED PRIMATE STUDIES.

DR. ROBERT TAYLOR: NOT FOR STEM CELL YET, BUT THEY CERTAINLY ARE IN A LOT OF OTHER DRUG DEVELOPMENT TRIALS.

DR. WAGNER: BUT, AGAIN, WE DON'T KNOW WHAT THE FUTURE IS GOING TO BRING. SO WE'LL HAVE TO SPECIFY. JUST SAY STUDIES REQUIRED BY THE FDA FOR CLINICAL TRIALS.

MR. SHEEHY: HONESTLY, I THINK IT SHOULD BE JUST A BLANKET EXEMPTION FOR FDA-MANDATED PRECLINICAL STUDIES.

THIS OTHER LAYER OF COMPLIANCE I JUST DON'T THINK IS NECESSARY AT THIS STAGE. I THINK 1 THROUGH 4 WILL HAVE BEEN ANSWERED. I DON'T THINK THAT'S AN ASSUMPTION. I THINK THAT'S A REALITY.

CHAIRMAN LO: JEFF, I THINK WE'RE ALL IN AGREEMENT WITH YOU.

MR. SHEEHY: BUT IF YOU LOOK AT THE WAY

YOU FRAMED IT, YOU'RE SAYING IF THE INVESTIGATOR CAN ASSURE THAT 1 THROUGH 4 --

CHAIRMAN LO: OKAY. WHY DON'T WE MAKE A SEPARATE EXCEPTION --

MR. SHEEHY: THIS WOULD JUST BE AN EXCEPTION FOR FDA-MANDATED PRECLINICAL STUDIES.

CHAIRMAN LO: THAT'S FINE. AND ANOTHER ONE IS IF THE INVESTIGATOR CAN SHOW THAT THE REQUIREMENTS 1, 2, 3, 4 HAVE ALREADY BEEN MET BY SOME OTHER REVIEW PROCESS.

DR. PATRICK TAYLOR: I THINK THIS IS WHAT YOU MEANT BY --

MR. SHEEHY: I JUST THINK THAT'S UNNECESSARY. REGULATIONS FOR THE SAKE OF REGULATION.

CHAIRMAN LO: NO. NO. JEFF, I THINK WE'RE ALL AGREEING.

DR. ROBERT TAYLOR: IF THE FDA, AND I'M NOT SURE THAT THE FDA IS THAT PROACTIVE. THAT'S MY PERSONAL EXPERIENCE. SO I DOUBT THAT THEY'RE GOING TO ACTUALLY --

CHAIRMAN LO: HERE'S WHAT I THOUGHT I HEARD, BUT CORRECT ME IF I'M WRONG. THAT IF THE FDA SAYS PRE-IND YOU GOT TO PROVIDE THESE STUDIES OR ELSE IT'S A NO-GO, AND WE CONFIRM THAT THAT'S FDA

POLICY, WE WILL SAY, OKAY, YOU DON'T HAVE TO HAVE A SCRO REVIEW. SO THAT'S WHAT ADDRESSES JEFF'S QUESTION.

AND THEN WE'RE SAYING IS THAT ALL WE'RE GOING TO DO. SO THERE WAS A PROPOSAL TO SAY WE'RE GOING TO REALLY SORT OF THROW EVERYTHING AWAY, REMOVED A LOT OF OTHER THINGS. AND JEFF SAID, WELL, WAIT A MINUTE. THAT MAY BE GOING TOO FAR. JOHN. SORRY. JOHN SAYING THAT THAT MAY GO TOO FAR BECAUSE THAT MAY HAVE A LOT OF UNINTENDED CONSEQUENCES.

SCOTT CAME UP WITH ANOTHER PROPOSAL SORT OF SAYING IT'S NOT JUST THE FDA-MANDATED STUDIES IN THE PRE-IND MEETING THAT WE'RE EXEMPTING. WE'RE ALSO THINKING TO EXEMPT IF YOU'VE ALREADY HAD THE FUNCTIONAL ISSUES IN THE REVIEW ADDRESSED, YOU DON'T HAVE TO GO THROUGH THE SCRO AGAIN.

DR. WAGNER: WHO WOULD HAVE DONE THAT REVIEW?

MR. TOCHER: IT WOULD HAVE BEEN EITHER THE SCRO OR THE IACUC, WHICHEVER HAS THE APPROPRIATE EXPERTISE, TO ENSURE THAT YOUR STANDARD -- IN OTHER WORDS, YOU'RE STILL KEEPING YOUR STANDARD. YOU WANT THESE FOUR ELEMENTS MET. YOU NEED TO DO IT WITH THE APPROPRIATE BODY.

CHAIRMAN LO: LET'S DO IT IN PIECES.

LET'S SAY WE AGREE WITH JEFF, AND WE HAVE TO CRAFT THE LANGUAGE. IF A SCRO HAS ALREADY REVIEWED AND SAID 1, 2, 3, 4 YOU PASS, YOU DON'T HAVE TO GO THROUGH A SECOND REVIEW. I THINK WE CAN ALL AGREE ON THAT, I HOPE.

THEN THE NEXT QUESTION IS ARE WE GOING TO ALLOW SOME OTHER BODY OTHER THAN A SCRO TO MAKE THESE FOUR REVIEW POINTS? AND THE QUESTION IS DO WE THINK AN AUGMENTED IACUC IS APPROPRIATE FOR THAT? THAT'S A QUESTION, I THINK, WE'RE NOT TOTALLY IN AGREEMENT ON.

CO-CHAIR LANSING: I HAVE A QUESTION. THAT'S FOUR. THAT WOULD BE FOUR.

CHAIRMAN LO: CAN SOMEONE GO BACK AND ACTUALLY PUT UP A NEW SET OF 1, 2, 3, 4?

CO-CHAIR LANSING: THAT WOULD BE NO. 4, THAT YOU'RE LETTING SOMEONE ELSE DO IT. AND NOT BEING AS SOPHISTICATED LIKE YOU ARE, I GUESS WHAT I THOUGHT, BECAUSE I DON'T UNDERSTAND IT, I GUESS, WELL ENOUGH, I'M NOT A SCIENTIST, IS THAT THERE'S CERTAIN THINGS THAT THEY WOULD HAVE HAD TO HAVE DONE, AND THEY'D HAVE TO DO A CHECKLIST AND SAY WE DID THIS, WE DID THIS, WE DID THIS, WE DID THIS. NOW, IF YOU DON'T BELIEVE THEM OR YOU DON'T THINK THAT THEY HAVE THE PROPER QUALITIES TO DO IT, THAT'S

A WHOLE OTHER THING.

BUT I JUST THOUGHT THAT THERE WERE STANDARDS AND THAT THERE WAS CERTAIN ETHICS, THAT THEY'RE NOT GOING TO LIE TO YOU, AND THAT YOU COULD TRUST OTHER ORGANIZATIONS TO DO IT. BUT MAYBE I'M WRONG. THAT'S WHEN I WAS COMBINING 1 AND 4. I WAS SAYING OKAY.

DR. WAGNER: THE MAJOR THING IS THAT THE REASON SCRO'S WERE DEVELOPED IS BECAUSE IT WAS BELIEVED THAT THERE NEEDED TO BE A BODY OF INDIVIDUALS WHO ARE KNOWLEDGEABLE ABOUT THE FIELD. OTHERWISE, WE WOULD HAVE JUST RELIED ON THE IRB AND THE IACUC ALL ALONG. THOSE BODIES, IF THERE'S STEM CELL RESEARCH, RELY ON A SCRO TODAY TO AT LEAST ADDRESS CERTAIN ASPECTS, NOT THE WHOLE THING, BUT CERTAIN ASPECTS OF THE STEM CELL RESEARCH.

CO-CHAIR LANSING: SO THEN WHAT YOU GUYS ARE SAYING -- I ACCEPT THIS BECAUSE YOU'RE THE EXPERTS. WHAT YOU GUYS ARE SAYING THAT NOBODY BESIDES THE SCRO CAN DO THIS.

CHAIRMAN LO: WE'RE DEBATING.

DR. PATRICK TAYLOR: WE'RE DISCUSSING. THERE'S THIS NEW BODY OF RULES, COMPLEX RULES, NOBODY IS GOING TO THE IACUC TO MASTER.

CO-CHAIR LANSING: I UNDERSTAND. I

RESPECT WHAT YOU'RE SAYING.

DR. PATRICK TAYLOR: IT HAD TO BE LIMITED TO INTERPRETATION AND OTHER STUFF, DISCUSSION AMONG BODIES.

CHAIRMAN LO: LET ME AGAIN TRY. SO NO. 1 IS BASICALLY JEFF'S ISSUE. IF IT'S FDA MANDATED, IT'S OKAY. SECOND, IF A SCRO HAS ALREADY REVIEWED ESSENTIALLY THE STUDY, YOU DON'T HAVE GO THROUGH IT AGAIN. I THINK WE PROBABLY SAY MAYBE NOT JUST YOUR SCRO, BUT A SCRO AT AN EQUIVALENT INSTITUTION, YOU DON'T WANT TO SAY I DON'T TRUST HARVARD. SO I THINK --

CO-CHAIR LANSING: ARE NOT ALL SCRO'S EQUAL?

CHAIRMAN LO: THAT'S WHAT WE HAVE TO CRAFT. THE TENDENCY NOW IN IRB'S, YOU WILL ACCEPT OTHER IRB REVIEW. WE CAN THINK ABOUT ACCEPTING OTHER SCRO REVIEW.

NOW, A THIRD ISSUE IS CAN AN INSTITUTION SAY -- THIS GETS TO JEFF'S POINT -- WE DON'T HAVE A SCRO, BUT WE DO HAVE AN IACUC. IF WE PUT A COUPLE OF STEM CELL SCIENTISTS ON THE SCRO, IS THAT GOOD ENOUGH? AND I GUESS THERE'S SOME CONCERNS RAISED ABOUT WHETHER THAT GROUP WILL HAVE THE SORT OF DEEP BACKGROUND ON SORT OF ALL THE CASES THAT HAVE COME

THROUGH, UNDERSTANDING SORT OF PRIOR HISTORY, I THINK THAT JOHN -- I'M HEARING JOHN AND PAT HAD SOME RESERVATIONS ABOUT THE ALTERNATIVE TO A SCRO, THE IACUC BEING EQUIVALENT TO A SCRO.

DR. PATRICK TAYLOR: FOR SOME CASES I THINK IT'S PRETTY CLEAR THAT ESCRO'S KNOW THEY'RE WASTING THEIR TIME REVIEWING STUFF. (INAUDIBLE) INSTITUTIONS, PROBABLY BE A TREMENDOUS HELP PROVIDING AN EXPERT REVIEW. THESE THINGS THAT ARE EXEMPT NOW, WE KNOW. THE FDA ONE IS AN EXAMPLE. THERE ARE OTHERS TOO WHERE THEY REALLY HAVE TO (INAUDIBLE.) PROBABLY NOT AND SO ON. WE HAVE TO ACKNOWLEDGE THE EXEMPTIONS THAT ARE CONCRETE. IT'S NOT SUCH A BIG LIFT FOR AN INSTITUTION TO SAY, OKAY, WE'LL HAVE SOME IACUC PEOPLE PLUS. IT'S A GREAT UNKNOWN NOT LEFT OPEN FOR...

DR. LEE: SO MAYBE WE SHOULD GIVE EXAMPLES OF STUFF THAT YOU'RE COMFORTABLE EXEMPTING BECAUSE THAT'S THE MAJORITY OF STUDIES THAT COMPANIES ARE GOING TO BE, AND THAT'S WHO WE'RE TRYING TO HELP. ALL COMPANIES HAVE ESCRO'S. I BELIEVE THAT WAS YOUR INTENTION. AND MOST COMPANIES ARE DOING STUFF THAT ARE GOING TO CLINICAL TRIALS, AND THEY'LL BE FDA EXEMPT ANYWAY. THEY'RE NOT DOING THESE FAR-OUT STUFF THAT WE WERE DISCUSSING EARLIER.

CO-CHAIR LANSING: I'M SO NAIVE ON THIS. ISN'T THERE A WAY IF YOU SET UP -- WE HAVE OUR REGULATIONS. AND IF YOU ARE GOING TO BE EXEMPT, YOU HAVE TO SHOW TO US THAT YOU MET OUR REGULATIONS. MAYBE HARVARD'S IS BETTER THAN PODUNK U, BUT IF PODUNK U GOT A BUNCH OF PEOPLE TOGETHER TO SHOW THAT THEY WERE ABLE TO MEET THOSE STANDARDS, WE WOULD HAVE TO ACCEPT THAT. ISN'T THERE A WAY OF DOING THAT?

DR. WAGNER: I'M GOING TO MAKE IPS CELLS AND I'M GOING TO MAKE GAMETES. AND THE FDA IS JUST SAYING TO ME, OKAY, WELL, I'M GOING TO MAKE GAMETES FROM YOUR SKIN. AND SO FOR THE SAFETY STUDIES, THAT'S ALL STRAIGHTFORWARD. THAT'S ALL OKAY. DOES THAT BOTHER ANYBODY ELSE, THAT I'M NOW MAKING GAMETES?

DR. BOTKIN: NO. WE'RE TALKING ABOUT ADULT ANIMALS, INJECTION OF STEM CELLS INTO ADULT ANIMALS HERE.

DR. WAGNER: I AM. BUT I GUESS I'M SAYING I'M DOING SAFETY STUDIES. I'M TRYING TO FIGURE OUT WAYS OF JUST SAYING WHAT WE DON'T WANT TO DO IS TRY TO PREDICT EVERYTHING. I THINK I AGREE WITH YOU. THERE MIGHT BE SPECIFIC STUDIES THAT WE CAN SAY ARE EXEMPT. RATHER THAN TRYING TO PREDICT ALL THE

THINGS THAT COULD GO WRONG WITH THIS, WHY NOT FOLLOW YOUR ADVICE AND SAY LET'S JUST TALK ABOUT THE THINGS THAT WE KNOW OR FEEL COMFORTABLE WITH, AND JUST PUT IN THE EXEMPTION LIST. AND MAYBE A YEAR FROM NOW WE HAVE OTHER EXAMPLES OF EXEMPTIONS. BUT I DON'T KNOW THAT WE CAN ACTUALLY RELY ON IACUC TO MAKE CERTAIN DECISIONS WHEN THE THINGS ARE MUCH MORE COMPLEX. THAT WAS THE GAMETE THING. MAYBE THEY CAN, MAYBE THEY CAN'T. WE'RE JUST SAYING WHO ELSE CAN BE REVIEWING THIS OTHER THAN AN ESCRO? I'M TRYING TO COME UP WITH AN EXAMPLE OF SOMETHING THAT PARTS OF THIS MIGHT BE OKAY FROM AN FDA POINT OF VIEW, BUT THEN THERE'S OTHER PARTS OF THAT SAME EXPERIMENT THAT MIGHT BE UNCOMFORTABLE.

CO-CHAIR LANSING: IF WE JUST GO -- I'M ASKING YOU. DOES THIS SLOW US UP IF WE JUST LET OTHER ESCRO'S REVIEW IT, NOT JUST TO BE DEPENDENT ON OURSELVES? IS THAT GOING TO SLOW US UP A LOT? I'M ASKING YOU.

DR. WAGNER: ANSWER TO THAT QUESTION. I THINK AN ESCRO DOES. IT DOESN'T MATTER.

DR. PATRICK TAYLOR: (INAUDIBLE.) YOU DON'T WANT TO SAY EXEMPT, BUT THESE ARE THINGS TO THINK ABOUT, JUST THE THINGS (INAUDIBLE).

CHAIRMAN LO: GEOFF HAS CONCERNS ABOUT

TRYING TO SPECIFY --

DR. LOMAX: SCOTT CAN CHIME IN ON THIS. THIS IS ACTUALLY -- IT'S NOT JUST ISSUE SPECIFIC TO THE ISSUE WE'RE TRYING TO TACKLE, BUT IT'S A PRINCIPLE IN REGULATORY POLICY IN THAT, IN GENERAL, IT'S CONSIDERED BETTER TO SET A PERFORMANCE STANDARD; I.E., WHAT ARE THE TYPES OF THINGS YOU SHOULD CONSIDER, THAN CREATING LISTS OF EXEMPTIONS WHICH ARE SORT OF -- THEY DON'T HAVE THAT QUALITY OF -- YOU'RE STRIVING FOR SOMETHING AS OPPOSED TO LISTING. IT ACTUALLY CREATES CONFUSION ON THE GRANTEE SIDE AS WELL.

DR. PATRICK TAYLOR: EXEMPTION IS AN EXCEPTION TO THE RULE. SO WE HAVE A BODY OF ESTABLISHED QUALIFICATIONS. LIKE THE IRB'S, FOR EXAMPLE, HAVE AN EXCEPTION LIST. THERE'S A LIST FOR THAT REASON. THAT A BODY WAS -- IT'S A QUESTION OF WHETHER OR NOT THE STANDARDS (INAUDIBLE). IT WOULDN'T BE SUCH AN UNUSUAL THING TO HAVE A LIST OF REGULAR EXCEPTIONS. EVERY AGENCY IN THE UNITED STATES DOES THAT.

DR. LOMAX: THE DIFFICULTY WE RUN INTO, BECAUSE HISTORICALLY WE'VE HAD THIS PROBLEM, IS THERE IS A DIFFERENCE BETWEEN WHEN YOU'VE GOT A PROCEDURAL REQUIREMENT, WHICH IS WHAT WE'RE TALKING

ABOUT, AND TRYING TO TIE A LIST OF EXEMPTIONS TO A PROCEDURAL REQUIREMENT AS OPPOSED TO -- LIKE WE HAVE A LIST OF EXEMPTIONS FOR PROVENANCE WE BROUGHT UP EARLIER. IF IT'S IN THIS BANK BECAUSE YOU CAN DRAW A VERY CLEAR BOX AROUND, IT'S A STATIC, QUANTITATIVE, VERIFIABLE. BUT WHEN YOU START DRAWING EXEMPTIONS AROUND PROCEDURAL REQUIREMENTS, IT INEVITABLY JUST BECOMES VERY DIFFICULT.

DR. MILLAN: GEOFF, CAN I MAKE ONE COMMENT? SO, DR. WAGNER, JOHN, YOU BROUGHT UP THE CONCERN OF THINGS THAT CAN HAPPEN, SOME ACTIVITIES THAT CAN HAPPEN IN THE FUTURE THAT COULD BE OF CONCERN. PRESUMABLY EVERYTHING THAT'S GOING TO GO TO MEET THESE REQUIREMENTS HAVE GONE THROUGH PEER REVIEW. THAT IS THE OPPORTUNITY TO ACTUALLY REVIEW WHAT CIRM WOULD FUND, FOR INSTANCE. THE POLICIES DRIVING WHAT KIND OF THINGS WE WOULD FUND WOULD BE ONE KIND OF GATE THAT ONE WOULD HAVE TO GO THROUGH EVEN BEFORE THEY WOULD HAVE TO MEET THIS REQUIREMENT TO START THE ACTIVITIES FOR FUNDED AWARDS.

SO IF AN INVESTIGATOR SAID I'M GOING TO MAKE IPS CELLS AND MAKE GAMETES OUT OF IT, IT WILL GO THROUGH CIRM REVIEW. SO THAT WILL BE AN OPPORTUNITY TO TAKE A LOOK AND SAY IS THIS SOMETHING THAT WE WOULD FUND? DOES IT MEET OUR OWN

REQUIREMENTS?

AND THEN DR. BOTKIN HAD BROUGHT UP THE POINT THAT THE NATURE OF THE THINGS THAT THE SCRO REALLY LOOKS AT, AND I AGREE THAT HAVING STEM CELL EXPERTISE IS IMPORTANT, BUT THE QUESTION IS WILL THEY REALLY BE ADDRESSING SOME OF THE CONCERNS ABOUT HUMAN QUALITIES. ONCE THEY REVIEW IT, THEY'RE NOT ACTUALLY DOING THE FOLLOW-UP TO SEE IF THESE ANIMALS PROSPECTIVELY ARE GAINING HUMAN QUALITIES. IN ADDITION, GEOFF HAD DONE THE SURVEY, AND THOSE THAT UNDERWENT THE SCRO REVIEW REALLY DIDN'T HAVE ANY CHANGES TO THOSE PROTOCOLS. SO MAYBE THERE'S THINGS THAT HAVE HAPPENED THAT WE DON'T KNOW ABOUT JUST FROM THE OUTCOME SURVEY THERE.

SO I THINK -- AND WITH JEFF BRINGING UP THE INTRODUCTION OF INEFFICIENCIES, BY THEN TRYING TO GO TO THE EXEMPTION LIST, I THINK THAT IS GOING TO ADD A LOT OF COMPLEXITY. AND WHAT WE'RE TRYING TO DO IS STREAMLINE WHILE STILL MAINTAINING THE STANDARDS.

SO I GUESS WHAT I'M ASKING IS SOME OF THE CONCERNS THAT HAVE BEEN BROUGHT UP, NO. 1, DOES THE SCRO TRULY ADDRESS THEM? AND NO. 2, ARE THERE NOT OTHER WAYS THAT WE ARE ACTUALLY KEEPING TRACK OF THE ACTIVITIES SO THAT THESE KIND OF FAR-OFF ACTIVITIES

DON'T JUST START HAPPENING?

DR. WAGNER: MAYBE THAT WAS NOT THE BEST EXAMPLE BECAUSE SOME ARE REALLY FAR OFF. AT LEAST IN THE GRANT REVIEW, I'M NOT SAYING WHAT CIRM STAFF DO, BUT IN THE GRANT REVIEW, THERE ARE NO BIOETHICISTS TO BRING UP CERTAIN ASPECTS OF THIS. IT'S A GROUP OF SCIENTISTS AND PATIENT ADVOCATES TYPICALLY, AND PERHAPS OTHERS, BUT NOT BIOETHICISTS, AT THESE REVIEWS TYPICALLY. SO THAT'S ONE THING. SO I'M NOT SURE THAT THAT PART OF THE PROCESS REALLY ADDRESSES THE QUESTION.

I COULD THINK SCIENTIFICALLY THIS IS A GREAT IDEA, BUT YET THERE'S A LOT OF OTHER FACTORS ASSOCIATED WITH IT.

THE SECOND THING IS THAT I DON'T DISAGREE WITH YOU. I CAN'T SAY THAT THE SCRO'S NECESSARILY MAKE CHANGES, AND MAYBE THAT NEEDS TO BE REEVALUATED, WHAT WE THINK THEY SHOULD BE DOING VERSUS WHAT THEY ARE DOING. BUT MY GUESS IS IS THAT THERE'S A LOT OF THINGS THAT HAPPEN BEFORE THE ACTUAL FINAL REVIEW TAKES PLACE. AT MY CENTER, FOR EXAMPLE, WE HAVE A WHOLE AREA OF PEOPLE WHO ARE WORKING ON BASICALLY DEVELOPING HUMAN PANCREASES, PANCREATA, IN PIGS. AND THE ANIMAL FARMING IDEA MAKES THE COMMUNITY UNCOMFORTABLE.

SO THE POINT IS THAT WE NOW HAVE A BODY THAT JUST TACKLES A VARIETY OF THESE THINGS THAT WE THINK ABOUT BEFORE THEY ACTUALLY DO IT, AND IT'S ALREADY GONE THROUGH A SERIES ALMOST LIKE YOUR CIRM 2.0 ITERATIVE PROCESS. AND SO, YES, IT MAY NOT BE THAT YOU SEE -- I DON'T KNOW HOW THE QUESTIONNAIRE WAS ASKED OF THE ESCRO'S, BUT I WONDER IF NOT SOME OF THOSE FIXES TOOK PLACE ACTUALLY BEFOREHAND AND, THEREFORE, YOU'RE NOT PICKING IT UP.

DR. MILLAN: THAT IS A QUESTION.

DR. PATRICK TAYLOR: IT SEEMS TO ME IF THERE ARE EXEMPTIONS, IT'S PROBABLY CONFUSING. WE CAN'T GIVE EXEMPTIONS BECAUSE THAT'S WHAT WE'RE DOING. WE'RE GIVING AN EXEMPTION OF ONE ALREADY. WE CAN DO ONE. IT SEEMS TO ME IN SITUATIONS WHERE REVIEW IS ACTUALLY REDUNDANT AND WE KNOW IT'S REDUNDANT AND IS REDUNDANT, AND IT'S SAFE, A STANDARD EXEMPTION LIKE THAT, ALL THOSE STATES, THERE OUGHT TO BE MORE EXEMPTIONS. THESE ARE THE QUESTIONS WE'RE ASKING TO ANSWER. I HAVE A HARD TIME BELIEVING THAT A GRANTEE INSTITUTION WOULD HATE THE IDEA OF EXEMPTIONS FOR PERFORMING CERTAIN WORK. IT WORKS IN SOME OTHER CONTEXTS. IT SEEMS THAT THIS WORKS ASKING THE QUESTION AND ANSWERING AS AN EXAMPLE A SPECIES THAT WAS PROBABLY (INAUDIBLE.)

DR. LOMAX: I'M JUST NOT UNDERSTANDING THE SPECIFIC EXEMPTION THAT'S PROPOSED. I'M NOT SAYING --

DR. PATRICK TAYLOR: MY PROPOSAL WAS HAVING GIVEN ONE EXEMPTION, ACTUALLY ASK THE QUESTION, VIA SYMPOSIUM OR OTHERWISE, TO SEE WHERE EXPERIENCE AND SCIENTIFIC EVIDENCE INDICATES THAT EXEMPTIONS OR DIFFERENT KINDS OF REVIEW OUGHT TO BE GIVEN. THE QUESTION IS ACTUALLY WELL OVERDUE. TEN YEARS AFTER THIS STARTED. NOBODY KNOWS WHAT THE RULES ARE GOING TO BE.

CHAIRMAN LO: TAKING INTO ACCOUNT JOHN'S QUESTION AS TO WHETHER THERE WAS A PRE-SCRO APPROVAL DISCUSSION THAT LED TO SOME MODIFICATION TO THE PROTOCOL TO ADDRESS THE ISSUE.

DR. WAGNER: SO YOU HAVE TO GIVE THE CELLS -- THE SAME NUMBER OF CELLS YOU'RE GIVING TO A HUMAN YOU HAVE TO GIVE TO AN ANIMAL. YOU HAVE TO HAVE THE APPROPRIATE ANIMAL MODEL TO EVALUATE WHATEVER THE INDICATION IS. THE FDA WILL TELL YOU TO DO ALL THESE THINGS. YOU HAVE TO FIND OUT WHERE THE DISTRIBUTION OF CELLS ARE. SO WHERE IN THE BODY DID THEY GO? SO ALL THOSE THINGS WILL BE MANDATED. AND WHAT WE'RE SAYING, I THINK, IS THAT IF YOU CAN DEMONSTRATE THAT THIS IS WHAT WAS MANDATED BY THE

FDA IN ORDER TO MOVE IT FORWARD TO A CLINICAL TRIAL, OTHERWISE YOU CAN'T GO FORWARD.

DR. PATRICK TAYLOR: I WAS PROBABLY UNCLEAR. I ACTUALLY THINK STRONGLY TO GIVE AN EXEMPTION. I WAS USING IT AS AN EXAMPLE OF WHY WE CAN'T MAKE OTHER EXEMPTIONS WHICH MAY NOT BE TRUE. SO TO MAKE ONE DEFINABLE, THERE ARE OTHER CANDIDATES PROBABLY OUT THERE. IT SEEMS LIKE NOW IS A FINE TIME TO LOOK AT THE QUESTION TO GATHER EVIDENCE ON IT.

DR. LOMAX: I APOLOGIZE IF I IMPLIED -- I THOUGHT I HEARD SOMETHING ABOUT THAT CERTAIN CATEGORIES OF EXEMPTIONS ARE CLEAR AND OTHER ONES ARE UNCLEAR.

CHAIRMAN LO: LET ME TRY AND SEE WHERE WE ARE AT THIS POINT. MAYBE WE SHOULD JUST CONSIDER A MOTION TO EXEMPT FDA-MANDATED STUDIES, STUDIES OF INJECTING HUMAN STEM CELLS INTO VERTEBRATE ANIMALS REQUIRED BY THE FDA IN A PRE-IND MEETING WILL BE DEEMED TO MEET THE FOUR CRITERIA IN, WHATEVER, PAGE 4, SECTION (E)(1), (2), (3), (4). SO THAT TAKES OUT FROM SCRO REVIEW A WHOLE CLASS OF STUDIES. I'M NOT HEARING ANY OPPOSITION. WE WANT THE SCRO TO DO THAT. SO MAYBE WE APPROVE THAT, AND THEN SEE IF THERE'S ANYTHING ELSE WE WANT TO CHANGE.

DR. ROBERTS: AT ONE POINT, THOUGH, THERE WAS A DISCUSSION OF CONFIRMING THAT THE FDA ACTUALLY WOULD HAVE REQUIRED ALL OF THIS.

CHAIRMAN LO: ASSUMING THAT WE TASK THE STAFF WITH CONFIRMING WITH THE FDA THAT THIS IS PART OF THEIR POLICY AND NOT JUST SOMETHING THEY DO.

DR. WAGNER: THEY GIVE YOU A WRITTEN DOCUMENT.

CHAIRMAN LO: WE DO THAT DUE DILIGENCE. ASSUMING THAT COMES THROUGH, WE WOULD RECOMMEND TO THE ICOC THAT WE CHANGE THAT PART OF THE REGULATION AND ISSUE AN EXEMPTION. WE NEED TO WORK ON THE LANGUAGE, BUT I THINK WE'RE IN AGREEMENT. I HAVEN'T HEARD AGREEMENT SAYING, NO, NO, WE WANT THE SCRO TO REDO.

MR. SHEEHY: SO THE ONLY THING IS THE DEFINITION OF THE PRE-IND MEETING. WE CAN HAVE AN PRE-PRE-IND MEETING. SO I WOULD JUST SAY THAT SPECIFICALLY FDA MANDATED WHERE THEY SAY YOU HAVE TO DO THOSE.

DR. WAGNER: DOCUMENTABLE.

MR. SHEEHY: YEAH. AND NOT LIKE, WELL, I KNOW THE FDA IS GOING TO REQUIRE ME TO DO THAT. BUT WHEN THE FDA SAYS, OKAY, HERE YOU ARE. I NEED A TOX STUDY, I NEED A TUMORGENICITY STUDY, I NEED THIS AND

THIS AND THIS BEFORE YOU ARE GOING TO BE ABLE TO GET YOUR IND, IT'S CLEARLY MANDATED.

CHAIRMAN LO: LET ME ASK. RATHER THAN OUR TRYING TO DRAFT LANGUAGE ON THE FLY, LET ME ASK SCOTT AND GEOFF WITH ADVICE FROM OTHERS TO SORT OF DRAFT THIS. I THINK THIS IS SOMETHING THAT CAN CIRCULATE AROUND. AND I DON'T KNOW WHAT THE RULES ARE, WHETHER WE CAN VOTE ELECTRONICALLY, WE HAVE TO HAVE A CONFERENCE CALL, BUT I THINK THE GIST OF WHAT WE'RE TRYING TO DO IS RIGHT, AND WE JUST -- I DON'T WANT TO TRY AND CRAFT LANGUAGE ON THE FLY NOW.

MR. TOCHER: MY FIRST QUESTION WOULD BE IF THE MEETING IS GOING THROUGH TO TOMORROW MORNING, WE CAN CERTAINLY DO IT THEN. IF THERE'S A QUORUM, WE COULD JUST TAKE IT IN THE NORMAL COURSE OF THIS ITEM. OR WE COULD TAKE A VOTE ON A MOTION TO ENSURE THAT IT REFLECTS THE SENTIMENTS THAT YOU'VE EXPRESSED. AND THEN IT WOULD JUST BE A MATTER OF AFTER THE MEETING JUST CONFIRMING THAT THIS DOES INDEED REFLECT WHAT THE INTENT OF THE COMMITTEE IS.

DR. LOMAX: ONE PROCEDURAL QUESTION. WE COULDN'T GET PEOPLE LIKE VOTE THIS WITHOUT CONVENING ANOTHER MEETING. COULD WE DO SOMETHING LIKE WE GET THE MANDATE FROM THE COMMITTEE, WE DRAFT SOMETHING. AND THEN IF SOMEBODY FINDS IT TO BE OUTSIDE THAT

MANDATE, THAT WOULD TRIGGER US TO THEN HAVE TO MEET. SOMETHING LIKE THAT.

MR. TOCHER: I THINK WE'RE OVEREMPHASIZING THE BAGLEY-KEENE REQUIREMENTS, WHICH WE'RE NOT REALLY SUBJECT TO. WHAT I'M SAYING IS I THINK IT'S SUFFICIENT THAT WE GET THE SENTIMENTS EXPRESSED IN A MOTION OF WHAT YOU WANT THE LANGUAGE. AND THEN THE WORDSMITHING CAN BE CIRCULATED JUST TO ENSURE THAT IT, IN FACT, EMBODIES IT. IT WILL GO TO THE BOARD FOR APPROVAL AS TO WHETHER OR NOT IT WILL BE --

CHAIRMAN LO: DOES SOMEONE WANT TO DRAFT THAT LANGUAGE THAT WE CAN TAKE AS A MOTION? SCOTT, DO YOU WANT TO DO IT?

MR. TOCHER: I'M HAPPY TO WRITE IT AND CIRCULATE IT TO EVERYBODY THIS EVENING, IN FACT. AS I UNDERSTAND IT, IT WOULD BE A MOTION TO AMEND THE DRAFT LANGUAGE TO EXEMPT FROM SCRO REVIEW FOR COMPLIANCE WITH SUBSECTIONS (E)(1) THROUGH (4) THOSE FDA-MANDATED PRECLINICAL STUDIES.

CHAIRMAN LO: I THINK THAT'S THE GIST OF IT.

MR. TOCHER: IF IT'S PLACED WITHIN THAT REGULATION, IT WILL INCORPORATE ALL OF THE --

DR. BOTKIN: JUST TO BE CLEAR. SO THE SLIDE SAID WE WERE TALKING ABOUT TRANSPLANT OF STEM

CELLS INTO ADULT ANIMALS. AND THIS SECTION (E) IS TRANSPLANT OF STEM CELLS INTO ANIMALS REALLY AT ANY STAGE OF DEVELOPMENT. SO I WANT TO BE CLEAR ABOUT WHAT CLASS OF STUDIES WE'RE TALKING ABOUT.

CHAIRMAN LO: WELL, I THINK WE WERE SPECIFICALLY EXCLUDING BLASTOCYSTS. BUT THE FDA REQUIRES YOU TO DO EMBRYONIC OR FETAL INJECTIONS INTO A FETAL ANIMAL. I THINK WE'RE KEEPING THIS REQUIREMENT AND JUST SAYING IT IS A BIG EXEMPTION FOR FDA-MANDATED CELLS.

DR. BOTKIN: OKAY. SO THEY ARE TALKING ABOUT -- THIS IS TALKING ABOUT STEM CELL LINES IN NONHUMAN ANIMALS OR INTO THE BRAIN OF NONHUMAN ANIMALS AT ANY STAGE OF EMBRYONIC, FETAL, OR POSTNATAL DEVELOPMENT.

CHAIRMAN LO: WHEN YOU SAY THIS, DO YOU MEAN THE RESOLUTION OF THE FDA?

DR. BOTKIN: YES. IS THAT AN EXEMPTION TO THAT SECTION OR WHAT WE WERE REALLY PREVIOUSLY TALKING ABOUT, WHICH WAS TRANSPLANT OF ADULT ANIMALS?

DR. ROBERTS: WELL, THE EXEMPTION COULD JUST APPLY TO ADULT ANIMALS AND STILL BE UNDER HERE. THIS IS AN EXEMPTION TO THIS BROADER LANGUAGE, BUT I THINK WE SHOULD BE CLEAR WHAT WE'RE EXEMPTING.

CHAIRMAN LO: WE'VE BEEN TALKING ABOUT ADULT. WE'VE DISCUSSED INJECTION INTO EMBRYONIC OR FETAL. SO I'M NOT SURE WE'RE READY -- WE MAY GET THERE EVENTUALLY, BUT IT SEEMS TO ME WE NEED TO THINK THAT THROUGH.

MR. TOCHER: CAN I MAKE A SUGGESTION? THAT WE EXEMPT FROM SCRO REVIEW FOR COMPLIANCE WITH SUBDIVISIONS (E)(1) THROUGH (4) THOSE STUDIES INVOLVING TRANSPLANTATION OF STEM CELLS INTO ADULT ANIMALS THAT ARE FDA MANDATED FOR PRECLINICAL STUDY.

DR. PATRICK TAYLOR: HOW ABOUT THE ADOLESCENT ANIMALS?

DR. MARSALA: WE CALL DEVELOPMENT INTO SEXUALLY MATURE ANIMALS.

DR. WAGNER: IT'S REALLY ANY ANIMAL THAT'S POSTNATAL.

DR. MILLAN: POSTNATAL.

DR. WAGNER: ADULT STEM CELLS IS ANYTHING THAT'S NOT FETAL.

CHAIRMAN LO: NOT JUST ADULT. IT'S POSTNATAL ANIMALS MANDATED BY FDA.

DR. MILLAN: SHOULD IT BE MANDATED BECAUSE AT THE PRE-IND, SOMETIMES THEY'RE JUST YOUR PROPOSED STUDIES.

DR. WAGNER: NO. NO. NO. WHAT WE'RE

SAYING IS THAT THERE'S A DOCUMENT THAT THE FDA GIVES YOU. SO THE ONLY WAY YOU GET THAT DOCUMENT IS IF YOU DO A PRE-IND MEETING, AND THEN THEY WILL MODIFY WHATEVER YOU SAY. SO LET'S SAY ALL I WAS GOING TO BE ASKING -- I PROPOSED TO THEM I WOULD ONLY DO A TERATOMA ASSAY. THEY'RE GOING TO COME BACK AND SAY THAT'S NOT GOOD ENOUGH, AND YOU MUST DO THESE OTHER FIVE THINGS. WHEN THEY GET THAT DOCUMENT, THEN THAT'S WHAT CAN GO TO YOU ALL.

DR. MILLAN: RIGHT. IN THOSE SITUATIONS THAT'S CLEAR. BUT OFTEN WHAT WILL HAPPEN IS YOU'LL GO IN AND YOU'LL SAY WHAT WE PROPOSE TO DO IS THIS, AND YOU MAKE COMMENTS. THEY MAY NOT SAY ANYTHING ABOUT THOSE. THEY MAY MANDATE, THEY MAY SAY YOU DEFINITELY NEED TO DO THIS, BUT THEN WHAT HAPPENS TO THOSE OTHER PROPOSED ACTIVITIES?

DR. WAGNER: THEY GO THROUGH A SCRO THEN. IF THEY DON'T HAVE THAT DOCUMENT, THEN THEY GO TO SCRO.

CHAIRMAN LO: I THINK WE WANT DOCUMENTATION FROM THE FDA.

DR. MILLAN: BUT THEY HAVE AN AGREEMENT. IF THE FDA IS IN AGREEMENT WITH YOUR PROPOSED STUDIES, IS THAT CALLED MANDATED?

DR. WAGNER: NO. THERE WILL BE A

DOCUMENT.

DR. MILLAN: OKAY. JEFF.

MR. SHEEHY: I REALLY DON'T KNOW WHAT GAP WE'RE TRYING TO COVER. CELLS AT THAT POINT WILL HAVE BEEN HEAVILY EXAMINED. AND I ALSO HAVE AN ISSUE WITH THE PRECLINICAL LIMITATION BECAUSE AREN'T ANIMAL STUDIES SOMETIMES ORDERED UP IN DIFFERENT CLINICAL STAGES? SO IT SHOULD BE PRECLINICAL AND CLINICAL. I REALLY THINK WE'RE OVERREGULATING.

BEFORE THESE CELLS ARE GOING TO GO INTO PEOPLE, THEY'RE GOING TO BE REALLY LOOKED AT. AND THE FDA -- WE THINK THE FDA IS GOING TO BE WAY AHEAD OF EVERYBODY ELSE. THIS IS THE FDA. IF THEY'RE MANDATING -- THEY'RE GETTING PEOPLE TO DO STUDIES IN ANIMALS, THEY HAVE MORE POLITI- --

DR. MILLAN: NO. NO. MANDATING IS -- I MEAN THAT'S A PRETTY CLEAR THING. THE THING IS OFTEN IN A PRE-IND YOU'LL SAY WE ARE PROPOSING THIS BODY OF PRECLINICAL STUDIES. AND THE FDA MAY NOT HAVE COMMENTS TO IT OR MAY SAY WE ARE IN GENERAL AGREEMENT, AND THEN THERE'LL BE OTHERS THAT THEY'LL SAY DEFINITELY DO THIS.

DR. WAGNER: IT'S WRITTEN IN A WAY WHERE THEY HAVE RESPOND TO IT. THERE HAS TO BE A DOCUMENT. SO THERE WILL BE ONE. HOWEVER, IF YOU

DON'T HAVE THAT DOCUMENT, THEN THEY HAVE TO GO THROUGH A SCRO. THIS IS ALL DRIVEN BY IF YOU'RE A PHARMACEUTICAL COMPANY WHERE YOU'RE BRINGING THIS FORWARD TO CLINICAL TRIALS AND THEY DON'T HAVE A SCRO RIGHT THERE. THIS IS THE MAJORITY OF WHAT THEY'VE BEEN DOING; ISN'T THAT RIGHT?

MR. SHEEHY: IN REALITY IT'S HOW MANY PROJECTS ARE WE REALLY GOING TO SEE THAT INVOLVE COVERED LINES?

HOW MANY PROJECTS ARE WE GOING TO SEE? I MEAN WE'RE TALKING ABOUT A RELATIVELY FEW NUMBER OF PROJECTS. YOU'RE TALKING ABOUT LINES THAT ARE DERIVED FROM EMBRYOS, POTENTIALLY IPS LINES, BUT THAT'S IT. JUST THE AMOUNT OF STUFF YOU HAVE TO DO TO EMBRYONIC DERIVED CELLS AND IPS CELLS TO EVEN GET TO THE POINT WHERE YOU WANT TO TALK TO THE FDA LEADS ME TO BELIEVE THAT ALMOST ALL OF THIS, HUNDRED PERCENT OF THIS HAS REALLY BEEN WORKED THROUGH BECAUSE IT'S INCREDIBLY EXPENSIVE. IT'S INCREDIBLY -- IT'S JUST THE STAGE OF DEVELOPMENT. BY THE TIME -- AND YOU KNOW. YOU'VE SEEN THIS. BY THE TIME YOU GET THOSE CELLS THAT CLOSE TO THE LINE, THE ETHICAL ISSUES HAVE BEEN ADDRESSED ABOUT THOSE CELLS. THE SCRO HAS BEEN INVOLVED ALL THE WAY UP TO THAT POINT.

DR. WAGNER: THAT'S RIGHT.

MR. SHEEHY: NOW THAT YOU'RE GOING TO THE FDA, YOU'RE JUST ADDING ANOTHER LAYER. ONCE YOU START ENGAGING WITH THE FDA, ALL THE ETHICAL ISSUES AROUND THE PROJECT WILL HAVE BEEN ADDRESSED.

DR. PATRICK TAYLOR: WHAT ARE YOU SAYING THAT'S DIFFERENT?

DR. MARSALA: JUST AMENDMENT BASICALLY TO WHATEVER WAS ALREADY BEING STUDIED FOR TWO YEARS PROBABLY BEFORE THAT.

MR. SHEEHY: SO YOU'RE JUST ASKING FOR ANOTHER LAYER OF REVIEW. YOU'RE ASKING FOR ONE MORE REVIEW OF A PROJECT THAT'S BEEN REVIEWED ENDLESSLY BECAUSE YOU PROPOSED ANOTHER STUDY.

DR. WAGNER: THE WAY THIS ALL STARTED WAS THAT HOW DO WE SPEED THE PROCESS FORWARD. SO I DID THIS WORK IN AN ACADEMIC INSTITUTION. I GOT AN AWARD FROM CIRM. I HAD TO GO THROUGH THE SCRO. I DID DO ALL THAT STUFF. NOW I'M READY TO PASS IT TO YOU. YOU HAVE A COMPANY. OKAY. YOUR COMPANY IS NOT GOING TO BE WORKING WITH THIS CELL. RATHER THAN THAT COMPANY NOW DOING NEW ASSAYS WITH IT, RATHER THAN HAVING TO GO THROUGH A SCRO, WE'RE SAYING YOU DON'T HAVE TO GO TO A SCRO ANY LONGER. YOU HAVE GOTTEN YOUR IND PLAN, IT'S ALL READY TO GO. WE'RE

TRYING TO SAVE YOU TIME SO YOU DON'T HAVE TO GO THROUGH ANOTHER REVIEW PROCESS BECAUSE WE AGREE WITH YOU. IT'S REDUNDANT. YOU HAVE TO DO IT. SO YOU DON'T HAVE TO WORRY ABOUT IT. I THINK WE'RE TRYING TO SAVE THE HANDOFF IN A SENSE, THAT YOU DON'T HAVE TO DO IT AGAIN.

IF I WAS DOING IT FROM BEGINNING TO END, I'VE ALREADY GOTTEN SCRO APPROVAL, SO LET'S MOVE.

MR. SHEEHY: SO I WAS JUST TRYING TO FIGURE OUT WHERE THAT LINE IS, WHEN THAT LINE IS REACHED.

CHAIRMAN LO: NOW, LET ME MAKE SURE WE UNDERSTAND. IF YOU'RE GOING TO GO INTO STUDIES TO GET FDA APPROVAL FOR A PRODUCT, YOU'RE GOING TO HAVE TO GO TO THE FDA. WE'RE SAYING SINCE YOU'RE GOING TO GO TO THE FDA, GET THIS PIECE OF PAPER JOHN'S TALKING ABOUT, AND THEN YOU DON'T HAVE TO DO ANOTHER SCRO.

I HAD ORIGINALLY PROPOSED THAT IF YOU'VE ALREADY BEEN TO THE SCRO FOR THE LINE AND THE TYPE OF EXPERIMENT YOU'RE DOING, YOU DON'T NEED TO GO BACK TO SCRO AGAIN. YOU'RE DONE. SO THAT'S THE SECOND EXEMPTION. YOU'VE ALREADY GOT SCRO REVIEW FROM A SCRO --

MR. TOCHER: IF YOU'VE ALREADY GOT THE

SCRO REVIEW, YOU'RE FINE UNDER THE REGULATION EVEN AS IT IS. WE'RE TALKING ABOUT A SITUATION WHERE YOU DON'T.

CHAIRMAN LO: THAT TAKES CARE OF JEFF'S CONCERN. YOU'VE ALREADY DONE A SIMILAR EXPERIMENT AND YOU DON'T HAVE TO GO BACK. WE'RE NOW SAYING IF YOU HAVEN'T GONE TO A SCRO FOR SOME REASON, IF YOU'RE GOING TO THE FDA, GET THE FDA PIECE OF PAPER, YOU DON'T HAVE TO GO TO THE SCRO.

IF WE ALL AGREED ON THAT, THEN I THINK WE SHOULD RATIFY THAT.

CO-CHAIR LANSING: THAT'S AS FAR AS WE CAN GO BECAUSE NO ONE WANTED TO HAND IT OFF TO ANOTHER INSTITUTION THAT WASN'T A SCRO. THERE WAS TOO MANY QUESTIONS ABOUT IT.

MR. TOCHER: CAN I READ WHAT I THINK WE HAVE SO FAR?

EXEMPT FROM SCRO REVIEW FOR COMPLIANCE OF SUBDIVISIONS (E)(1) THROUGH (4) THOSE FDA-MANDATED STUDIES INVOLVING TRANSPLANTATION OF HUMAN STEM CELLS INTO POSTNATAL ANIMALS.

CHAIRMAN LO: THAT'S A MOTION.

CO-CHAIR LANSING: I'LL SECOND.

MR. TOCHER: WHO MADE THE MOTION?

CHAIRMAN LO: SHERRY MADE THE MOTION. WHO

SECONDS IT?

MR. SHEEHY: SECOND.

CHAIRMAN LO: JEFF SECONDS IT. OKAY. ANY PUBLIC DISCUSSION? IS THERE ANY MEMBER OF THE PUBLIC WE HAVEN'T DRIVEN AWAY? OKAY. ANY FURTHER DISCUSSION BY THE COMMITTEE? WE CAN DO A ROLL CALL VOTE.

MR. TOCHER: WE CAN JUST DO A VOICE VOTE.

CHAIRMAN LO: ALL THOSE IN FAVOR OF THE MOTION WITH THE UNDERSTANDING THAT WE NEED TO CHECK ON WHAT THIS PIECE OF PAPER IS CALLED. ALL THOSE IN FAVOR SAY AYE. ANY ABSTENTIONS? ANY NAYS?

MR. TOCHER: LET'S GO TO THE PHONE.

CHAIRMAN LO: ANYBODY ON THE PHONE STILL? ART? FRANCISCO?

MR. TORRES: AYE.

DR. PRIETO: AYE.

MR. TOCHER: MOTION CARRIES.

CHAIRMAN LO: MOTION CARRIES.

AND THEN SCOTT PROVIDED SOME CLARIFICATION, WHICH I THINK WE SHOULD PUT INTO THE RECORD, THAT IF YOU'VE ALREADY GOTTEN SCRO APPROVAL FOR THAT LINE FOR BASICALLY THOSE EXPERIMENTS, YOU DON'T NEED TO GO BACK TO THE SCRO. SO THAT'S ALREADY COVERED IN THE -- IT'S ALREADY AN EXEMPTION.

SO THAT TAKES CARE OF JEFF'S CONCERN.

MR. TOCHER: IT'S NOT AN EXEMPTION.

CHAIRMAN LO: IT'S ALREADY DONE. I JUST WANT THE RECORD TO SHOW THAT YOU DON'T HAVE TO KEEP GOING BACK FOR THE SAME LINE.

SO THEN WE WERE SORT OF KICKING AROUND THIS IDEA BECAUSE SHERRY SAID I DON'T HEAR OVERWHELMING SUPPORT FOR AN AUGMENTED -- FOR ALLOWING ANOTHER ENTITY, WHETHER IT'S SOMEBODY ELSE'S -- SOME OTHER INSTITUTION'S SCRO OR AN AUGMENTED IACUC TO SERVE THE FUNCTIONS OF DOING THE REVIEW FOR POINTS 1 THROUGH 3.

CO-CHAIR LANSING: I THOUGHT IT WAS A GOOD IDEA, BUT I CAN SEE THAT THE GROUP SAID THERE'S NO WAY TO MONITOR IT ENOUGH. ISN'T THAT THE CONSENSUS WAS THAT -- IT'S WHAT I HEARD WAS THERE WASN'T ENOUGH TRUST THAT ANOTHER INSTITUTION OTHER THAN A SCRO COULD DO IT WELL.

DR. BOTKIN: MY ONLY THOUGHT THERE IS THAT IT SOUNDS LIKE WE'RE LOADING ONTO THE SCRO SORT OF AN UNARTICULATED SET OF STANDARDS. WE'RE SAYING THAT WE WANT THEM TO SORT OF SIGN OFF ON THE ETHICS OF THESE THINGS, BUT NOBODY -- WE HAVEN'T HAD A SOCIALLY DETERMINED SET OF CONCLUSIONS OR REGS ABOUT WHAT THE ETHICS REALLY ARE HERE.

MAYBE WE WANT THEM TO SERVE AS SORT OF A RED FLAG. WAIT A SECOND. THERE'S SOMETHING WEIRD GOING ON WITH THIS. WE NEED TO THINK MORE ABOUT IT, WHICH IS A HARD PLACE TO PUT COMMITTEES IN IF YOU DON'T HAVE A SET OF CRITERIA BY WHICH THEY'RE SUPPOSED TO EVALUATE STUDIES.

AND I, AT LEAST, FIND 1, 2, 3, 4 HERE NOT PARTICULARLY COMPELLING. I THINK BERNIE POINTED OUT NO. 3 IS SORT OF THE KEY ONE, BUT I WOULD NOTE THAT (E)(3), EVALUATE THE PROBABLE PATTERN AND EFFECTS OF DIFFERENTIATION AND INTEGRATION OF HUMAN CELLS INTO NONHUMAN ANIMAL TISSUES, EVEN AS EXPRESSED THERE, THAT'S PROSPECTIVELY. DOESN'T ACTUALLY SAY YOU SHOULD DESIGN AN EXPERIMENT TO MAKE SURE THAT YOU ACTUALLY EVALUATE WHAT THE PATTERN IS OF EFFECTS AND DIFFERENTIATION WHICH COULD BE A MUCH MORE SORT OF TECHNICAL CHALLENGING ASPECT THAT YOU COULD LOOK TO A COMMITTEE FOR. I DON'T KNOW HOW -- WELL, PROBABLY ENOUGH SAID THERE.

WHERE DID THOSE FOUR COME FROM?

DR. LOMAX: I BELIEVE THAT'S DRAWN FROM THE NATIONAL ACADEMIES' GUIDELINES, BUT I'D HAVE TO CONFIRM THAT.

DR. BOTKIN: SO I GUESS PART OF THE POINT OF MY -- I GUESS I'M LESS CONVINCED THAT YOU

COULDN'T AUGMENT SOMETHING LIKE IACUC TO HELP ADDRESS SOME OF THESE SORTS OF ISSUES. I HAVEN'T BEEN CONVINCED THAT HAVING THE SCRO -- THE KIND OF RESEARCH WE'RE TALKING ABOUT REALLY DOES THE KIND OF WORK THAT WE WOULD WANT IT TO DO.

DR. WAGNER: I THINK THAT WE NEED TO LOOK THEN -- WE NEED TO GO BACK AND LOOK AT THE LANGUAGE OF THE SCRO, WHICH IS NOT HERE. ARE THERE CERTAIN EXPECTATIONS THAT LETS US KNOW WHAT THE SCRO'S FUNCTION IS, BUT IT'S JUST NOT DOCUMENTED IN THE PART THAT YOU HAVE.

DR. BOTKIN: RIGHT. YEAH. I'M CERTAINLY ON BOARD WITH THE WHOLE NOTION OF DEALING WITH EMBRYOS, AND THAT SORT OF STUFF ISN'T ADEQUATELY COVERED IN THE CURRENT SYSTEM, AND THAT ADDITIONAL OVERSIGHT PROBABLY MAKES A LOT OF SENSE. IN THE CONTEXT OF POSTNATAL ANIMALS, ONES WE WERE TALKING ABOUT...

DR. WAGNER: IT ALL CENTERS AROUND THE ISSUE OF CHIMERISM. AND WHEN WE TALKED ABOUT IT EARLIER, IT WAS THE PUBLIC'S FEAR LIKE THE *LIFE MAGAZINE* WITH THE EAR COMING OUT THE SIDE AND THE CHIMERISM STATUS AND CHANGES IN HUMANNESS AND ALL THAT. SO IT WAS DRIVEN BY THAT ASPECT OF IT. IT WAS HOPING THAT SINCE WE CAN'T ANTICIPATE WHAT ALL

THE STUDIES MIGHT BE, THAT IN A PROSPECTIVE WAY THAT INFORMATION WOULD BE DISCOVERED AS THESE NEW STUDIES AND NEW TECHNIQUES BECAME AVAILABLE BY THIS COMMITTEE, HAVING MONITORED THE FIELD, WHICH AN IACUC OR AN IRB DOESN'T NECESSARILY HAVE THE EXPERTISE TO DO. AT LEAST THAT WAS THE INTENT.

CHAIRMAN LO: SO I DON'T THINK WE'RE IN A POSITION TO APPROVE ANY FURTHER REVISIONS. LIKE SHERRY, I DON'T SENSE UNANIMITY ON THAT. BUT THE ISSUE THAT WAS RAISED BY SHERRY EARLIER IN THE MEETING WAS IN KEEPING WITH THIS NOTION THAT WE WANT -- CIRM 2.0 WANTS TO BE EFFICIENT, BUT PROTECTIVE OF HUMAN PARTICIPANTS AND ALSO SORT OF THE ETHICAL SORT OF PROBLEMS, DO WE WANT TO SORT OF DO MORE IN THE FUTURE TO SEE ARE THERE OTHER WAYS OF EITHER DELINEATING CLASSES OF RESEARCH WHERE WE THINK SCRO REVIEW IS NOT EFFECTIVE AND PRESENTS DELAY? AND THERE WAS SOME CONCERN ABOUT ARE PEOPLE WILLING TO ACCEPT OTHER BODIES OR SOME WAY WE COULD DEFINE THAT OTHER BODY? IS THERE A WAY OF MOVING TOWARDS ACCEPTING ANOTHER SCRO'S REVIEW? CERTAINLY IT SEEMS TO ME WOULD YOU ACCEPT ANOTHER CIRM GRANTEE INSTITUTION'S SCRO, SOMETHING LIKE THAT? WE CAN CHIP AWAY AT IT A LITTLE BIT.

I HEARD A MUCH MORE RADICAL PROPOSAL WHICH

IS MAYBE WE SHOULD REALLY TAKE A DEEPER DIVE INTO WHAT DO SCRO'S DO THAT ARE VALUABLE AND WHAT DO SCRO'S DO THAT IS INEFFICIENT AND NOT HELPFUL. AND JOHN WAGNER RAISED A SUGGESTION THAT MAYBE IT'S THE INFORMAL INTERACTION. IRB'S WILL OFTEN DO THAT AS WELL. LET'S TALK ABOUT WHAT YOU SUBMITTED AND CONCERNS ABOUT THIS. AND BY THE TIME IT GETS TO THE FORMAL IRB, IT GOES THROUGH.

I DON'T KNOW IF WE WANT TO HIGHLIGHT CERTAIN TYPES OF RESEARCH THAT ARE NOT THE KINDS OF THINGS SHERRY USED TO MAKE MOVIES ABOUT, BUT COMING UP OUT OF THE LAB IN A COUPLE OF YEARS, NOT NECESSARILY TO PUT NEW REGULATION, BUT TO SAY THESE ARE THE KINDS OF THINGS WE THINK SCRO'S, IF THEY THINK ABOUT AND MAKE A CONTRIBUTION, SO IT'S NOT REGULATORY, BUT IT'S MORE THIS IS THE KIND OF THING WE WANT YOU TO FOCUS ON.

I'M JUST THINKING THAT MAYBE -- WE'VE DONE QUITE A LOT HERE TO SORT OF CLEAR AWAY SOME UNDERBRUSH. I'M JUST WONDERING IF WE WANT TO AT LEAST HAVE GEOFF AND OTHERS EXPLORE OTHER APPROACHES. THEY MAY COME BACK AND SAY NO.

CO-CHAIR LANSING: I PERSONALLY WOULD JUST LIKE TO UNDERSTAND WHY NOBODY ELSE BUT A SCRO CAN DO THE WORK THAT WE'RE DOING. NO. 4. YOU ASSIGN IT --

IF AN INSTITUTION CAN PROVE TO YOU THAT THEY HAVE THE RIGHT PEOPLE TO DO WHAT THE SCRO DID, I DON'T HAVE THE KNOWLEDGE. I JUST WOULD BE CURIOUS, GEOFF, IF YOU COULD FIND OUT IF OTHER PEOPLE THAN THE SCRO CAN DO IT. NO. 4, COULD THEY PROVE IT TO US IN SOME WAY? IF THEY COULDN'T, THEY COULDN'T.

DR. LOMAX: IN PREPARATION FOR THIS MEETING IN TERMS OF EXPLORING WHAT ROADBLOCKS PEOPLE ARE RUNNING INTO AND HOW THEY COULD REMEDY IT, THE CASE WAS MADE THAT BECAUSE THEY ALREADY HAVE EXISTING IACUC COMMITTEES, THEY COULD ADD THE EXPERTISE AND GIVE SOME STATEMENT OF COMMITMENT TO MEETING THESE REQUIREMENTS. BUT WE CAN TRY TO DO A MORE ELABORATE SURVEY.

THE TROUBLE WE GET INTO -- THE POINT THAT GETS A LITTLE BIT OF PULL-BACK IS IF YOU ASK MOST OF OUR GRANTEES WHO ARE VERY RESPONSIVE TO SURVEYS, BECAUSE THEY HAVE SCRO'S, THEY WOULD JUST SAY WE DON'T NEED THIS. THE HARDER PART IS FINDING --

CO-CHAIR LANSING: YOU KNOW WHAT, THEN, I THINK WE SHOULD LEAVE IT ALONE. IT DOESN'T SOUND LIKE -- I HAVE TO ASK RANDY, BUT IT SOUNDS LIKE WHAT WE'VE DONE IS ENOUGH TO -- I'M LOOKING AT YOU.

DR. MILLAN: WE'RE ADDRESSING THE CLINICAL STAGE PROJECT, THAT POTENTIAL ROADBLOCK, THAT'S BEEN

ADDRESSED BY THE MOTION THAT WAS JUST PASSED.

CO-CHAIR LANSING: YOU FEEL GOOD. YOU FEEL LIKE WE'VE DONE ENOUGH. IF YOU FEEL GOOD, THEN I FEEL GOOD. BECAUSE I'M LOOKING -- YOU'RE THE EXPERTS. I'M SAYING, OKAY, IF WE HAVE NOT DONE ANYTHING TO HARM OUR STANDARDS, TO HARM SAFETY, AND WE HAVE UNTANGLED THE BUREAUCRACY AND THE ROADBLOCKS, THAT'S WHAT WE WERE SUPPOSED TO DO TODAY, SO THEN I THINK WE SHOULD FEEL GOOD AND GO TO DINNER.

DR. BLEDSOE: I HAVE ONE QUESTION. GIVEN THE FACT THAT A LOT OF WHAT WAS DRIVING THIS WAS THAT SOME INSTITUTIONS DID NOT HAVE A SCRO, I'M WONDERING IF IT'S STILL WORTH LOOKING INTO THIS ISSUE OF RELYING ON ANOTHER INSTITUTION'S SCRO WOULD BE SOMETHING.

CHAIRMAN LO: WE COULD SAY, TO FOLLOW UP ON THAT, YOU CAN CERTAINLY RELY ON THE SCRO OF A CIRM-FUNDED INSTITUTION.

DR. LOMAX: POINT OF FACT. WE DO ALLOW THAT. WHAT'S HAPPENED IS, FOR WHATEVER REASON, THERE'S BEEN AN UNWILLINGNESS AMONGST A NUMBER OF INSTITUTIONS TO ASSUME, QUOTE, UNQUOTE, THE LIABILITY ASSOCIATED WITH THAT TASK.

DR. BLEDSOE: SOUNDS LIKE SIMILAR TO THE

IRB SITUATION. NOT SURPRISING.

DR. ROBERTS: IS THERE A WAY TO ADDRESS THAT, THEN, THAT WE COULD DO SOMETHING? I DON'T KNOW IF IT WOULD BE A REGULATION OR A POLICY TO ADDRESS THAT CONCERN. THAT SEEMS LIKE AN OBVIOUS WAY OF RESOLVING THIS PROBLEM, JUST USE ANOTHER CIRM-FUNDED INSTITUTION.

CHAIRMAN LO: THE RELUCTANCE OF THE SCRO WHO IS THE RECIPIENT OF, OH, WON'T YOU BE OUR SCRO OF RECORD, AT LEAST IN THE IRB WORLD, THERE WAS A LONG HAUL TO SAY, YEAH, I'LL TAKE RESPONSIBILITY FOR SOMETHING GOING ON IN THE OTHER INSTITUTION.

DR. ROBERT TAYLOR: THIS IS SOME EXTRA WORK AND THE LIABILITY, SO IT'S KIND OF A BAD DEAL.

DR. BOTKIN: BUT IT DOES WORK FOR NETWORKS. WHEN YOU HAVE AN ESTABLISHED GROUP THAT IS GOING TO BE WORKING TOGETHER OVER TIME, THEN SETTING UP THOSE AGREEMENTS --

DR. ROBERT TAYLOR: IT STRIKES ME THAT THIS KIND OF HIGH OCTANE IACUC SHOULDN'T BE THAT HARD TO ACCOMPLISH. THIS ISN'T REALLY KIND OF A PIONEERING TECHNOLOGY. STEM CELL BIOLOGY IS REALLY OUT THERE. ALMOST EVERY PLACE THAT'S WORTH ITS SALT HAS GOT THAT EXPERTISE. IT WOULD SEEM TO ME THAT IT MIGHT BE HARD FOR THE INDUSTRY KIND OF COMPONENTS.

CHAIRMAN LO: BEFORE WE ADJOURN FOR DINNER, THERE'S STUFF HAPPENING TOMORROW, BUT THERE'S ONE VOTE GEOFF WOULD US TO TAKE TODAY, WHICH IS HOPEFULLY A SMALL ONE. IF NOT, WE'LL JUST POSTPONE IT TILL TOMORROW. THAT'S ON PAGE 2, THE LEFT-HAND COLUMN, LINE 32.

DR. LOMAX: AGAIN, THIS IS ANOTHER -- THIS IS A CASE WHERE THE NATIONAL ACADEMIES HAS ACTUALLY MODIFIED ITS REQUIREMENT AROUND BREEDING OF ANIMALS. ORIGINALLY THEY SAID THE BREEDING OF ANY ANIMAL, YOU COULDN'T BREED ANIMALS. THEY SUBSEQUENTLY AMENDED THAT TO INCLUDE THE PHRASE "SUCH THAT IT COULD CONTRIBUTE TO THE GERMLINE." AGAIN, THIS ISN'T A BURNING ISSUE. I'VE TRIED TO GET THE BACK HISTORY IN TERMS OF LOOKING THROUGH THE NATIONAL ACADEMIES' REPORTS.

THE SENSE I GOT IS THAT IN THE FUTURE IT MAY BE SORT OF WHAT I CALL THE THALIDOMIDE EXAMPLE. IT MAY BE IMPORTANT TO HAVE SAFETY PROTOCOLS WHERE YOU HAVE IMPLANTATION OF CELLS AND THEN YOU HAVE A BREEDING CYCLE TO SEE IF THERE'S ANY GENERATIONAL EFFECTS FROM THE CELL THERAPY.

DR. PATRICK TAYLOR: THE ISSCR REACHED (INAUDIBLE) CONCLUSION, SO THEY INCORPORATED THE ISSCR CHANGE.

DR. LOMAX: THAT WAS THE ISSCR. SO THAT PROBABLY MIGHT HAVE COME FROM THE ISSCR. AGAIN, UNLIKE THE PREVIOUS CONVERSATION WHERE WE HAD THINGS DRIVING -- EXPERIENCE DRIVING IT, THIS HASN'T COME UP YET, BUT IT IS ONE OF THE AREAS WHERE OTHER REGULATIONS DO DEVIATE NOW FROM THE NATIONAL ACADEMIES AND THE ISSCR.

DR. PETERS: COMMENT AND QUESTION. JUST TO REDUCE ANY AMBIGUITY, WE COULD SAY THAT THEY COULD CONTRIBUTE TO THE ANIMAL'S GERMLINE.

THEN I HAVE A QUESTION AS TO -- WE DID ACTUALLY DISCUSS THIS SOME TIME BACK. AND WHAT'S THE MOTIVE, WHAT'S THE REASON THAT WE DON'T WANT TO INFLUENCE THE GERMLINE OF AN ANIMAL MODEL? OR WHY DO THE GUIDELINES STIPULATE THAT? WHAT'S GOING ON? WHAT'S THE RATIONALE?

DR. ROBERT TAYLOR: SO THAT'S THE SUPER RAT PHENOMENA.

DR. PETERS: IS THAT WHAT IT IS? OKAY.

DR. WAGNER: THE CONCERN IS INTRODUCING HUMAN CELLS, MAKING -- THE CONCERN WAS IF YOU HAVE HUMAN GERMLINES BEING BRED IN ANIMALS, THAT'S THE CONCERN. THAT'S THE FEAR OF SOME OF THE PUBLIC.

DR. PETERS: A WHOLE BREED OF HUMANALS, HUH?

DR. WAGNER: REMEMBER THE PHOTOGRAPH OF THE SEMIPIG-HUMAN-DOG?

DR. PETERS: YEAH. I REMEMBER ALL OF THOSE ISSUES, BUT WHAT IS DISTINCTIVE ABOUT THE ANIMAL GERMLINE? I'M NOT GOING TO DEBATE IT. I JUST WOULD LIKE TO KNOW WHAT THE RATIONALE IS. I CAN SEE WHY YOU WOULDN'T WANT TO DO THAT TO A HUMAN GERMLINE. ANYWAY.

DR. ROBERTS: I THINK SOME OF THE CONCERNS WITH THE HUMAN GERMLINE IS NOT -- IT'S THAT YOU DON'T KNOW WHAT THE CONSEQUENCES WOULD BE. AND I THINK THERE'S SIMILAR CONCERNS ABOUT CHANGING ANIMAL GENOMES. YOU DON'T KNOW WHAT WILL BE THE CONSEQUENCE OF BREEDING ANIMALS THAT ARE COMPLETELY DIFFERENT FROM ANIMALS THAT EXIST NOW.

DR. MARSALA: I THINK THE REALLY CONCERN IS THAT HUMAN GERMLINE IN ADULT GROW THEM, FOR EXAMPLE, AND THEN YOU WOULD BREED THE ANIMAL WITH WILD-TYPE ANIMAL WHICH DOESN'T HAVE HUMAN GERMLINE, AND YOU WOULD HAVE A SEMI-HUMAN, SEMI-RODENT.

DR. ROBERT TAYLOR: THE MOST PART IS THE PROBLEM IF YOU USE A RAT OR A MOUSE LINE TO GET YOUR SPERM FOR SPERM DONATION, THAT PROBABLY WOULD BE OFFENSIVE TO SOME PEOPLE.

DR. WAGNER: FIRST OFF, I DON'T THINK THAT

YOU CAN HAVE A VIABLE EMBRYO BY MIXING HUMAN AND MOUSE, BUT COULD YOU THEN CREATE A HUMAN EMBRYO IN A MOUSE?

DR. LEE: CHANGE THE LANGUAGE TO PROHIBIT.

DR. LOMAX: RIGHT NOW IT'S A HARD LIMIT ON BREEDING. AND THE IDEA IS THAT YOU -- ACTUALLY THERE MAY BE CERTAIN CASES WHERE YOU WANT TO DO AN INTERGENERATIONAL STUDY. AS LONG AS YOU'VE EVALUATED THE POTENTIAL TO CONTRIBUTE TO THE GERMLINE, YOU CAN'T DO THAT. YOU CAN'T.

DR. ROBERT TAYLOR: I GUESS IF WE DO SOMETHING LIKE THIS, THERE SHOULD PROBABLY ALSO BE SOME MANDATE TO INVESTIGATE GERMLINE TRANSMISSION BECAUSE EVEN WITHOUT INTENTIONAL --

DR. WAGNER: MY NOTE IS HOW DO WE KNOW?

DR. ROBERT TAYLOR: BONE MARROW-DERIVED STEM CELLS THAT GET INTO THE -- I DON'T REALLY KNOW WHERE THESE.

DR. WAGNER: IN REALITY IT WAS REALLY TO PROVIDE SOME REASSURANCE TO THE COMMUNITY THAT IT WAS NOT AN INTENDED ACT. BUT YOU'RE ABSOLUTELY RIGHT. HOW DO WE KNOW IF WE DON'T LOOK?

DR. LOMAX: AGAIN, THAT IS A CASE WHERE HAVING AN OVERSIGHT COMMITTEE, THAT'S THEIR JOB. THEY EMBODY THESE REGULATIONS. THEY'RE CHARGED.

THERE'S LOTS OF ISSUES LIKE THAT. THEY'RE TASKED WITH KNOWING THESE REGULATIONS AND APPLYING THEM IN INSTITUTIONAL STUDIES.

DR. BOTKIN: BUT THIS DOES SAY SUCH THAT THEY COULD CONTRIBUTE TO THE GERMLINE. THE QUESTION IS DO WE KNOW ENOUGH TO KNOW WHEN THAT MIGHT HAPPEN? SHOULD THERE BE EXACTLY THAT REQUIREMENT, AND YOU, IN FACT, EVALUATE. IF YOU'RE BREEDING THE ANIMALS, YOU BETTER LOOK TO FIND OUT WHETHER IT'S BEEN TRANSMITTED.

DR. ROBERT TAYLOR: I THINK THAT'S A PRETTY SIMPLE REQUEST.

DR. PATRICK TAYLOR: THE EXAMPLE THAT CAME UP WAS SAYING CERTAIN KIND OF GROWTH FACTORS. THE THOUGHT WAS WE MAY NOT KNOW WHEN THEY DO CONTRIBUTE. WE KNOW WHEN THEY DON'T. SO IF YOU'RE NEW TO THE ANIMALS, THEN BETTER FOLLOW THEM.

CHAIRMAN LO: WHERE ARE WE ON THIS PARTICULAR? GEOFF HAD PROPOSED AN AMENDMENT TO THE REGULATIONS. HAVE WE REACHED A POINT --

CO-CHAIR LANSING: FINISH THAT.

CHAIRMAN LO: WE WERE TALKING ABOUT TOMORROW. THERE IS A POSSIBILITY THAT WE MAY NOT NEED TO MEET IN PERSON.

CO-CHAIR LANSING: OR AT ALL. BUT FIRST

FINISH IT.

CHAIRMAN LO: FIRST FINISH GEOFF'S REQUEST TO AMEND THAT PART OF THE -- I WASN'T CLEAR FROM THE DISCUSSION HERE WHETHER THERE WAS AGREEMENT TO MAKE WHAT PRIMARILY I THOUGHT WAS AN EDITORIAL CHANGE, MOVING THE COVERED TO A DIFFERENT PART OF THE --

DR. LOMAX: THE FUNDAMENTAL POLICY CHANGE WOULD BE REMOVING A HARD RESTRICTION ON ANIMAL BREEDING.

DR. ROBERTS: WHERE IS THAT?

DR. LOMAX: PAGE 2, LINE 32 THROUGH 35.

DR. ROBERTS: BUT THE PROHIBITION IS STILL THERE.

DR. LOMAX: THAT'S RIGHT. THE TEXT IN PURPLE HAS BEEN ADDED. SO THERE IS A RESTRICTION ON BREEDING.

DR. WAGNER: SO RIGHT NOW THERE'S NO BREEDING.

DR. LOMAX: NO BREEDING, PERIOD. THE CHANGE WOULD ALLOW BREEDING.

CHAIRMAN LO: AS LONG AS NO GERM -- CONTRIBUTION OF THE HUMAN STEM CELL TO THE GERMLINE.

DR. LOMAX: CORRECT.

DR. ROBERTS: NOW I SEE. IT'S OKAY. I'M SORRY. I CAN SEE NOW. I NEED TO TAKE MY GLASSES

OFF AND HOLD IT CLOSE UP TO DETECT THE PURPLE AS DISTINGUISHED FROM THE BLACK INK. VERY SORRY.

CO-CHAIR LANSING: IT DOESN'T BOTHER YOU, AND YOU WANT TO BE SURE --

DR. ROBERTS: LET ME SEE.

DR. ROBERT TAYLOR: I THINK THERE SHOULD BE SOME LEVEL OF --

DR. MARSALA: I HAVE A QUESTION RELATED. PATRICK, YOU MADE A COMMENT, YOU HAVE A TERATOMA, HIGHLY LIKELY YOU HAVE SOME GERM CELLS.

DR. PATRICK TAYLOR: ACTUALLY I DIDN'T SAY THAT. I SAID (INAUDIBLE). SO THE ESCRO HAS TO QUESTION ABOUT THAT. THEY DID ACTUALLY GET AN ANSWER TO IT. QUESTION IS WHETHER THERE WAS NO GERMLINE TRANSMISSION. IT WAS IMPOSSIBLE IN TERATOMA CASES, BUT THEY HAD A PROCESS SIMILAR TO WHAT HE'S DESCRIBING NOW WHERE THEY LOOKED AT THE QUESTION.

CHAIRMAN LO: ROB TAYLOR, YOU RAISED THE CONUNDRUM THAT YOU HAVE TO PROVE -- THEY COULD CONTRIBUTE IS PRETTY PROBABILISTIC IF YOU THINK -- HOW DO YOU PROVE THAT THEY COULDN'T CONTRIBUTE OTHER THAN DOING THE EXPERIMENT?

DR. ROBERT TAYLOR: DOING THE EXPERIMENT, LOOKING FOR THOSE.

MR. TORRES: IS THERE A MOTION ON THE BREEDING LANGUAGE?

CHAIRMAN LO: NOT YET. WE'RE TRYING TO GET THERE.

DR. BOTKIN: SO I THINK THE NOTION WAS IF YOU DO GO AHEAD AND BREED, THERE SHOULD BE AN OBLIGATION TO CHECK AND SEE WHETHER THERE HAS BEEN ANY TRANSMISSION. OTHERWISE YOU'RE JUST GUESSING.

CHAIRMAN LO: IS THAT COVERED BY THIS LANGUAGE IN PURPLE?

DR. BOTKIN: NO.

DR. ROBERTS: NO.

CHAIRMAN LO: HOW WOULD YOU AMEND IT?

DR. ROBERTS: IS THE REASON FOR THE ORIGINAL BAN ON BREEDING TO AVOID THE CONTRIBUTION TO THE GERMLINE? IN OTHER WORDS, IS THE ORIGINAL CONCERN COVERED NOW BY THIS PURPLE LANGUAGE?

DR. LOMAX: AGAIN, PAT, YOU WERE PART OF THAT PROCESS. MY UNDERSTANDING WAS IT WAS MODIFIED BECAUSE THE THOUGHT WAS HAVING A BLANKET RESTRICTION WAS PROBLEMATIC. THEREFORE, THE CONCERN WAS, YES, IF THE GERMLINE BECAME HUMANIZED, THAT'S THE PROBLEM, SO YOU NEED TO AVOID THAT OUTCOME, BUT BREEDING ITSELF IS OKAY.

DR. PATRICK TAYLOR: THE USE OF GERMLINE

LANGUAGE, WASN'T THAT PEOPLE MINDED THE IDEA (INAUDIBLE) CELSS AND BE SURE THERE WAS NO CONTRIBUTION, WAS THEY DID IT WITH A GERMLINE IN THE CLASSIC SENSE IN ORDER TO MODIFY THE SPECIES. SO THIS LANGUAGE ACTUALLY WORKS. DOESN'T REALLY CARE WHETHER THEY USE AN ANIMAL AS GERMLINE. (INAUDIBLE) TO SPECIES.

DR. ROBERTS: SO, IN FACT, THEN, IN ESSENCE, THIS LANGUAGE ACTUALLY YOU CAN SAY PINPOINTS WHAT THE CONCERN WAS AND DOESN'T REALLY CHANGE THE PROHIBITION. IT CHANGES THE LANGUAGE. IT'S NO LONGER A BLANKET PROHIBITION. BUT WHAT IT'S SPECIFICALLY PROHIBITING IS WHAT THE ORIGINAL PROHIBITION WAS CONCERNED ABOUT. IF THAT'S THE CASE, I'M FINE WITH IT. MY ONLY CONCERN IS IF THERE WAS SOME OTHER ISSUE WITH BREEDING ANIMALS INTO WHICH COVERED STEM CELLS HAVE BEEN INTRODUCED BEYOND THE CONCERN ABOUT GERMLINE WHICH I'M JUST NOT AWARE OF. I DON'T KNOW. BUT IT SOUNDS LIKE WHAT PATRICK IS SAYING, THAT WAS THE ORIGINAL CONCERN.

DR. ROBERT TAYLOR: I THINK I COULD PROPOSE LANGUAGE HERE, AND THAT WOULD BE BREEDING ANY ANIMAL INTO WHICH COVERED STEM CELLS HAVE BEEN INTRODUCED SHOULD BE INTERROGATED TO DEMONSTRATE THAT THEY DO NOT CONTRIBUTE TO THE GERMLINE. I

THINK THAT KIND OF SOLVES THE ISSUE MUCH MORE EXPLICITLY THAN IS STATED HERE.

MR. TOCHER: COULD YOU JUST REPEAT?

DR. ROBERT TAYLOR: STEM CELLS HAVE BEEN INTRODUCED SHOULD BE INTERROGATED TO DEMONSTRATE THAT THEY DO NOT CONTRIBUTE TO THE GERMLINE.

DR. ROBERTS: THAT WOULD HAVE TO -- IT WOULD HAVE TO BE CHANGED SO ITS PLACEMENT, BECAUSE THIS IS A LISTING OF ACTIVITIES THAT ARE NOT ELIGIBLE. SO IF YOU WORK ON THE WORDING.

DR. WAGNER: UNLESS YOU CAN DEMONSTRATE.

CHAIRMAN LO: DO YOU WANT TO READ THAT OUT AND WE CAN VOTE ON IT.

MR. TOCHER: THE MOTION WOULD BE TO REPHRASE PROHIBITION TO READ "BREEDING ANY ANIMAL INTO WHICH COVERED STEM CELLS HAVE BEEN INTRODUCED UNLESS THEY HAVE BEEN INTERROGATED TO DEMONSTRATE THAT THEY DO NOT CONTRIBUTE TO THE GERMLINE."

CHAIRMAN LO: UNLESS IT HAS BEEN -- I KNOW INTERROGATING IS A FANCY TERM. UNLESS IT HAS BEEN DEMONSTRATED THAT THE HUMAN STEM CELLS DO NOT CONTRIBUTE TO THE ANIMAL'S GERMLINE.

DR. PETERS: I THINK THERE ARE A FEW MORE WRINKLES TO WORK OUT BECAUSE IT'S REALLY THE EXTENSION OF A SENTENCE THAT BEGINS "THE FOLLOWING

ACTIVITY IS NOT ELIGIBLE." AND IT LOOKS LIKE --

DR. ROBERT TAYLOR: I THINK BREEDING IS THE ACTIVITY PROBABLY.

CHAIRMAN LO: YOU CAN'T FUND BREEDING UNLESS YOU'VE SHOWN THAT THERE'S NO HUMAN COMPONENT TO THE ANIMAL'S GERM CELLS.

DR. BOTKIN: YOU HAVE TO BREED TO DO THAT. THERE'S SOME VERB TENSE ISSUES.

CHAIRMAN LO: COULDN'T YOU -- I ASSUME YOU WOULD DO IT BY SACRIFICING THE ANIMAL BEFORE THEY BREED.

DR. BOTKIN: SO YOU DO IT BY EVALUATING THE GERMLINE ALONE PRIOR TO BREEDING.

CHAIRMAN LO: READ IT BACK.

MR. TOCHER: A LITTLE SHORTER. BREEDING ANY ANIMAL INTO WHICH COVERED STEM CELLS HAVE BEEN INTRODUCED, UNLESS IT IS DEMONSTRATED THAT THE CELLS DO NOT CONTRIBUTE TO THE GERMLINE.

DR. ROBERT TAYLOR: YEAH.

CO-CHAIR LANSING: SO I MOVE THAT.

DR. ROBERT TAYLOR: SECOND.

CHAIRMAN LO: ANY DISCUSSION FROM THE PUBLIC? ANY DISCUSSION IN THE ROOM?

DR. PETERS: COULD I HEAR IT AGAIN BECAUSE I WORRY IT MAY BE SAYING THE OPPOSITE OF WHAT WE

WANT. OKAY. THE FOLLOWING ACTIVITY IS NOT ELIGIBLE FOR FUNDING, AND...

MR. TOCHER: BREEDING ANY ANIMAL INTO WHICH COVERED STEM CELL LINES HAVE BEEN INTRODUCED, UNLESS IT IS DEMONSTRATED THAT THE CELLS DO NOT CONTRIBUTE TO THE GERMLINE.

DR. PETERS: THANK YOU. GOOD WORDS. TRUST A LAWYER, RIGHT.

CHAIRMAN LO: ANYBODY ON THE PHONE HAVE A QUESTION, COMMENT?

MR. TORRES: SHERRY'S MOTION WAS SECONDED?

CHAIRMAN LO: YES.

MR. TORRES: I'M READY TO VOTE.

CHAIRMAN LO: ALL THOSE IN FAVOR IN THE ROOM? AYE. ANY ABSTAIN? ANY NAYS? THOSE OF YOU ON THE PHONE, COULD YOU STATE YOUR VOTE, PLEASE.

MR. TORRES: AYE.

DR. PRIETO: AYE.

CHAIRMAN LO: OKAY. THANK YOU. MOTION PASSES.

OKAY. NOW WE HAVE A REAL FORK IN THE ROAD. THERE'S A DINNER BEING HOSTED; HOWEVER, IN TERMS OF TOMORROW, WE HAVE A VERY SHORT AGENDA. AND SHERRY SUGGESTED THAT WE ALLOW PEOPLE TO PHONE INTO THE MEETING TOMORROW.

CO-CHAIR LANSING: FROM WHAT I UNDERSTAND, THERE'S NO VOTES AND IT'S PURELY INFORMATIONAL. AND I'M NOT IN ANY WAY MINIMIZING THE INFORMATION, BUT MAXIMUM IT'S AN HOUR. IT MAY BE AS LITTLE AS A HALF HOUR IS WHAT I WAS TOLD. AND I JUST FEEL THAT SOME OF YOU, SOME OF YOU WILL ENJOY STAYING OVER AND WOULD ENJOY, I HOPE, LOS ANGELES AND SITTING BY THE POOL OR WHATEVER YOU WANT TO DO OR DOING OTHER WORK, AND SOME PEOPLE WANT TO GO HOME, AND SOME PEOPLE ARE SAYING, WOW, CAN I CALL IN IF IT'S JUST AN HOUR. WITH ONE CAVEAT, AND THAT IS THAT JEFF WANTS TO MAKE AN ANNOUNCEMENT OF SOMETHING THAT WE WILL DEFINITELY BE DOING.

MR. SHEEHY: I JUST THINK WE NEED TO TAKE ON THE GENE MODIFICATION OF THE GERMLINE ISSUE. AND I KIND OF PUT -- IT ONLY ENDED UP IN THIS MEETING BECAUSE IT WAS HAPPENING. SUDDENLY WE HAD THE ARM, THE ISSCR, THE BALTIMORE ARTICLE, BUT I THINK WE SHOULD TAKE IT UP. WE SHOULD CLARIFY WHERE CIRM STANDS ON IT, BUT WE SHOULD ALSO DISCUSS THE ISSUE BECAUSE I'VE HEARD FROM BOTH SIDES. AND THIS IS SOMETHING THAT IS HAPPENING. THERE ARE PAPERS IN PRESS. ONE APPARENTLY WHERE THEY REMOVED THE CYSTIC FIBROSIS GENE, ANOTHER WHERE THEY REMOVED THE BRCA2 GENE.

SO PEOPLE ARE TREATING DISEASE BY GENETICALLY MODIFYING EMBRYOS. AND WHERE CIRM STANDS ON THAT I THINK IS NOT CLEAR, AND WE NEED TO ADDRESS THAT, BUT THAT PROBABLY IS A WHOLE MEETING. IT'S NOT SOMETHING TACKED ON, WHICH I'M HAPPY TO DO, BUT I WANTED, AT LEAST FOR THIS MEETING, TO GET OUT THERE THAT CIRM IS GOING TO ADDRESS IT. IF EVERYBODY HERE IS COMFORTABLE WITH THAT, BY THE WAY.

DR. PETERS: I HEARTILY CONCUR. THE PAGES OF *NATURE* AND *SCIENCE* ARE JUST RED HOT WITH THIS STUFF. THE ISSUE HAS BEEN AROUND FOR 20 YEARS, BUT NOW, BECAUSE OF NEW RESEARCH, IT'S GOING TO BE REALISTIC. WHEN WE THINK OF SHERRY AND RANDY'S REMARKS THIS MORNING ABOUT ANTICIPATING THE FUTURE, EVEN IF WE DON'T PASS ANY MOTIONS, I REALLY THINK IT SHOULD BE DISCUSSED AND SEE WHAT PEOPLE THINK ABOUT IT.

DR. ROBERT TAYLOR: THIS IS BEING COMMERCIALIZED NOW. THERE ARE COMPANIES THAT ARE OFFERING TO DO THIS FOR YOUR CELL LINE, SO IT'S REALLY OUT THERE.

CHAIRMAN LO: I THINK JEFF HAS RAISED A REALLY IMPORTANT, COMPLEX, AND BREAKING TOPIC. I THINK THE IDEA OF HAVING A SYMPOSIUM TO DEAL WITH BOTH THE SCIENCE AND THE ETHICS POLICY COULD BE A

REALLY IMPORTANT THING TO DO. I GUESS I'D JUST LIKE TO GET THE SENSE OF THIS GROUP THAT WE WOULD LIKE TO ASK GEOFF TO SORT OF TAKE THE LEAD WITH CIRM.

DR. LOMAX: I THINK ANOTHER ROUTE, THOUGH, WOULD ACTUALLY BE THROUGH THE BOARD. WHERE IS THE APPROPRIATE ASK COMING FROM? AND IS IT A RECOMMENDATION?

CO-CHAIR LANSING: WE'RE RECOMMENDING IT TO THE BOARD, AND THEN IT WOULDN'T JUST BE NECESSARILY THIS GROUP. YOU WANT TO REALLY ADDRESS THIS, HAVE A SYMPOSIUM OF EXPERTS DISCUSSING THIS ISSUE.

MR. SHEEHY: I THINK EXPERTS, BUT I ALSO LIKE THE TYPES OF DISCUSSIONS THAT WE HAVE WHERE PEOPLE -- WHEN YOU HAVE A SYMPOSIUM WITH EXPERTS, EVERYONE GETS UP AND GIVES THEIR OPINION, AND THERE'S NO REAL DIALOGUE.

DR. PETERS: I THOUGHT WE WERE THE EXPERTS.

CO-CHAIR LANSING: JEFF, I MISUNDERSTAND YOU. ALL WE NEED TO DO, THEN, IF WE WANT TO DO THAT, IS JUST SCHEDULE ANOTHER MEETING. WE DON'T --

MR. SHEEHY: THAT WOULD BE MY PREFERENCE. WE CAN BRING IN OUTSIDE PEOPLE IF WE NEED THEM TO PROVIDE THEIR EXPERTISE.

CO-CHAIR LANSING: IN OTHER WORDS, WE ARE GOING TO SCHEDULE ANOTHER MEETING, AND YOU ARE GOING TO ORGANIZE IT, AND THAT'S GOING TO BE THE SUBJECT OF THE MEETING.

DR. ROBERTS: BUT IT WOULD BE NICE TO HAVE EXPERTS, JUST LIKE DR. MARSALA CAME IN.

MR. SHEEHY: I AGREE.

CO-CHAIR LANSING: THIS COMMITTEE -- WE DON'T NEED TO ASK THE BOARD FOR ANYTHING. WE'RE ENTITLED TO SCHEDULE ANOTHER MEETING. SO WE'LL GET EVERYBODY'S SCHEDULE. THAT'S YOUR RECOMMENDATION, AND I THINK EVERYONE IS APPROVING IT, SO WE CAN DO THAT.

DR. PATRICK TAYLOR: THERE ARE VARIOUS THINGS THAT COVER (INAUDIBLE) STEM CELLS. THE ONE THING THAT WAS LISTED ON THE AGENDA FOR THIS MEETING WAS THIS, THE FACT THAT THIS IS GOING TO BE ON THE AGENDA AND WOULD BE DISCUSSED. WOULDN'T SURPRISE ME IF THERE'S SOME PUBLIC (INAUDIBLE).

CHAIRMAN LO: SO THERE WAS A BLOG THAT SAID, OH, CIRM IS GOING TO TAKE UP THIS TOPIC TOMORROW. WE CAN JUST SAY WE'RE DEFERRING IT TO A LARGER, WE'RE GOING TO SPEND A WHOLE DAY.

CO-CHAIR LANSING: WE THOUGHT WE COULDN'T DO IT IN AN HOUR AND A HALF. IT TOOK US LONGER TO

DEAL WITH OTHER THINGS, SO IT'S OUR NEXT MEETING.

MR. SHEEHY: IT WAS ONLY ADDED TO THE AGENDA A WEEK AGO. THE BOARD KIND OF SENT THE REQUEST TO THE GROUP.

CO-CHAIR LANSING: I LIKE THAT BETTER, SCHEDULING A WHOLE DAY. THEY'LL LIKE THAT.

DR. ROBERT TAYLOR: THIS DEVELOPMENT HAS TAKEN ALL THE PRESSURE OFF MITOCHONDRIAL TRANSPLANTATION.

CO-CHAIR LANSING: BEFORE WE LEAVE, IT'S 5:30, SO THE REAL QUESTION IS I GUESS WE NEED TO KNOW THE OTHER ISSUES.

DR. LOMAX: HERE'S THE QUESTION REALLY. WE HAVE SOME MATERIALS PREPARED. THEY ARE BACKGROUND ISSUES. WE DON'T NEED THE FORMALITIES AND ALL THE BUSINESS END OF THINGS, BUT WE DO HAVE MATERIALS PREPARED SPECIFICALLY TALKING ABOUT THE IMPLEMENTATION OF OUR STEM CELL BANK WHICH IS SORT OF A REPORT BACK TO YOU ALL ON WORK THAT WE SPENT QUITE A BIT OF TIME ON. WE ARE STILL PREPARED TO GIVE THAT REPORT IF THERE IS AN AUDIENCE THAT'S INTERESTED IN THAT REPORT. WE DON'T NEED THE ENTIRE COMMITTEE. PEOPLE CAN LISTEN ON THE PHONE, BUT IF PEOPLE'S SCHEDULES PERMIT AND YOU ARE INTERESTED IN THAT REPORT BACK, WE ARE PREPARED TO PROVIDE IT TO

YOU.

MR. TOCHER: THAT'S TOMORROW.

CHAIRMAN LO: THAT WOULD BE THE ONLY THING ON THE AGENDA.

CO-CHAIR LANSING: SO LETS TALK ABOUT THIS FOR A SECOND BECAUSE I THINK THERE'S A WAY TO HAVE EVERYBODY GET TO DO WHAT THEY WANT. SO YOU HAVE THE REPORT, SO YOU CAN EMAIL IT TO US AS WELL, RIGHT?

DR. LOMAX: IT'S A POWERPOINT.

CO-CHAIR LANSING: IS IT AVAILABLE NOW THAT WE CAN TAKE IT IF WE PREFER TO DO IT OVER THE PHONE?

DR. LOMAX: WE CAN MAKE IT AVAILABLE. NO PROBLEM.

CO-CHAIR LANSING: SO I GUESS WHAT WE SHOULD KNOW, JUST MY OFFICE JUST NEEDS TO KNOW, WHO'S GOING TO HERE. AND EVERYBODY ELSE CAN BE ON THE PHONE. AND WE WANT TO ALLOW FROM NINE TO TEN TO DO THAT IS WHAT YOU WANT, OR DO YOU WANT LONGER? WHATEVER YOU WANT.

DR. LOMAX: I THINK NINE TO TEN WOULD BE AMPLE.

DR. ROBERTS: IF WE WANT, WE CAN COME?

CO-CHAIR LANSING: ABSOLUTELY. I JUST NEED TO KNOW -- THAT'S FINE. HOW MANY PEOPLE, AND

I, WHO HAD A CONFLICT ANYWAYS, WOULD LOVE, I'M JUST BEING REALLY HONEST WITH YOU AS MUCH AS I LOVE SEEING YOU, IF I CAN DO IT ON THE PHONE, I CAN GET TO THE THING THAT I WAS SUPPOSED TO GET TO AND DO BOTH THINGS. HOW MANY PEOPLE ARE GOING TO BE HERE? GREAT. I'M GOING TO BE ON THE PHONE.

CHAIRMAN LO: ANOTHER QUESTION FOR SHERRY'S STAFF. HOW MANY OF YOU ARE GOING TO BE ATTENDING THE DINNER TONIGHT?

MS. CHEUNG: DINNER IS AT THE HOTEL DOWNSTAIRS IN THE GRILL, SO 6:30.

CHAIRMAN LO: SO COULD I JUST SEE ANOTHER SHOW OF HANDS OF WHO'S GOING TO BE HERE TOMORROW? SO THERE BEING NO FURTHER BUSINESS, LET'S ADJOURN THE MEETING.

(THE MEETING WAS THEN CONCLUDED AT 05:35 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 TO THE INDEPENDENT CITIZEN'S OVERSIGHT COMMITTEE OF THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE IN THE MATTER OF ITS REGULAR MEETING HELD AT THE LOCATION INDICATED BELOW

2121 AVENUE OF THE STARS
GROUND FLOOR CONFERENCE ROOM
LOS ANGELES, CALIFORNIA
ON
APRIL 2, 2015

WAS HELD AS HEREIN APPEARS AND THAT THIS IS THE ORIGINAL TRANSCRIPT THEREOF AND THAT THE STATEMENTS THAT APPEAR IN THIS TRANSCRIPT WERE REPORTED STENOGRAPHICALLY BY ME AND TRANSCRIBED BY ME. I ALSO CERTIFY THAT THIS TRANSCRIPT IS A TRUE AND ACCURATE RECORD OF THE PROCEEDING.

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