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

ANNUAL MEETING

LOCATION: HOTEL PALOMAR LOS ANGELES-WESTWOOD
10740 WILSHIRE BOULEVARD
LOS ANGELES, CALIFORNIA

DATE: FRIDAY, APRIL 29, 2011
9:45 A.M.

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

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I N D E X

LOS ANGELES, CALIFORNIA; FRIDAY, APRIL 29, 2011

09:54 A.M.

CHAIRMAN LO: GOOD MORNING. SO I'D LIKE TO FORMALLY CALL TO ORDER THE MEETING OF THE CIRM STANDARDS WORKING GROUP. I WANT TO WITH THAT WONDERFUL, INSPIRING PRESENTATION BY CHRIS HEMPEL, I THINK WE REALLY HAVE A LOT OF IMPORTANT AND GNARLY, TO USE CHRIS' WORD, ISSUES TO TRY AND ADDRESS.

FIRST THING I WANT TO DO IS TO WELCOME OUR NEWEST MEMBER, TIM KAMP FROM THE UNIVERSITY OF WISCONSIN MADISON, IS A PROFESSOR OF MEDICINE, AND HE'S AN EXPERT IN CARDIAC DISEASE, HEART FAILURE, ARRHYTHMIAS, EXTREMELY ACTIVE AREA OF STEM CELL RESEARCH, AND ONE WHERE WE'RE BEGINNING TO SEE THE VALUE OF IPS MODELS AS A WAY TO SORT OF PUSH FORWARD OUR UNDERSTANDING OF DISEASES AND ALSO ACTUAL TRANSPLANTATION THERAPIES IN CARDIAC DISEASE. SO, TIM, WELCOME VERY MUCH. AT SOME POINT WE WILL SORT OF GRAB YOU AT LUNCH AND HEAR ABOUT WHAT'S REALLY GOING ON IN MADISON, WISCONSIN.

DR. KAMP: I'M NOT SURE I CAN ANSWER THAT, NOT BECAUSE I DON'T WANT TO. I'M NOT SURE I KNOW.

CHAIRMAN LO: GEOFF WANTS TO DO A FORMAL ROLL FOR THE RECORD.

DR. LOMAX: THANK YOU, DR. LO. YES, FOR THE RECORD, TO ACKNOWLEDGE THE WORKING GROUP MEMBERS THAT ARE HERE: PAT TAYLOR, DOROTHY ROBERTS, JEFF SHEEHY, ANN KIESSLING, BERNARD LO, SHERRY LANSING, ROBERT TAYLOR, MARCY FEIT, AND TIMOTHY KAMP.

CHAIRMAN LO: GREAT. IS THERE ANYONE WHO'S GOING TO BE CALLING IN, OR THIS IS -- I WANTED TO TRY AT THE ONSET TO JUST KIND OF FRAME WHAT THIS MEETING HOPES TO ACCOMPLISH. AND TOGETHER WITH GEOFF AND STAFF, WE WANT TO REALLY SEEK THE GUIDANCE OF THE SWG FOR A PROPOSAL THAT CIRM IS PUTTING TOGETHER TO BE INVOLVED WITH IPS BANKING, PRIMARILY I THINK AT THIS POINT FOR TOOLS FOR RESEARCH, BUT NOT CLOSING OFF THE POSSIBILITY THAT SOME OF THESE LINES MIGHT IN THE FUTURE BE USEFUL FOR THERAPY FOR TRANSPLANTATION.

I WANT TO TRY AND PUT WHAT WE'RE GOING TO DO TODAY IN CONTEXT. WE'RE NOT HERE TO WRITE REGULATIONS, UNLIKE WHAT WE'VE DONE PREVIOUSLY AT OTHER MEETINGS. WE'RE REALLY TRYING TO RECOMMEND GUIDANCE THAT CIRM CAN USE FOR REQUESTS FOR APPLICATIONS FOR FUNDING, FOR CONTRACTS AND GRANTS THAT THEY MAKE, AND FOR GRANTEES APPLYING FOR CIRM FUNDING TO KNOW WHAT THEY NEED TO DO TO BE ELIGIBLE. AND I THINK AT THIS MEETING WHAT I'D LIKE TO DO IS,

FIRST OF ALL, MAKE SURE WE'VE IDENTIFIED REALLY IMPORTANT ETHICAL ISSUES SO THAT THEY ARE TAKEN INTO CONSIDERATION AS CIRM MOVES FORWARD IN THIS PLANNING PROCESS.

ALSO I THINK THERE ARE SOME AREAS OF CONSENSUS, AND WHERE WE CAN IDENTIFY THOSE AND POINT THE WAY TO HOW MORE SPECIFIC GUIDANCE MAY BE FORTHCOMING, I THINK THAT WOULD BE USEFUL TO THE ICOC AND CIRM STAFF. AND I THINK WE ARE GOING TO IDENTIFY AREAS WHERE WE DON'T HAVE AGREEMENT YET, WHERE THESE ARE DIFFICULT, GNARLY ISSUES, BUT NEED FURTHER DISCUSSION. AND I THINK AT LEAST WE CAN TRY AND DEFINE THE PARAMETERS OF CONSIDERATIONS THAT THAT DISCUSSION IS GOING TO NEED TO INVOLVE.

WE HAVE OVER THE YEARS ACTUALLY DEVELOPED AN APPROACH, IF YOU WILL, A PHILOSOPHY OF OVERSIGHT. I JUST WANTED TO REMIND US OF WHAT WE'VE DONE IN THE PAST, WHICH I THINK IS A GOOD MODEL. ONE IS THAT WHAT WE PUT FORTH, WHETHER IT'S REGULATIONS AS WE'VE DONE IN THE PAST, OR GUIDANCE, WE WANT TO BE COMPATIBLE WITH OTHER STANDARDS, WITH FEDERAL STANDARDS, WHETHER IT'S REGULATION LIKE THE COMMON RULE OR NIH GUIDELINES.

NOW, COMPATIBLE DOESN'T MEAN IDENTICAL. THERE MAY WELL BE TIMES WHERE CIRM MAY WANT TO GO

BEYOND WHAT OTHER STANDARDS ARE. AND WE'VE CERTAINLY DONE THAT, FOR EXAMPLE, WITH INFORMED CONSENT FOR OOCYTE DONATION AND COMPENSATION FOR RESEARCH INJURIES AFTER OOCYTE DONATION. I WANT TO MAKE SURE THAT A CIRM GRANTEE CAN FULFILL BOTH OUR STANDARDS AND, SAY, FEDERAL STANDARDS FROM OHRP OR FOR NIH. WE DON'T WANT OUR RESEARCH GRANTEES TO BE CAUGHT IN A DOUBLE BIND.

WE HAVE TAKEN A RIGOROUS, BUT I THINK FLEXIBLE APPROACH TO OVERSIGHT, AND IT'S BEEN FLEXIBLE IN SEVERAL WAYS. WE'VE REALLY BEEN COMMITTED TO REVISITING OUR OVERSIGHT AS THE SCIENCE CHANGES. AND SHERRY HAS SAID OVER AND OVER AGAIN WE NEED TO, AS THE SCIENCE PROGRESSES, RETHINK WHETHER THE ETHICS HAS CHANGED AND WHETHER THE REGULATIONS SHOULD CHANGE. WE'VE ALSO BEEN FLEXIBLE LOOKING BACKWARDS, THAT THERE ARE MATERIALS, AND WE'LL SEE THIS PARTICULARLY WITH BIOBANKING, MATERIALS DONATED A NUMBER OF YEARS AGO --

THIS MAY BE JOHN WAGNER.

-- MATERIALS DONATED A NUMBER OF YEARS AGO WHERE THE STANDARD OF CONSENT WAS NOT WHAT IT IS TODAY. AND WE HAVE NEVER WANTED TO WAIVE THE IDEA OF CONSENT, BUT THE SORT OF SPECIFICS OF WHAT CONSTITUTES A VALID CONSENT, THAT MAY CHANGE OVER

TIME. SO THE TERMS IN THE CONSENT PROCESS MAY BE CHANGING.

WE'VE ALSO ALLOWED INSTITUTIONAL VARIATION. WE HAVE TRIED TO SHY AWAY FROM PRESCRIBING EXACTLY WHAT INSTITUTIONS MUST DO TO BE IN COMPLIANCE. I THINK THIS GETS AT WHAT CHRIS HEMPEL WAS SUGGESTING WHERE REGULATIONS CAN DETER VALUABLE AND ETHICAL RESEARCH RATHER THAN PROTECT SUBJECTS. AND I THINK THE FEEDBACK WE'VE GOTTEN FROM THE INSTITUTIONAL GRANTEES IS THAT THEY APPRECIATE OUR WILLINGNESS TO ALLOW INSTITUTIONS TO FIGURE OUT HOW BEST TO MEET THE CIRM POLICY AND ETHICS STANDARDS.

WE'VE ALSO REALIZED THAT STEM CELL RESEARCH INTERSECTS WITH A LOT OF OTHER RESEARCH. AND I THINK THE EXAMPLE OF WHOLE GENOME SEQUENCING IS GOING TO COME UP A LOT AS THIS MOVES FORWARD AS THAT TECHNOLOGY BECOMES MORE FEASIBLE AND AFFORDABLE. WE HAVE STRUGGLED WITH HOW TO MAKE STEM CELL RESEARCH COMPARABLE TO OTHER CELL AND TISSUE RESEARCH. WE HAVE NOT BEEN WILLING TO SAY THERE'S SOMETHING SO SPECIAL ABOUT STEM CELLS JUST BECAUSE THEY'RE STEM CELLS. THAT MEANS WE HAVE TO HAVE A TOTALLY DIFFERENT SYSTEM OR VERY STRICTER SYSTEM.

SO MANY OF THE THINGS WE DO WITH STEM

CELLS, WE IMMORTALIZE THEM SO THEY'RE KEPT ALIVE AT CORIELL. WE'RE GOING TO DO WHOLE GENOME SEQUENCING. THEY'RE DONE BY SCIENTISTS STUDYING THINGS WITHOUT STEM CELLS. AND WE WANT TO BE CONSISTENT WITH, ONE, THE SAME TECHNOLOGY IN DIFFERENT SCIENTIFIC CONCEPTS.

A PARTICULAR ISSUE THAT WE'RE GOING TO BE ADDRESSING THIS MEETING AND AS THIS BIOBANK IDEA MOVES FORWARD IS THE USE OF DEIDENTIFIED EXISTING MATERIALS WITHOUT SPECIFIC CONSENT FOR IPS DERIVATION, FOR EXAMPLE, OR WHOLE GENOME SEQUENCING. AND WE'LL SEE LATER HOW THE CURRENT FEDERAL REGULATIONS, WHICH ACTUALLY WERE PROMULGATED IN 1974 AND 1975, ALMOST 40 YEARS AGO, REALLY COULD NOT HAVE ANTICIPATED THAT WHOLE GENOME SEQUENCING MAY ACTUALLY RENDER DEIDENTIFIED MATERIALS, WE STRIPPED OFF ALL THE IDENTIFIERS, MAKE IT IDENTIFIABLE BECAUSE THE WHOLE GENOME SEQUENCE IS A UNIQUE BIOLOGICAL MARKER, WHICH NOW INCREASINGLY WE MAY BE ABLE TO WORK BACK TO THE ACTUAL IDENTITY OF THE PERSON.

SO THAT'S NOTHING. THAT'S JUST TO REMIND ME THAT I'M DONE.

SO WITH THAT, I WANT TO SORT OF GO AHEAD WITH THE MAIN PART OF OUR MEETING. AND FIRST, I'M

GOING TO CALL ON SOHEL TALIB TO GIVE US AN UPDATE AND REPORT ON THE SCIENTIFIC RECOMMENDATIONS FOR A CIRM IPSC RESEARCH REPOSITORY.

DR. TALIB: THANK YOU, DR. LO. WHAT I THOUGHT I WOULD DO TODAY FOR NEXT FEW MINUTES IS TO GIVE YOU AN OVERVIEW OF A WORKSHOP, A SCIENTIFIC WORKSHOP, THAT WAS HELD IN SAN FRANCISCO IN NOVEMBER TO SPECIFICALLY ADDRESS THE ISSUE OF IPS INITIATIVE THAT CIRM IS PROPOSING.

AND THE PURPOSE OF THIS WORKSHOP WAS TO GET INPUT FROM THE THOUGHT LEADERS IN THE FIELD OF STEM CELL RESEARCH AND REGENERATIVE MEDICINE ON THIS SPECIFIC PROPOSAL. AND THE PURPOSE OR THE FOCUS OF THIS INITIATIVE IS TO INCREASE THE NUMBER OF IPS LINES AS WELL AS THE QUALITY OF IPS LINES FOR A NUMBER OF DISEASES. AND SPECIFICALLY FOR THE PURPOSE OF DISEASE MODELING AS WELL AS FOR DRUG SCREENING.

I SHOULD POINT OUT THAT IN THE LAST COUPLE OF YEARS THERE HAS BEEN A LOT OF INTEREST IN THIS PARTICULAR AREA, BUT I THINK IT WILL BE FAIR TO SAY THAT MOST OF THESE EFFORTS ARE KIND OF FRAGMENTED SPECIFICALLY AS IT RELATES TO THE QUALITY AND STANDARDS BOTH ON THE SIDE OF THE PROCUREMENT OF THE MATERIAL WHICH IS USED FOR IPS GENERATION AS WELL AS

THE PRODUCT WHICH IS BEING GENERATED IN TERMS OF THE QUALITY. SO THE PURPOSE OF THIS INITIATIVE IS TO CHANGE THAT.

AND WHAT CIRM WOULD LIKE TO DO BY PUTTING THIS INITIATIVE FORWARD IS BOTH TO ENABLE THE PRODUCTION AND AVAILABILITY OF IPS CELL LINES FROM A NUMBER OF DISEASES SO THAT THEY CAN BE UTILIZED AND HAS ALL THE INFORMATION WHICH IS NEEDED AND THAT CAN BE UTILIZED FOR THE PURPOSE OF DISEASE MODELING AND FOR DRUG SCREENING. AT THIS STAGE CIRM IS NOT PROPOSING THAT THESE CELL LINES TO BE USED FOR CELL THERAPY PURPOSES.

SO WITH THAT THINGS IN MIND, THIS PARTICULAR WORKSHOP ACTUALLY FOCUSED ON A NUMBER OF SPECIFIC TOPICS; FOR EXAMPLE, THE GLOBAL EFFORTS. SO A NUMBER OF COUNTRIES HAVE ALREADY STARTED ACTIVITIES IN IPS BANKING, AND THESE COUNTRIES INCLUDE JAPAN, CANADA, SPAIN, UK, AND, IN FACT, NIH ITSELF. SO THE REPRESENTATIVES FROM THE INSTITUTIONS, FROM THESE COUNTRIES, THEY PROVIDED THEIR EXPERIENCE IN STARTING THESE INITIATIVES AND SOME OF THE CHALLENGES THEY ARE FACING. AND I SHOULD POINT OUT THE WHOLE IDEA IS THAT WE SHOULD NOT BE DUPLICATING WHAT HAS ALREADY BEEN GOING ON IN DIFFERENT PLACES.

IN THAT DIRECTION WE ARE ALREADY -- AT THIS TIME CIRM IS CONSIDERING TO WORK WITH NIH, NINDS, AND TO PARTICIPATE IN THEIR CONSORTIUM ON NEURODEGENERATIVE DISEASES SO THAT WE DO NOT REALLY DUPLICATE SOME OF THE WORK WHICH IS ALREADY GOING ON.

SECONDLY, THERE WAS A WHOLE DISCUSSION ABOUT THE SCIENTIFIC AND TECHNICAL CONSIDERATIONS. AS YOU KNOW, THERE'S A LOT OF DISCUSSIONS AND A LOT OF NEW METHODS HAVE BEEN DEVELOPED. SO THE EXPERTS IN THE FIELD, THEY DISCUSS ABOUT THE NEW METHODS OF IPS GENERATION AND ALSO IN TERMS OF TECHNICAL CONSIDERATION OF THE CHARACTERIZATION OF THESE IPS LINES. AND IT WAS RECOMMENDED THAT EACH AND EVERY CELL LINE SHOULD HAVE A VERY SPECIFIC SCORECARD WHICH WILL PROVIDE ALL THE INFORMATION IN TERMS OF THE PHENOTYPE, THE GENOTYPES, THE VIABILITY, ALL ISSUES, WHICH IS ALL THE INFORMATION WHICH IS NEEDED FOR THE PURPOSE OF USING THESE IPS LINES FOR DISEASE MODELING AS WELL AS FOR DRUG SCREENING.

CLINICAL CONSIDERATIONS WERE DISCUSSED. A NUMBER OF THE CLINICIANS, PHYSICIAN/SCIENTIST, THEY TALKED ABOUT WHICH PARTICULAR DISEASES TO TARGET AND WHAT IS THE ADVANTAGES OR DISADVANTAGE OF USING A MONOGENIC DISEASES VERSUS POLYGENIC DISEASES AND

WHAT KIND OF INFORMATION WE NEED TO HAVE, WHAT KIND OF PATIENT INFORMATION IS NEEDED, WHAT KIND OF FAMILY HISTORY IS NEEDED IN ORDER THAT THESE CELL LINES, WHEN THEY ARE GENERATED, THEY CAN BE UTILIZED FOR THE PURPOSE THEY'RE INTENDED TO.

THERE WAS DISCUSSION ABOUT THE GENOMIC AND EPIGENOMIC CONSIDERATIONS IN MAKING THESE IPS LINES AND THEIR IMPORTANCE IN DISEASE MODELING. AND SOME OF THE WORK, WHICH WAS, IN FACT, DISCUSSED ABOUT THE GENOMIC AND EPIGENOMIC PART IN THIS MEETING, HAS RECENTLY BEEN PUBLISHED BY THE SCIENTIST WHO PARTICIPATED IN THIS MEETING FROM THE SALK INSTITUTE FROM TORONTO AS WELL AS FROM UC SAN DIEGO.

OF COURSE, THERE WAS A WHOLE DISCUSSION ABOUT THE CELL BANKING, DISTRIBUTION, AND DATA MANAGEMENT WHICH ARE VERY PRACTICAL AND VERY OPERATIONAL ISSUES IN CELL BANKING. AND SOME OF THE EXPERTS WHO ARE MANAGING THESE CELL BANKS, FOR EXAMPLE, UK STEM CELL BANK, UNIVERSITY OF WISCONSIN STEM CELL BANK, AS WELL AS FROM TORONTO, THEY PROVIDED SOME OF THE ISSUES AND SOME OF THE CONSIDERATIONS IN MAKING AN IPS CELL BANK OPERATIONAL AND ALSO IN TERMS OF THE DATA MANAGEMENT BECAUSE A NUMBER OF INFORMATION WHICH WILL BE GENERATED NEEDS TO HAVE INFORMATION WHICH CAN BE

MANAGED.

AND, OF COURSE, AND BUT NOT LEAST, THERE WAS A WHOLE DISCUSSION ABOUT THE ETHICS AND LEGAL ISSUES WHICH, IN FACT, WAS IN THAT DISCUSSING PREVIOUS WORKSHOP WHICH WAS DONE PREVIOUSLY BY CIRM.

SO IN TERMS OF THE OUTPUT OF THIS PARTICULAR WORKSHOP, SPECIFICALLY THERE WERE TWO RECOMMENDATIONS. AND THOSE RECOMMENDATIONS WERE, FIRST OF ALL, AN IPS CELL REPOSITORY FOR EXISTING CELL LINES. SO A NUMBER OF CELL LINES HAVE ALREADY BEEN GENERATED BY THE INVESTIGATORS FROM THE CIRM RFA WHICH HAVE BEEN ISSUED PREVIOUSLY, AND WOULD LIKE TO HAVE -- THOSE INVESTIGATORS WOULD LIKE TO HAVE THOSE CELL LINES DEPOSITED IN AN IPS REPOSITORY, WHICH CIRM WILL PROVIDE MONEY FOR AND BECAUSE SOME OF THESE CELL LINES HAVE BEEN GENERATED, BUT THE INVESTIGATOR DON'T HAVE MEANS TO EITHER STORE THEM OR FOR THE DISTRIBUTION.

SECOND RECOMMENDATION IS THE GENERATION OF NEW IPS LINES FOR TARGETED DISEASES FOR DISEASE MODELING AND IN VITRO SCREENING AND FOR PREDICTIVE TOXICOLOGY. SO THOSE ARE THE TWO RECOMMENDATIONS WHICH THIS WORKSHOP PUT FORWARD.

NOW LET ME DESCRIBE TO YOU THE ISSUES WHICH ARE MORE RELATED TO THE CELL SOURCE AND DONOR

INFORMATION AND THAT GEOFF WILL GO MORE INTO DETAIL ABOUT THIS SPECIFIC ASPECT OF IT.

NOW, IN TERMS OF THE CELL BANKING, BASICALLY IT'S A THREE-STEP PROCESS. THAT IS CELL PROCUREMENT, IPS DERIVATION/CHARACTERIZATION, AND THE BANKING AND DISTRIBUTION, AND THE DATA MANAGEMENT. SO THE FRONT END, THAT IS, CELL PROCUREMENT AREA, IS VERY IMPORTANT IN TERMS OF CELL SOURCE AND DONOR INFORMATION. THOSE ISSUES WERE VERY HEAVILY DISCUSSED AND RECOMMENDATIONS WERE MADE.

SINCE THE IDEA IS TO GENERATE IPS LINES FROM A NUMBER OF DISEASES WITH DIVERSE POPULATION IN CALIFORNIA, THE ISSUES WHICH SHOULD BE TAKEN INTO CONSIDERATION, AND THEY ARE VERY OBVIOUS, BUT THEY ARE VERY IMPORTANT; THAT IS, THE AGE, GENDER, RACE, ETHNICITY OF THE POPULATION FROM WHICH THE DONORS ARE PROVIDING THE SAMPLES, GENOTYPE AND HLA HAPLOTYPE WHICH WILL BE VERY IMPORTANT IF ONE HAS TO REALLY CORRELATE THE DISEASE MODELING TO THE SAMPLE FROM WHICH THEY ARRIVED FROM, THE DONOR THEY ARRIVED FROM. MEDICAL HISTORY OF THE PATIENT AND FAMILY WAS CONSIDERED TO BE EXTREMELY IMPORTANT BECAUSE THAT PROVIDES, AGAIN, A DATABASE FROM WHICH ONE CAN MAKE CORRELATIONS WITH AND WOULD BE EXTREMELY IMPORTANT

FOR DISEASE MODELING AS WELL AS FOR DRUG SCREENING.

SINCE SOME OF THIS INFORMATION IN TERMS OF THE GENOMICS WILL BE AVAILABLE, SO THERE'S A POSSIBLE NEED TO RECONTACT THE DONORS NEEDS TO BE CONSIDERED AND AS WELL AS THE LEGAL AND INTELLECTUAL PROPERTY ISSUES NEED TO BE CONSIDERED. LEGAL ISSUES IN TERMS OF THE DONOR CONSENT. INTELLECTUAL PROPERTY AND MTA, SOME OF THE ISSUES, WHICH WERE DISCUSSED THIS MORNING BY MS. HEMPEL ALSO.

SO IN TERMS OF THERE ARE TWO THINGS THAT WE POINTED OUT, THAT ONE IS THE EXISTING CELL LINES; THAT IS, SOME OF THE INFORMATION FROM THE DONOR ALREADY IS AVAILABLE FROM THE EXISTING IPS CELL LINES BECAUSE THESE LINES IN CALIFORNIA HAS BEEN GENERATED BY USING A SCRO, GUIDELINES FROM CIRM, BUT SOME MORE INFORMATION MAY BE NEEDED. FOR THE NEW COLLECTION, THERE'S NEW CELL LINES WHICH WILL BE DEVELOPED FOR THE TARGETED DISEASES AND ALSO FOR THE CONTROLS.

I SHOULD POINT OUT THAT ONE OF THE THINGS WHICH WERE EXTREMELY EMPHASIZED, AND IT IS REALLY IMPORTANT, IS THE COLLECTION OF CONTROL SAMPLES. AND THAT IS CONTROL SAMPLES FROM THE NONAFFECTED FAMILY INDIVIDUALS, CONTROL SAMPLES FROM MATCH CONTROLS AS WELL, SO THAT WOULD BE NEEDED. SO IT IS

IMPORTANT THAT THE DATA IS COLLECTED, BUT THE INFORMATION IS THERE FROM THE DONORS WHICH ARE AFFECTED BY THE DISEASE AS WELL AS FROM THE FAMILY MEMBER DONORS. SO THEIR INFORMATION IS NEEDED BOTH IN TERMS OF THE DONOR AND AS WELL AS ALSO IN TERMS OF THE IPS CELL LINES WHICH WILL BE DERIVED.

SO THOSE INFORMATION WOULD NEED TO BE COLLECTED, AND THEY NEED TO BE PUT IN THE REGISTRY AND INTO THE DATABASE FOR THAT SO THAT THOSE INFORMATION WILL BE AVAILABLE WHEN THESE SAMPLES ARE UTILIZED FOR THEIR INTENDED USE; THAT IS, FOR DISEASE MODELING AND DRUG SCREENING.

I THINK AT THIS STAGE, I WILL HAND IT OVER TO GEOFF, WHO WILL GO MORE INTO THE DETAILS ABOUT THE ETHICAL ISSUES.

CHAIRMAN LO: BEFORE THAT, WHY DON'T I JUST ASK ALAN OR ELLEN IF YOU HAVE ANY UPDATES OR ANYTHING YOU WANTED TO ADD.

DR. TROUNSON: WELL, I THINK THIS FIELD IS MOVING VERY QUICKLY, OF COURSE. THERE ARE ISSUES AROUND -- THERE ARE SOME ISSUES AROUND THE INTEGRITY OF IPS CELLS, WHICH THE BASIC SCIENTISTS ARE WORKING HARD ON. AND I IMAGINE THAT THEY'RE GOING TO DEVELOP PERHAPS BETTER METHODS TO RETAIN THE INTEGRITY -- THE GENOMIC INTEGRITY OF THE CELLS, BUT

THERE ARE MORE AND MORE MODELS APPEARING. THESE ARE DISEASE-IN-A-DISH MODELS, IF YOU LIKE. AND SO THERE'S MORE AND MORE ENCOURAGEMENT IN THIS AREA, MORE AND MORE SCIENTISTS MOVING INTO IT, BERNIE.

AND SO IT IS GOING TO BE A HUGE FORCE OF RESEARCH, I THINK, OVER THE NEXT COUPLE OF DECADES AT THE VERY LEAST TO FIND OUT HOW WELL THESE CELLS WILL PERFORM IN THE DISCOVERY PROCESS, DISCOVERY ABOUT THE NATURE OF THE DISEASE AND ALSO ABOUT WHETHER YOU CAN ACTUALLY FIND SMALL MOLECULES, BIOLOGICS, OR OTHER TREATMENTS USING THOSE CELLS.

PERHAPS MORE IMPORTANTLY, I THINK THEY MAY END UP OR LIKELY TO END UP AS A REPLACEMENT FOR THE BIG PHENOMICS STUDIES THAT ARE DONE ON MOUSE MODELS BECAUSE A MOUSE MODEL OF A HUMAN DISEASE IS A MOUSE MODEL OF A HUMAN DISEASE. IT IS NOT THE HUMAN DISEASE. SO THIS IS -- YOU WILL BE ABLE TO PLUMB, IF YOU LIKE, THE HETEROGENEITY OF A HUMAN DISEASE. MOST OF THE HUMAN DISEASES ARE COMPLEX BECAUSE THEY HAVE AT LEAST VARIOUS GENETIC CONTRIBUTIONS EVEN IF THERE IS A MAIN MUTATION. PATIENTS WITH A MUTATION WERE VARIABLE IN THEIR RESPONSE, AND THAT'S USUALLY BECAUSE THEY'RE EITHER SUBJECT TO ENVIRONMENTAL DIFFERENCES OR THERE ARE OTHER GENES PLAYING INTO THE EFFECTOR OF THE PHENOTYPE, THE APPEARANCE OF THE

DISEASE PHENOTYPE IN THE PATIENT.

SO IT'S A HUGE AREA OF BASIC SCIENCE DISCOVERY, AND I THINK WE SHOULD LEAVE A FOOTPRINT OVER THIS. SO I'M VERY, VERY STRONGLY SUPPORTIVE, AS YOU KNOW, OF ESTABLISHING BANKING.

AND MAYBE I COULD JUST PASS QUICKLY TO ELLEN FEIGAL BECAUSE WE'VE ACTUALLY GOT AN ARRANGEMENT OVER SOME OF THE NEURODEGENERATION DISORDERS WITH THE NIH, SO WE'RE JOINING TOGETHER WITH THE NATIONAL INSTITUTES OF HEALTH FOUNDATION TO DO SOMETHING FOR SOME OF THE NEURODEGENERATIVE DISEASES. IT DOESN'T COVER EVERYTHING, BUT IT COVERS SOME IMPORTANT AREAS IN NEURODEGENERATIVE DISEASES.

DR. FEIGAL: MAYBE I CAN JUST SAY A FEW WORDS ABOUT THAT. SO WE'RE WORKING IN A PUBLIC/PRIVATE PARTNERSHIP WITH THE NATIONAL INSTITUTE OF NEUROLOGIC DISORDERS AND STROKE. WE'LL ACTUALLY BE PRESENTING IT TO OUR ICOC BOARD NEXT WEEK, BUT WE PRESENTED IT TO OUR SCIENCE COMMITTEE AND TO THE GRANTS WORKING GROUP PART OF CIRM TO ACTUALLY BE PART OF A PUBLIC/PRIVATE PARTNERSHIP WITH PATIENT ADVOCACY FOUNDATIONS, ACTUALLY WITH COMPANIES, AND WITH THE NATIONAL INSTITUTE -- WELL, WITH NINDS TO ACTUALLY DEVELOP REALLY NEW CELL LINES

AND A SUSTAINABLE RESOURCE FOR RESEARCHERS AND ALSO FOR COMPANIES TO HAVE ACCESS TO THESE TYPE OF CELL LINES FOR DISEASE MODELING, BUT AT THE END OF THE DAY, TO REALLY DEVELOP TREATMENTS.

SO THE IN VITRO SCREENING IS REALLY IN A CLINICALLY APPLICABLE WAY TO TRY AND DEVELOP SOME NEW THERAPIES. SO WE'LL BE PRESENTING THAT NEXT WEEK, AND HOPEFULLY WE'LL BE ABLE TO MOVE FORWARD WITH THAT INITIATIVE.

CHAIRMAN LO: QUESTIONS OR COMMENTS FROM ANY MEMBERS OF THE SWG? DO YOU WANT TO -- WHY DON'T WE AT LEAST ASK A FEW QUESTIONS. WE WANT TO NOT GET INTO THE DETAILS OF THE SPECIFIC PARTNERSHIP AS MUCH AS THE BIG PICTURE OF WHAT ARE THE ETHICAL POLICY CONSIDERATIONS THAT SHOULD GUIDE ANY CIRM INVOLVEMENT. MAYBE YOU COULD SAY A FEW MORE WORDS ABOUT THIS PARTNERSHIP.

DR. KIESSLING: PART OF IT WAS BECAUSE OF WHAT OUR SPEAKER TOLD US ABOUT THE LOGISTICS OF TRYING TO GET CELLS BACK FROM NIH. SO WHAT IS THE NATURE OF THE PARTNERSHIP WITH NINDS? WHY DO YOU EVEN HAVE IT?

DR. FEIGAL: THIS IS REALLY PART OF WHAT SOLEL WAS TALKING ABOUT, THAT CIRM HAS BEEN WORKING ON ACTUALLY DEVELOPING THIS TYPE OF RESEARCH

RESOURCE. AND SO THE DETAILS OF SOME OF THE ISSUES THAT WERE BROUGHT UP TODAY, THESE CAN BE BROUGHT UP IN FURTHER DISCUSSIONS WITH THE PARTNERS FOR THIS PROGRAM. BUT BASICALLY IT'S REALLY TO JUMP-START THE THINGS THAT WE'RE INTERESTED IN LOOKING AT. THIS IS SPECIFICALLY FOCUSED ON NEURODEGENERATIVE DISEASES. IT WILL BE LOOKING AT PARKINSON'S DISEASE, HUNTINGTON'S DISEASE, AND ALS.

DR. KIESSLING: BUT THE BASIC QUESTION IS IS THE NATURE OF THE PARTNERSHIP TO PROVIDE MORE ROBUST TYPES OF CELLS, MORE TYPES OF CELLS? WHAT'S THE NATURE OF THE PARTNERSHIP?

DR. FEIGAL: CORRECT. I MEAN IT'S TO DEVELOP NEW CELL LINES.

DR. ROBERT TAYLOR: I GUESS WE'RE GOING TO BE HEARING LATER FROM THE NICOLE, BUT I'M CURIOUS. IS THIS GOING TO BE A ONE-BY-ONE INSTITUTE DECISION? SOME INSTITUTES WILL KEEP BANKING INTERNAL. OTHERS WILL PART IT OUT. I'M JUST KIND OF CURIOUS WHAT SORT OF THE OVERALL THINKING IS ABOUT THAT.

DR. FEIGAL: ARE YOU ASKING ME OR ARE YOU ASKING NICOLE?

DR. ROBERT TAYLOR: MAYBE BOTH.

DR. FEIGAL: ACTUALLY I WASN'T WORKING WITH NICOLE ON THIS PROGRAM. IT'S ACTUALLY WITH A

DIFFERENT INSTITUTE.

DR. ROBERT TAYLOR: EXACTLY. MAYBE WE SHOULD WE WAIT TILL WE HEAR ABOUT THE NCI, BUT IT SEEMS LIKE THIS IS GOING IN MULTIPLE DIRECTIONS.

DR. LOCKHART: I WOULD BET HONESTLY IT WOULD BE INSTITUTE BY INSTITUTE, DEPENDING ON WHETHER THERE WAS OVERLAPPING RESEARCH INTEREST. SO WOULD THE NATIONAL CANCER INSTITUTE HAVE RESEARCH RESOURCES THAT WOULD BE OF INTEREST? I THINK THAT PROBABLY WOULD HAVE TO BE ON AN INSTITUTE-BY-INSTITUTE BASIS.

I WOULD ALSO SAY IN REGARDS TO SOME OF THE MATERIAL TRANSFER ISSUES THAT WERE DISCUSSED EARLIER, I SPOKE WITH CHRIS KIND OF ON A SIDELINE. AROUND THAT TIME SHE WAS HAVING DIFFICULTIES. THE NIH WAS BEING INVESTIGATED AND REPRIMANDED BY CONGRESS FOR SOME VIOLATIONS BASICALLY WHERE SAMPLES LEFT THE NIH WITHOUT PROPER DOCUMENTATION AND WERE GIVEN TO INDUSTRY RESEARCHERS. AND IT WAS BASICALLY A BAD ACTOR. THE IMPLICATION WAS THAT SAMPLES WERE BASICALLY OBTAINED WITH GOVERNMENT FUNDS AND THEN SOLD TO INDUSTRY. SO THERE WAS A CRACKDOWN WITHIN NIH. A LOT OF NEW POLICIES ARE BEING IMPLEMENTED. THERE ARE A LOT OF NEW REQUIREMENTS AS TO TRACKING, DOCUMENTATION, ANNUAL REPORTS TO CONGRESS.

I THINK A LOT OF THAT SHOULD BE BETTER NOW THAN WHEN THIS WAS ALL GOING ON. THERE WAS UPHEAVAL ON CAMPUS, TRYING TO MAKE SURE THAT WE'RE MEETING THESE CONGRESSIONAL -- THESE NEW CONGRESSIONAL MANDATES. AS YOU DEVELOP YOUR PPP, I THINK IT WILL BE IMPORTANT TO MAKE SURE ALL OF THAT IS CLEAR IN TERMS OF WHO HAS ACCESS, HOW THAT WILL BE SHARED, HOW IT WILL BE MANAGED AND CONTROLLED. AND YOU CAN DO THAT WITHIN YOUR PUBLIC/PRIVATE PARTNERSHIP UP FRONT.

DR. FEIGAL: THERE'S A STEERING COMMITTEE. WE WON'T GET INTO TOO MANY DETAILS REALLY RIGHT NOW, BUT THERE'S AN OVERSIGHT PART. AND YOU'RE BRINGING UP SOME GOOD QUESTIONS. AND HOW THEY WILL BE ADDRESSED AND ANSWERED, IT WILL BE VERY IMPORTANT. I THINK THE IMPORTANT THING FOR THIS INITIATIVE IS THAT CIRM WILL HAVE A SEAT AT THE TABLE.

DR. ROBERTS: I WAS WONDERING ABOUT THE RELATIONSHIP BETWEEN THE LINES THAT WOULD BE DERIVED IN THESE BANKS AND FUTURE TREATMENT OF PATIENTS IN A COUPLE WAYS. SO THESE LINES ARE GOING TO BE USED TO UNDERSTAND DISEASE BETTER AND TO DEVELOP TREATMENTS. ARE THE LINES -- THE PEOPLE WHO DONATE TO DERIVE THESE LINES, ARE THEY THE SAME PEOPLE WHO WILL BENEFIT FROM THE TREATMENT? AND ARE THESE THE SAME

LINES THAT WILL BE USED FOR THE ACTUAL TREATMENT, OR WOULD THERE BE DIFFERENT LINES USED FOR THE ACTUAL TREATMENT?

WHAT'S THE NEXT STEP, I GUESS, I'M ASKING, AND WHAT'S THE RELATIONSHIP BETWEEN THESE LINES? BECAUSE I WAS STRUCK BY CHRIS HEMPEL'S PRESENTATION. THE LINES THAT ARE DERIVED FROM HER SAMPLES ARE GOING TO BENEFIT HER CHILDREN. IS THAT ALWAYS THE CASE?

DR. FEIGAL: NO. PARTLY I THINK I WANT TO ASK BERNIE BECAUSE I KNOW THERE'S A SET OF ISSUES TO DISCUSS AT THE MEETING TODAY, AND THESE ARE VERY GOOD QUESTIONS. I JUST WANT TO FIND OUT --

DR. ROBERTS: THEY MIGHT COME LATER ON.

DR. FEIGAL: MAYBE WE COULD DO THIS AT A DIFFERENT TIME.

DR. ROBERTS: THAT WOULD BE FINE.

CHAIRMAN LO: MY UNDERSTANDING IS THAT RIGHT NOW THE REAL DRIVER FOR THESE BANKS IS THE BASIC SCIENCE VALUE AS A RESEARCH TOOL. IF IT SHOULD HAPPEN THAT THESE IPS CELLS ARE USEFUL FOR THERAPY, THAT'S A BIG UNKNOWN. THERE ARE A LOT OF SCIENTIFIC ISSUES THAT WOULD HAVE TO BE ADDRESSED, GOOD MANUFACTURING PROCESS ISSUES. SO I THINK RIGHT NOW WE NEED TO FOCUS ON THE BANK AS A REPOSITORY OF

LINES FOR SCIENTISTS TO USE IN UNDERSTANDING THE PATHOPHYSIOLOGY, DRUG DISCOVERY, AND SCREENING.

DR. FEIGAL: I JUST DO WANT TO SAY THERE'S THREE DIFFERENT ISSUES ON THE TABLE. YOU KNOW, ONE IS THIS BASIC SCIENCE AND THE DISEASE MODELING SO WE UNDERSTAND THE DISEASE BETTER. THE SECOND IS AS A DRUG DISCOVERY TOOL FOR A VARIETY OF AGENTS. AND THEN A THIRD, WHICH I THINK IS A DIFFERENT, SEPARATE, BUT IMPORTANT ISSUE, IS THE USE OF THE LINES AS THERAPIES IN AND OF THEMSELVES.

RIGHT NOW WITH NINDS, THE FOCUS RIGHT NOW IS ON THE FIRST TWO.

DR. ROBERTS: I GUESS I THINK WE HAVE TO KEEP IN MIND THE THIRD STEP BECAUSE THAT'S RELEVANT TO THE QUESTIONS ABOUT DEIDENTIFICATION AND INFORMATION GIVEN TO PEOPLE WHO ARE DONATING THE LINES, THE TISSUE FOR THE LINES.

CHAIRMAN LO: SO WE NEED TO KEEP THAT IN MIND.

DR. ROBERTS: KEEP IT IN MIND EVEN THOUGH WE'RE NOT DISCUSSING IT DIRECTLY NOW.

DR. PATRICK TAYLOR: JUST A FAST QUESTION. IS THE THOUGHT AS PART OF THE COLLABORATION TO DEVELOP A UNIFORM CONSENT? AND SO IF, WHAT STANDARDS WILL GUIDE THAT FOR ACCESS TO THIS

REPOSITORY?

DR. FEIGAL: AT THIS POINT I CAN'T GIVE YOU A LOT OF DETAILS BECAUSE IT HASN'T EVEN GONE OUT. THE APPLICATIONS HAVEN'T COME IN. SO I IMAGINE WHETHER IT'S UNIFORM, SOME SORT OF BROAD PRINCIPLES THAT ARE FOLLOWED. YOU KNOW, WE COULD GET BACK TO YOU AS THE BOARD DEVELOPS, THE STEERING COMMITTEE DEVELOPS. SO RIGHT NOW I CAN'T ANSWER THE QUESTION WHETHER IT WILL BE ONE. I IMAGINE, SINCE THIS GOES THROUGH A VARIETY OF DIFFERENT INSTITUTIONS, THERE'LL SOME SORT OF TEMPLATE, BUT I DON'T ENVISION THEY'LL BE IDENTICAL.

CHAIRMAN LO: THIS IS SOMETHING THAT WHEN WE GET -- WE'VE SORT OF ORGANIZED THE REST OF THE MEETING AROUND TOPICS. INFORMED CONSENT IS GOING TO BE A BIG TOPIC. I THINK WE'RE GOING TO NEED TO TALK ABOUT THIS. WHY DON'T WE MAKE SURE WE GET THAT DISCUSSION IN.

OTHER COMMENTS? OKAY. SO WHY DON'T WE -- GEOFF, DID YOU WANT TO --

DR. LOMAX: JUST A COUPLE OF NOTES ON THE PROCESS HERE JUST TO REMIND EVERYONE AND BRING EVERYONE UP TO SPEED. I'D LIKE TO USE THE PARALLEL TRACKS ANALOGY THAT AS AN ORGANIZATION WE'VE BEEN THINKING SIMULTANEOUSLY ABOUT SCIENTIFIC NEEDS AND

THE ETHICS AND POLICY CONSIDERATIONS. AND AS A REMINDER, ALMOST A YEAR AGO TODAY WE HAD A WORKSHOP ON THE OTHER SIDE OF THE FREEWAY. AND I THINK WE DID SORT OF CAPTURE -- THE REPORT FROM THAT WORKSHOP, I THINK I'D LIKE TO SORT OF SUGGEST A CONCLUSION AND SUGGEST THAT WE'RE ACTUALLY ON PRETTY FIRM GROUND IN TERMS OF OUR EXISTING POLICIES WITH REGARD TO THINGS LIKE CONSENT AND IP, AND THE EXISTING POLICY FRAMEWORK WITHIN CIRM IS FIRM, BUT CERTAINLY THERE'S VALUE IN IMPROVEMENT.

AND SO WE CAME OUT OF THAT EXPERIENCE GOING INTO THE NOVEMBER WORKSHOP, WHICH SOHEL JUST DESCRIBED TO YOU, AND NOW WE'RE BACK HERE IN APRIL.

AGAIN, THE END GAME IS A BANKING PROPOSAL; BUT, AGAIN, AS YOU'VE HEARD, IT MIGHT BE A SET OF DISTRIBUTED PROPOSALS THAT ARE WORKS IN PROCESS. AGAIN, A VERY DYNAMIC ENVIRONMENT, BUT ONE I THINK WE'RE EXTREMELY FAMILIAR WITH AS AN ORGANIZATION AND HAVE A HISTORY OF SORT OF USING THESE PROCESSES AS COMING BACK TO THE TABLE TO GET IT RIGHT. SO THAT'S SORT OF THE HISTORY OF THIS CONVERSATION.

AND THIS WAS A REMINDER, IT WAS PART OF YOUR BRIEFING MATERIALS, THAT WE'RE ONE ORGANIZATION OR A VOICE IN A LARGER SET OF DISCUSSIONS THAT ARE GOING ON NATIONALLY. AND WE'RE GOING TO HEAR ABOUT

SOME OF THOSE DISCUSSIONS TODAY. BUT, AGAIN, A LOT OF THE TOPICS THAT HAVE COME UP THIS MORNING ARE ON THE SORT OF POLICY AGENDA AT THE NATIONAL LEVEL. AGAIN, THAT'S REALLY REFLECTED IN YOUR BRIEFING MATERIALS. AND AS ALWAYS, I THINK CIRM HAS ALWAYS BEEN ABLE TO PLAY A PRODUCTIVE ROLE IN A RANGE OF SCIENCE POLICY DISCUSSIONS. I WOULD HOPE WE WOULD CONTINUE.

AS BERNIE INDICATED, BASED ON A REVIEW OF BOTH OUR PREVIOUS DISCUSSIONS AND WHERE WE FELT WE NEEDED TO COME BACK AND THE SORT OF CONVERSATIONS GOING ON NATIONALLY AT THE POLICY LEVEL, WE'VE ORGANIZED INTO FOUR TOPIC AREAS, WHICH I THINK WILL CAPTURE THINGS. AND THE POWERPOINT SEEMS TO INSIST WE HAVE TWO NO. 1S, BUT IT'S ACTUALLY FOUR TOPIC AREAS.

WITH THAT SAID, I THINK THAT'S KIND OF THE FRAMEWORK NOW WHICH WE WANT TO SORT OF INITIATE SORT OF THE DELIBERATIONS WITH THE PRECEDING MATERIAL AS BACKGROUND. I THINK FROM THERE, WE CAN MOVE ON WITH ONE OF OUR GUEST SPEAKERS.

CHAIRMAN LO: OKAY. SO NEXT I'D LIKE TO TURN TO DR. NICOLE LOCKHART FROM NCI. SHE IS THE DIRECTOR OF ETHICAL AND REGULATORY AFFAIRS FOR AN NCI-SPONSORED BIOBANKING INITIATIVE CALLED CAHUB.

IS THAT THE WAY YOU PRONOUNCE --

DR. LOCKHART: THAT IS. IT'S CAHUB, NOT CAHUB.

CHAIRMAN LO: SO SHE'S LEADING A TEAM THAT'S REALLY RESPONSIBLE FOR THE DEVELOPMENT OF CAHUB POLICIES, INCLUDING THE ISSUES THAT GEOFF JUST SHOWED ON THE SLIDE, CONSENT, ACCESS TO DATA AND SPECIMENS, AND MATERIAL TRANSFER AGREEMENTS. SO, NICOLE, WE ARE GRATEFUL TO YOUR COMING HERE. WE LOOK FORWARD TO YOUR COMMENTS AND TO ACTUALLY WORKING CLOSELY WITH YOU, NCI, AND THE REST OF NIH AS WELL.

DR. LOCKHART: THANK YOU VERY MUCH FOR HAVING ME. I THINK THIS WILL BE A HAVING INTERESTING DISCUSSION TODAY. FIRST OF ALL, I FORGOT TO INCLUDE THE OFFICIAL DISCLAIMER, BUT FOR THE RECORD, MY VIEWS TODAY ARE SOLELY MY OWN AND SHOULD NOT BE CONSTRUED TO REPRESENT THE NATIONAL CANCER INSTITUTE, THE NATIONAL INSTITUTES OF HEALTH, OR THE DEPARTMENT OF HEALTH AND HUMAN SERVICES, OR ANY OTHER FANCY GOVERNMENT BODY.

A LITTLE BACKGROUND ABOUT ME. I AM TRAINED AS A PHYSIOLOGIST, BUT FOR THE PAST FIVE YEARS I'VE BEEN AT THE NATIONAL CANCER INSTITUTE IN THE OFFICE OF BIOREPOSITORIES AND BIOSPECIMEN

RESEARCH. SO I'M REALLY COMING AT THIS MORE FROM A BIOBANKING PERSPECTIVE. I DON'T HAVE AS MUCH EXPERIENCE WITH STEM CELL RESEARCH, SO HOPEFULLY I'LL BE ABLE TO PROVIDE RELEVANT, ALMOST AN OUTSIDER'S PERSPECTIVE.

I DID TRY TO STICK TO JUST FOUR ISSUES. SO FIRST, INFORMED CONSENT. I THINK ESPECIALLY WITH BIOBANKING IT'S REALLY ALMOST A BALANCING ACT HERE. WHAT DO PARTICIPANTS NEED TO KNOW IN ORDER TO BE FULLY INFORMED AND PROVIDE MEANINGFUL CONSENT? AND THERE'S A GREAT DEAL OF TENSION BETWEEN PROVIDING DETAILED INFORMATION ABOUT HOW SPECIMENS WILL BE USED VERSUS OVERWHELMING PARTICIPANTS BY PROVIDING SO MUCH INFORMATION THAT THE CONSENT IS 12 PAGES LONG AND THEY DON'T EVEN MAKE IT THROUGH, OR LIMITING FUTURE USES BY BEING VERY, VERY EXPLICIT, AND THEN NOT REALLY ALLOWING THAT FLEXIBILITY YOU MIGHT NEED IN THE FUTURE.

SOME BIOBANKS HAVE ATTEMPTED TO ADDRESS THIS ISSUE BY PROVIDING OPTIONS OR CHOICES FOR CONSENT IN ORDER TO PROMOTE AUTONOMY, WHICH IS SOMETIMES TERMS TIERED CONSENT. SO THOSE CHOICES MIGHT INVOLVE EITHER SPECIFIC DISEASES. IT IS OKAY TO USE MY SAMPLE FOR LUNG CANCER, ALL CANCER, ANY FUTURE RESEARCH. THAT IS A POPULAR APPROACH. IT

CAN LEAD TO DIFFICULTIES IN INTERPRETATION. SO WHEN YOU HAVE A FEW YEARS DOWN THE LINE A PARTICULAR RESEARCH PROJECT AND YOU'RE TRYING TO DETERMINE DOES THIS CONSENT ALLOW THIS TYPE OF RESEARCH, IT CAN BE DIFFICULT TO INTERPRET THOSE CHOICES. YOU NEED TO BE VERY CAREFUL ABOUT HOW YOU WORD ANY CHOICES YOU USE.

I ORIGINALLY WAS A BIG FAN OF TIERED CONSENT WHEN I CAME TO THE NCI BECAUSE IT MAKES A LOT OF INTRINSIC SENSE. I LATER BECAME INVOLVED IN THE CANCER GENOME ATLAS, WHICH IS SOMETIMES CALLED THE HUMAN GENOME PROJECT FOR CANCER, DOING DEEP SEQUENCING OF VARIOUS CANCER TUMOR TYPES. AND THEY WERE USING RETROSPECTIVE SAMPLES, SO SAMPLES THAT WERE ALREADY COLLECTED AND WITHIN ACADEMIC INSTITUTIONS. I WAS PART OF A TEAM THAT WAS REVIEWING CONSENTS AND REVIEWING THESE RETROSPECTIVE CONSENTS AND TRYING TO DETERMINE IF THEY WERE APPROPRIATE FOR TCGA. IT WAS VERY DIFFICULT, AND THE CHECK BOXES MADE IT WORSE, TRYING TO SAY WHAT WOULD THE PERSON HAVE HAD TO CHECK IN ORDER TO ALLOW THEIR SAMPLE TO BE USED. AND IN SOME CASES THEY'D BE CONFLICTING. SO IF SOMEONE CHECKED ONE, BUT NOT THREE, TRYING TO FIGURE OUT WHAT THE PERSON IS REALLY OBJECTING TO, IT CAN BE DIFFICULT.

AND THERE'S ALSO TRACKING IMPLICATIONS, MAKING SURE THAT YOU HAVE A MEANS OF TRACKING ALL THOSE CHOICES OVER TIME, MAKING SURE THAT WHATEVER CONSENT OPTIONS DON'T VARY OVER TIME BECAUSE THEN YOU MIGHT NEED TO TRACK DIFFERENT ITERATIONS. BASICALLY IF YOU'RE GOING TO USE THIS OPTION, YOU NEED TO BE ABLE TO FULFILL THE PROMISE YOU MAKE TO PATIENTS. IT'S NOT AN AUTONOMOUS CHOICE IF THE BANK IS UNABLE TO MEET THAT FULFILLMENT OF THE REQUEST.

THE ALTERNATIVE APPROACH IS TO USE BROAD CONSENT FOR BROAD FUTURE USE. IN THIS CASE YOU CAN DESCRIBE TYPES OF RESEARCH A SPECIMEN MAY BE USED FOR, PARTICULARLY ANYTHING THAT MIGHT BE CONSIDERED HIGHER RISK OR THAT PATIENTS MIGHT BE CONCERNED ABOUT, AS WELL AS OVERSIGHT MECHANISMS IN PLACE. SO IF YOU ARE GOING TO HAVE AN ACCESS COMMITTEE, WHO MIGHT SIT ON THAT ACCESS COMMITTEE? JUST LETTING PEOPLE KNOW THAT THERE IS A OVERSIGHT MECHANISM AND HOW THAT PROCESS WORKS.

IT'S IMPORTANT TO NOTE THAT DIFFERENT PEOPLE WILL BE CONCERNED ABOUT DIFFERENT ISSUES. AND SO IT'S DIFFICULT TO WRITE A CONSENT THAT WILL ADDRESS THE CONCERNS OF ALL POTENTIAL PARTICIPANTS. AND THIS STATEMENT IS ALSO MEANT TO IMPLY IN MANY CASES IT WOULD BE GOOD IF YOU KNEW SOMEONE,

SOMETHING ABOUT WHAT THOSE PARTICIPANTS MIGHT BE CONCERNED ABOUT. SO AS YOU MOVE FORWARD THINKING ABOUT TARGETING DIFFERENT DISEASE TYPES, ANY CHANCE WHERE YOU CAN DO COMMUNITY ENGAGEMENT WOULD BE HELPFUL.

JUST AS A SIDE NOTE, WHAT PATIENTS CARE ABOUT IS NOT NECESSARILY THE SAME AS WHAT IRB'S AND RESEARCHERS THINK IS IMPORTANT. THIS IS A CITATION FROM LAURA BESKOW WHO HAD A RECENT PAPER WHERE SHE BASICALLY ASKED PATIENTS AND RESEARCHERS AND IRB'S TO HIGHLIGHT WHICH PORTIONS OF A CONSENT THEY THOUGHT WERE MOST IMPORTANT. AND THEY WERE DIFFERENT. THEY WERE REALLY DIFFERENT. SO THAT'S JUST KIND OF A SIDE NOTE.

AND, AGAIN, THE CONSENT FORM IS JUST A PIECE OF PAPER. YOU ALSO HAVE TO THINK A LOT ABOUT THE PROCESS. HOW ARE PATIENTS APPROACHED? WHO WAS DOING THE CONSENT, ETC.?

I TRIED TO STICK TO JUST KEY QUESTIONS AS THERE'S OBVIOUSLY A LOT OF ISSUES HERE. SO IN TERMS OF CONSENT FOR WHOLE GENOME SEQUENCING, THERE'S A NEED TO MAKE SURE THAT PARTICIPANTS UNDERSTAND THESE VERY COMPLEX CONCEPTS. WHAT EVEN IS A GENE? WHAT IS WHOLE GENOME SEQUENCING? I INCLUDED A LINK. THE NATIONAL HUMAN GENOME RESEARCH INSTITUTE HAS A LOT

OF GOOD RESOURCES IN TERMS OF SAMPLE CONSENT LANGUAGE THAT MIGHT BE USEFUL.

SOME OF THE RISKS THAT ARE ASSOCIATED WITH WHOLE GENOME SEQUENCING, POTENTIAL CONFIDENTIALITY LOST, PSYCHOLOGICAL OR SOCIAL RISKS, INCLUDING POSSIBLE RECEIPT OF UNWANTED INFORMATION, POSSIBLE DISCRIMINATION RELATED TO YOUR GENETIC HISTORY, RISKS TO FAMILY SINCE THERE'S GENETIC RELATEDNESS, AS WELL AS POPULATIONS OR GROUPS.

IF YOU'RE INCLUDING RISKS, YOU ALSO NEED TO TRY AND INCLUDE ARE THERE PROTECTIONS IN PLACE? IT'S BECOMING MORE AND MORE COMMON FOR CONSENT FORMS TO DISCUSS THE GENETIC INFORMATION NONDISCRIMINATION ACT, AT LEAST IN PART. AND THERE IS SOME SAMPLE LANGUAGE FROM BOTH NHGRI AS WELL AS OHRP RELATED TO GINA THAT COULD BE INCLUDED. IF THERE'S A CERTIFICATE OF CONFIDENTIALITY IN PLACE, THAT COULD ALSO BE DESCRIBED AS A POSSIBLE PROTECTION, AS WELL AS WHATEVER DATA AND SECURITY PRACTICES YOU HAVE IN PLACE. SO IS THE DATA GOING TO BE LIMITED ACCESS ON A SECURE DATABASE? DESCRIBING THAT TO PATIENTS SO THEY HAVE SOME IDEA OF HOW THEIR INFORMATION WILL BE PROTECTED AS WELL AS ACCESS POLICIES. WHAT KINDS OF PEOPLE WILL HAVE ACCESS TO MY DATA? WILL THERE BE INTERNATIONAL RESEARCHERS? RESEARCHERS OUTSIDE MY

INSTITUTION?

AND I THINK ONE CONCEPT THAT IS BECOMING MORE IMPORTANT IS ENSURING THAT PARTICIPANTS UNDERSTAND THAT WHOLE GENOME SEQUENCING WILL INCLUDE STUDY OF GENES BEYOND THOSE DIRECTLY RELATED TO THEIR DISEASE. I THINK THERE MIGHT BE A PERCEPTION FOR PATIENTS THAT WHEN THEY CONTRIBUTE A SAMPLE, RESEARCHERS, IF I HAVE BREAST CANCER, RESEARCHERS ARE GOING TO LOOK AT BREAST CANCER BECAUSE WHAT ELSE WOULD THEY BE LOOKING AT? AND I DON'T THINK PATIENTS NECESSARILY REALIZE THAT IT'S THEIR WHOLE GENOME. IT WILL BE FAR BEYOND WHATEVER THEIR DISEASE OF INTEREST IS.

AND ALSO DESCRIBING MECHANISMS FOR DATA SHARING, SUCH AS SUBMISSION TO DBGAP OR OTHER DATABASES. PATIENTS CARE ABOUT DATA SHARING. THERE WAS A RECENT STUDY BY LUDMAN, ET AL., WHICH BASICALLY -- I CAN'T REMEMBER WHAT INSTITUTION. BUT AN INSTITUTION WAS GOING TO SUBMIT TO DBGAP, AND THEIR IRB REQUIRED RECONSENT FOR THAT. AND THEY TACKED ON A STUDY TO ASK PATIENTS HOW THEY FELT ABOUT BEING RECONTACTED. AND THE MAJORITY WERE WILLING TO HAVE THEIR DATA SUBMITTED, BUT THEY WERE VERY GLAD THEY WERE ASKED. AND THE TITLE OF THE PAPER IS ACTUALLY "GLAD YOU ASKED." IT WAS

SOMETHING LIKE MAYBE 70ISH PERCENT THOUGHT IT WAS VERY IMPORTANT TO BE ASKED. SO I THINK THERE IS A REAL INTEREST. PATIENTS ARE WILLING TO CONTRIBUTE TO RESEARCH, BUT THEY LIKE TO HAVE A CHOICE IN HOW THEIR DATA IS USED.

IN TERMS OF REPRODUCTIVE USE -- IF YOU WANT TO STOP ME, YOU CAN, OR WE CAN JUST HOLD QUESTIONS TO THE END.

IN TERMS OF REPRODUCTIVE USE OF MATERIALS, IF REPRODUCTIVE USE WILL OR MAY OCCUR, I THINK THERE'S A BURDEN TO MAKE SURE THAT IT'S SCIENTIFICALLY JUSTIFIED, THAT THERE'S SOME REASON TO BE USING MATERIALS IN THAT WAY. IT SHOULD BE DISCLOSED TO PATIENTS. AND I THINK DURING THE CONSENT PROCESS, THERE WILL NEED TO BE SIGNIFICANT EFFORT TO DISPEL MISCONCEPTIONS. I THINK THE SUBTLETIES OF STEM CELL RESEARCH ARE REALLY DIFFICULT FOR THE PUBLIC TO GRAPPLE WITH. AND IT'S NOT SOMETHING WHERE YOU COULD JUST HAVE A FEW LINES IN A CONSENT FORM AND EXPECT PATIENTS TO UNDERSTAND.

JUST AN OFFHAND THOUGHT IS THAT THIS MIGHT BE SOMETHING WHERE A BROCHURE OR SUPPLEMENTARY INFORMATION MIGHT BE HELPFUL WHERE YOU CAN PROVIDE A LITTLE BIT MORE INFORMATION TO PEOPLE WHO ARE EITHER PARTICULARLY INTERESTED OR PARTICULARLY CONCERNED.

YOU WOULD NEED TO DESCRIBE ANY PROTECTIONS IN PLACE, SUCH AS OVERSIGHT MECHANISMS, TO LET PATIENTS KNOW THIS IS HOW RESEARCHERS WILL GAIN ACCESS TO THESE MATERIALS. THIS IS HOW WE WILL MAKE SURE THAT NO PROHIBITED USES OCCUR. I THINK THIS WILL BE AN AREA WHERE YOU REALLY ARE GOING TO NEED KNOWLEDGEABLE CONSENTERS TO EXPLAIN THESE SCIENTIFIC CONCEPTS TO MAKE SURE PATIENTS ARE CLEAR AS TO HOW THEIR SAMPLES WILL BE USED.

IF REPRODUCTIVE USE WILL NOT OCCUR, I WOULD SUGGEST THAT THAT NEEDS TO BE CLEARLY DESCRIBED IN THE CONSENT. THIS SEEMS LIKE AN AREA THAT PATIENTS WOULD BE CONCERNED ABOUT; AND IF THEIR TISSUE WILL NOT BE USED IN THAT WAY, THEN THAT SHOULD BE DISCLOSED. WHAT PROTECTIONS ARE IN PLACE TO ENSURE THAT THIS PROHIBITED USE WILL NOT OCCUR SO THAT PATIENTS UNDERSTAND IT'S NOT JUST THE RESEARCHERS SAYING THIS. THERE'S A BODY IN PLACE WHO'S GOING TO MAKE SURE THAT MY TISSUE IS NOT USED IN THAT WAY, AND IT'S GOING TO BE WRITTEN INTO AN AGREEMENT OR WHATEVER THE PROCESS IS.

IN TERMS OF PEDIATRIC RESEARCH AND WHETHER CONSENT IS NEEDED AT THE AGE OF MAJORITY, THE THINKING HERE IS THAT PEDIATRIC SAMPLES WOULD BE COLLECTED UNDER PARENTAL PERMISSION. AND WHEN THE

CHILD TURNS 18, THAT PERMISSION WOULD NO LONGER BE VALID. OF COURSE, IF THE SAMPLES ARE FULLY IDENTIFIABLE OR IF THERE'S ONGOING INTERACTION OR INTERVENTION, SO IF YOU'RE CONTINUALLY GATHERING MORE DATA OR TAKING MORE SAMPLES, YOU WOULD NEED TO SEEK CONSENT, BUT A MAJORITY OF A LARGE PROPORTION OF RESEARCH IS CONDUCTED WITH DEIDENTIFIED OR CODED SAMPLES. SO THEY'RE CODED, YOU HAVE THE ABILITY TO GO BACK AND SEEK CONSENT; BUT ALSO, DEPENDING ON HOW IT'S STRUCTURED BECAUSE THEY'RE CODED, THEY COULD ALSO POSSIBLY BE CONSIDERED NOT HUMAN SUBJECTS RESEARCH.

SO HERE THERE'S BOTH KIND OF THE REGULATORY REQUIREMENTS AS WELL AS ETHICAL REQUIREMENTS. I VIEW THIS AS KIND OF A STRUGGLE BETWEEN AUTONOMY AND PRIVACY. YOU CAN ARGUE THAT THERE'S A STRONG CASE TO ASK FOR CONSENT BASED ON AUTONOMY. THIS PERSON NEVER MADE A CHOICE. THEY MAY NOT EVEN KNOW THAT THEIR SAMPLE IS INCLUDED IN THIS BIOBANK. HOWEVER, THERE'S ALSO A STRONG PRIVACY ARGUMENT. NOT EVERYBODY WOULD WANT TO BE RECONTACTED. THEY MAY JUST WANT TO GO ON AND LIVE THEIR LIFE.

AND THE SECOND BULLET ABOUT POTENTIAL HARM BY CONTACTING FOR CONSENT, THIS IS SOMETHING I'VE

THOUGHT A LOT ABOUT. AND I THINK THIS VARIES WIDELY BASED ON DISEASE TYPE AND INDIVIDUALS AS WELL. COULD THERE BE HARM IN CONTACTING SOMEONE? FOR EXAMPLE, IF THE FORMER CHILD DID NOT KNOW THAT THEIR SAMPLE WAS IN THE BIOBANK OR IF THEY DIDN'T KNOW THAT THEY HAD THAT DISEASE. THERE ARE SOME CHILDHOOD DISEASES, THERE ARE SOME TYPES OF CANCER WHERE THEY MIGHT HAVE BEEN VERY, VERY YOUNG, MAYBE THEY WERE NEVER TOLD. WOULD IT BE SHOCKING TO THEM TO FIND THAT OUT?

AND I THINK IN SOME CASES YOU MIGHT ALSO HAVE TO THINK ABOUT TRYING TO PREVENT HARM TO THE FAMILY AS WELL. YOU WOULDN'T WANT TO BE CONTACTING FAMILIES WHEN THEIR CHILD IS NO LONGER WITH THEM, AND THEY'RE RECEIVING THESE CALLS FROM RESEARCHERS, AND THAT COULD BE VERY TRAUMATIC. EVEN JUST THINKING ABOUT WOULD THERE BE ANY HARM FROM THE CONTACT ITSELF, AND THAT'S A VERY DIFFICULT QUESTION.

JUST FROM A PRACTICAL PERSPECTIVE, THERE CAN POTENTIALLY BE HUGE LOGISTICAL OBSTACLES. IS THE CONTACT INFORMATION YOU HAVE ACCURATE? AT THE AGE OF 18 MOST CHILDREN GO TO COLLEGE, AND THEY AREN'T -- THEY WOULD NOT BE AT -- THE ADDRESS INFORMATION AND PHONE INFORMATION YOU PROBABLY HAVE

IS FOR THEIR PARENTS. THEY WOULDN'T BE THERE ANYMORE.

AND IF YOU ARE PLANNING TO RECONTACT, THEN YOU PROBABLY NEED TO TRY AND HAVE SOME ONGOING RELATIONSHIP. YOU DON'T WANT TO CALL SOMEONE 16 YEARS AFTER A DONATION WHEN THEY MAYBE DON'T KNOW WHAT YOU'RE TALKING ABOUT, THEY DON'T REMEMBER DONATING. YOU WANT TO TRY AND HAVE SOME KIND OF ONGOING RELATIONSHIP.

AND ESPECIALLY FOR THIS ISSUE, I THINK COMMUNITY INPUT IS IMPORTANT. I PUT COMMUNITY IN QUOTES NOT TO DECREASE THE IMPORTANCE OF THE CONCEPT, BUT TO MAKE IT CLEAR THAT COMMUNITY CAN MEAN A LOT OF DIFFERENT THINGS. I THINK A LOT OF TIMES COMMUNITY ENGAGEMENT OFTEN REFERS TO MORE REGIONAL, THE COMMUNITY WHERE THE RESEARCH TAKES PLACE. AND I THINK IT'S VERY IMPORTANT TO ALSO THINK ABOUT ARE THERE GOING TO BE PARTICULAR GROUPS THAT ARE TARGETED, EITHER ETHNIC GROUPS OR RACIAL GROUPS OR DISEASE GROUPS. I THINK THERE CAN BE A LOT OF DIFFERENCES OF OPINION BASED ON THE DISEASE GROUP ITSELF.

IN REGARDS TO THIS ISSUE, IT IS VERY IMPORTANT TO PLAN AHEAD. HOW DO YOU PLAN TO APPROACH THIS ISSUE? IF YOU PLAN ON SEEKING CONSENT

AT AGE OF MAJORITY, YOU NEED TO HAVE THAT CONTACT INFORMATION. YOU MIGHT WANT TO TRY AND HAVE AN ONGOING RELATIONSHIP. AND TO DISCLOSE WHATEVER THE APPROACH FOR AGE OF MAJORITY IS IN THE CONSENT AND ASSENT DOCUMENT, IF APPROPRIATE.

I'VE HEARD STORIES FROM PEOPLE WHO ARE INVOLVED IN VARIOUS BIOBANKS WHERE THEY DIDN'T THINK ABOUT THIS ISSUE, AND THEN THEIR IRB ALL OF A SUDDEN REALIZED THEY HAD SUBJECTS TURNING THE AGE OF 18 OR THAT WERE OVER THE AGE OF 18, AND THINGS HAD TO STOP WHILE THEY THOUGHT ABOUT WHAT ARE WE GOING TO DO WITH THESE SAMPLES? YOU REALLY WANT TO TRY AND PREVENT THAT, AND YOU NEED TO EVEN THINK AHEAD IN TERMS OF WHAT IF WE DECIDE TO SEEK CONSENT AND WE CAN'T FIND SOMEBODY? DO WE THEN SAY, OKAY, WELL, WE TRIED, WE TRIED, AND WE WAIT 90 DAYS AND THEN WE USE THE SAMPLE? OR WE COULDN'T GET CONSENT, SO THEN WE DESTROY? WHAT IS GOING TO BE YOUR PROCESS THERE? YOU DON'T WANT TO WAIT UNTIL YOU'RE IN THE SITUATION AND THEN TRY AND FIGURE IT OUT.

GEOFF HAD ANOTHER QUESTION ABOUT DOES ANONYMIZATION OF MATERIALS MATTER. IT REALLY DEPENDS WHAT HARMS YOU'RE TRYING TO MINIMIZE. IF YOU ARE TRYING TO PREVENT OR PRODUCE PRIVACY RISKS, ANONYMIZATION HELPS WITH THAT. IF YOU ARE MORE

CONCERNED ABOUT LOSS OF AUTONOMY, ANONYMIZATION DOES NOT HELP. AND I THINK A LOT OF PEOPLE WOULD NOT NECESSARILY WANT THEIR TISSUE ANONYMIZED FOR VARIOUS REASONS. CHRIS WANTS THE RESEARCH TO HELP HER CHILDREN. ANONYMOUS RESEARCH CANNOT. OTHER GROUPS LIKE THE RECENT CASE WITH THE HAVASUPAI, IF THEIR SAMPLES WERE ANONYMOUS, THEY WOULDN'T HAVE BEEN ABLE TO HAVE THEM RETURNED, AND THEY WOULDN'T HAVE BEEN ABLE TO BURY THEM AS THEY THOUGHT WERE APPROPRIATE.

AND I BELIEVE GEOFF IS GOING TO TALK A LITTLE BIT MORE ABOUT THAT CASE, BUT THIS WAS A CASE WHERE SAMPLES WERE TAKEN. THE TRIBE UNDERSTOOD THAT THEY WERE GOING TO BE USED FOR DIABETES RESEARCH, WHICH WAS A MAJOR PROBLEM WITHIN THEIR TRIBE. AND THEN THEY WERE USED FOR SCHIZOPHRENIA AND MIGRATION RESEARCH WHICH THE TRIBE REALLY DISAGREED WITH. AND EVENTUALLY THE SAMPLES WERE RETURNED, AND THEY WERE RETURNED TO FAMILY MEMBERS, AND THE FAMILY MEMBERS THOUGHT IT WAS VERY IMPORTANT TO RESPECTFULLY BURY THOSE SAMPLES. SO IN ANONYMOUS SITUATIONS, THINGS CAN'T BE RETURNED.

IF YOU ARE PLANNING TO DO ANONYMIZATION, I THINK THAT NEEDS TO BE DISCLOSED IN THE CONSENT DOCUMENTS SO THAT PATIENTS KNOW THEY WON'T BE ABLE TO WITHDRAW IN THE FUTURE, AND THAT THEY WON'T BE

ABLE TO GET ANY RESEARCH RESULTS BACK.

IN TERMS OF WITHDRAWAL FROM PARTICIPATION FROM RESEARCH, SOME OF THE KEY QUESTIONS ARE IS THE WITHDRAWAL FULL OR PARTIAL? IN SOME CASES A PATIENT MAY JUST WANT TO PARTIALLY WITHDRAW. THEY MAY SAY I DON'T WANT ANY MORE INTERVENTIONS. I DON'T WANT TO GIVE ANY MORE BLOOD SAMPLES. I DON'T WANT TO FILL OUT ANY MORE SURVEYS. BUT WHATEVER YOU HAVE, YOU CAN KEEP USING. SO THAT WOULD BE AN INSTANCE OF PARTIAL WITHDRAWING. IT'S IMPORTANT TO FIGURE OUT WHAT THE PATIENT IS LOOKING FOR. ARE THE MATERIALS OR DATA IDENTIFIABLE? WHAT IS THE SCOPE OF ANALYSIS AND THE IRB-APPROVED PROTOCOL? AND THAT IS RELATED TO SOME OF OHRP'S CURRENT GUIDANCE. AND WHAT WAS PROMISED TO THE RESEARCH PARTICIPANT IN THE CONSENT DOCUMENT? OBVIOUSLY WHATEVER WAS PROMISED, YOU NEED TO FOLLOW THROUGH ON.

THESE ARE SOME KEY RESOURCES. THERE IS A FAIRLY RECENT OHRP GUIDANCE ON WITHDRAWAL OF SUBJECTS FROM RESEARCH, DATA RETENTION, AND OTHER RELATED ISSUES, AND THEN FDA GUIDANCE AS WELL.

SO THIS IS GOING TO BE A LITTLE -- I THOUGHT GEOFF WAS GOING TO GO IN FRONT OF ME, SO I'M RESPONDING TO SOME OF HIS RECOMMENDATIONS. HE LISTED OUT A NUMBER OF POSSIBLE OPTIONS FOR

WITHDRAWAL, AND THEN I ATTEMPTED TO KIND OF CORRELATE THE OHRP GUIDANCE TO THAT, AND THEN ALSO GIVE KIND OF MY OPINION AS TO WHAT I THOUGHT SHOULD HAPPEN.

SO ONE WITHDRAWAL OPTION WOULD BE NO FURTHER CONTACT BY THE REPOSITORY. THE OHRP GUIDANCE IS THAT INTERACTION OR INTERVENTION WITH A SUBJECT TO OBTAIN DATA MUST BE DISCONTINUED FOLLOWING THE WITHDRAWAL UNLESS, OF COURSE, THE ASTERISK SAYS, THE SUBJECT AGREES TO CONTINUED CONTACT OR RESEARCH ACTIVITY IN THE CASE OF A PARTIAL WITHDRAWAL. BUT IF IT'S A FULL WITHDRAWAL, YOU WOULD NEED TO STOP INTERACTING OR INTERVENING WITH THEM, SO IN MY MIND OPTION ONE SHOULD OCCUR.

OPTION 2 IS NO CONTACT AND NO FURTHER COLLECTION OF DONOR MEDICAL INFORMATION. ACCORDING TO THE OHRP GUIDANCE, OBTAINING ADDITIONAL IDENTIFIABLE INFORMATION ABOUT THE SUBJECT FOR THE RESEARCH STUDY MUST BE DISCONTINUED FOLLOWING WITHDRAWAL UNLESS, OF COURSE, IT'S PARTIAL. SO IN MY MIND OPTION 2 WOULD ALSO NEED TO OCCUR.

THEN IT BECOMES LESS CLEAR. WITHDRAWAL OF HUMAN -- ANOTHER OPTION WOULD BE TO WITHDRAW THE HUMAN SUBJECT STATUS OF THE MATERIAL, BASICALLY TO REMOVE INDIVIDUAL IDENTIFIERS AND RENDER THE DATA

AND SPECIMENS COMPLETELY ANONYMIZED. THE OHRP GUIDANCE IS THAT RETENTION AND ANALYSIS OF ALREADY COLLECTED IDENTIFIABLE DATA IS PERMITTED PROVIDING SUCH ANALYSIS FALLS WITHIN THE SCOPE OF THE ANALYSIS DESCRIBED IN THE IRB-APPROVED PROTOCOL. THE OHRP GUIDANCE REALLY ONLY DEALS WITH DATA. THEY DON'T CALL OUT SPECIMENS OR TRANSFORMED MATERIALS AT ALL. SO IT'S SOMEWHAT UNCLEAR AS TO WHAT THE STATUS OF CONTINUED USE OF COLLECTED SPECIMENS AND DERIVATIVES WOULD BE.

IN MY MIND THE ACTION IN TERMS OF OPTION 3 IS A BIT UNCLEAR. I PERSONALLY THINK IT'S ETHICALLY PROBLEMATIC TO REMOVE IDENTIFIERS IN ORDER TO CONTINUE USE. I THINK THAT IS REALLY JUST GOING AROUND THE PARTICIPANT'S REQUEST. THE REQUEST IS TO STOP USING THE MATERIAL FOR RESEARCH. TO STRIP IDENTIFIERS AFTER YOU RECEIVE THE REQUEST AND THEN CONTINUE TO USE IT REALLY SEEMS TO BE JUST IGNORING THEIR REQUEST.

IF YOU ALWAYS PLAN TO HAVE MATERIAL BE ANONYMOUS OR THE MATERIAL WAS RENDERED ANONYMOUS PREVIOUSLY, I THINK THAT'S A MUCH DIFFERENT CASE. BUT TO RECEIVE THE REQUEST AND THEN STRIP IDENTIFIERS, I THINK, IS REALLY NOT RESPECTING THE PARTICIPANT. REGARDLESS, YOU MUST ADHERE TO THE

CONSENT LANGUAGE IN WHATEVER YOU PROMISED. I THINK IT'S IMPORTANT TO NOTE THAT YOU DO NEED TO TRY TO BE EXPLICIT IN TERMS OF HOW YOU DESCRIBE THE ABILITY TO WITHDRAW. THERE ARE SOME CONSENTS THAT SAY YOU CAN WITHDRAW AT ANY TIME AND THEN DON'T SAY ANYTHING ELSE, AND THAT'S NOT NECESSARILY TRUE.

OPTION 4, WITHDRAWAL OF PRIMARY UNTRANSFORMED TISSUE SAMPLES. THE OHRP GUIDANCE WOULD BE ABOUT THE SAME AS OPTION 3. CONTINUED USE OF COLLECTED SPECIMENS AND DERIVATIVES ARE NOT EXPLICITLY ADDRESSED. HERE I THINK THE ACTION IS AGAIN NOT ENTIRELY CLEAR. FOR MOST BIOBANKS COMMON PRACTICE IS TO STOP DISTRIBUTION OF SPECIMENS THAT ARE WITHIN THE BANK AND EITHER OR SOMETIMES RETURN IT TO THE INSTITUTION IF IT'S LIKE A TISSUE BLOCK YOU MIGHT RETURN TO THE INSTITUTION BECAUSE THEY MIGHT BE ABLE TO USE IT, BUT NOT TO ATTEMPT TO RECALL SPECIMENS THAT ARE ALREADY IN USE. SO IF YOU HAVE DISTRIBUTED SPECIMENS OUT TO THE RESEARCHERS, MOST BANKS WILL NOT TRY TO RECALL THOSE.

THIS IS AN INSTANCE WHERE I THINK THE PLANNED ACTION SHOULD BE DESCRIBED IN THE CONSENT AND ADHERED TO. SO LET PEOPLE KNOW WE WILL DESTROY WHATEVER IS IN THE BANK. WE MAY HAVE ALREADY GIVEN THINGS OUT, AND YOU WON'T BE ABLE TO GET THOSE BACK.

AND IF A PARTICIPANT IS NOT COMFORTABLE WITH THAT, THEN THEY'LL KNOW AND THEY WILL NOT PARTICIPATE.

AND OPTION 5 IS NO FURTHER DISTRIBUTION OF TRANSFORMED MATERIALS. AGAIN, IN TERMS OF OHRP GUIDANCE, THERE'S NOTHING VERY CLEAR HERE. AND ADDITIONALLY, THE OHRP GUIDANCE DOES NOT REALLY ADDRESS TRANSFORMED MATERIALS. AND WHETHER THEY'RE STILL SPECIMENS, MUCH OF THIS GUIDANCE WAS WRITTEN AWHILE AGO. I THINK OHRP WAS REALLY TRYING TO ADHERE AS MUCH TO THE FDA GUIDANCE. THEY WERE TRYING TO MAKE SURE THEY WEREN'T IN CONFLICT. SO THAT'S ONE REASON WHY I DON'T THINK OHRP REALLY ADDRESSED SPECIMENS BECAUSE THEY WERE TRYING TO MAKE SURE THAT THEIR GUIDANCE WAS HARMONIZED.

THE ACTION HERE, AGAIN, IS UNCLEAR. YOU COULD APPLY KIND OF THE SAME COMMON BIOBANKING PRACTICE OF DESTROYING WHAT'S IN THE BANK, BUT NOT GOING AFTER WHAT'S BEEN RELEASED, OR YOU MAY DECIDE THAT TRANSFORMED MATERIALS ARE DISTINCT AND NOT QUITE THE SAMPLE AS A PRIMARY SPECIMEN. AGAIN, I WOULD JUST SAY WHATEVER THE PLANNED ACTION IS SHOULD BE DESCRIBED AND THEN ADHERED TO.

IN TERMS OF MATERIAL TRANSFER AND DATA USE AGREEMENTS, THEY CAN BE PROBLEMATIC, OF COURSE. BUT I THINK IN MANY CASES THEY ARE A USEFUL TOOL FOR

DELINEATING THE RESPONSIBILITIES OF PROVIDERS AND RECIPIENTS. SO WHO IS RESPONSIBLE FOR WHAT BASICALLY?

AND HERE THERE CAN BE KIND OF TIERS OF MTA'S. I THINK IT'S IMPORTANT TO UNDERSTAND AS WELL THERE MIGHT BE, DEPENDING ON THE MODEL OF THE BIOBANK, SO CIRM YOU MIGHT HAVE AN AGREEMENT BETWEEN THE COLLECTION SITE WHO'S INTERACTING WITH THE PATIENTS AND CIRM AND THEN ANOTHER AGREEMENT BETWEEN CIRM AND END USERS. GENERALLY I'M REFERRING TO PROVIDERS AS THE PEOPLE WITH THE MATERIAL AND RECIPIENTS AS THE PEOPLE RECEIVING IT.

MTA'S CAN ALSO SERVE SOMETIMES TO MAKE IRB'S MORE COMFORTABLE BECAUSE THEY THEN HAVE SOME MEANS OF KNOWING WHAT THE END USER IS AGREEING TO AND WHAT RESPONSIBILITIES ARE BEING PUT ON THE END USER. COMMON TERMS OFTEN INCLUDE THINGS LIKE NO FURTHER TRANSFER OF MATERIALS WITHOUT PRIOR APPROVAL. THE RECIPIENT WILL NOT SEEK TO IDENTIFY OR CONTACT DONORS OR FAMILIES. DESCRIPTION OF IP RIGHTS OF BOTH PARTIES. OFTEN THAT THE PROVIDER WILL NOT HAVE REACH-THROUGH RIGHTS TO THE RECIPIENT'S IP.

IN MANY CASES MTA'S WILL ALSO REQUIRE THAT END USERS ACKNOWLEDGE THE RESOURCE SO THAT THE

RECIPIENTS MIGHT HAVE TO SAY I OBTAINED THESE CELLS FROM CIRM UNDER GRANT XYZ, WHICH IS USEFUL FOR YOU BASICALLY SO YOU CAN TRACK HOW YOUR SAMPLES ARE BEING USED.

IF USING AN ACCESS OR APPROVAL PROCESS, THE MTA COULD ALSO OBLIGATE RECIPIENT TO LIMIT USE TO THE APPROVED RESEARCH PROTOCOL, WHICH I THINK MIGHT BE VERY IMPORTANT TO YOU IF YOU'RE TRYING TO HAVE PROCESSES TO LIMIT WHAT TYPES OF RESEARCH OR IF YOU'VE MADE PROMISES TO THE PARTICIPANT ABOUT HOW THEIR SAMPLE WILL BE USED. IT CAN BE A MECHANISM TO OBLIGATE THE END USER. AND YOU CAN ALSO COMBINE WITH A DATA USE AGREEMENT, IF NECESSARY, IF YOU'RE TRANSFERRING A LIMITED DATASET UNDER HIPAA.

THE CHALLENGE IS ENFORCEMENT. IF SOMEONE DOES VIOLATE THE MTA, WHAT ARE YOU GOING TO DO ABOUT IT? YOU PROBABLY ARE NOT GOING TO SUE THEM. IF THEY'RE A CIRM GRANT RECIPIENT, YOU MIGHT HAVE MORE LEVERAGE, BUT BEING REALISTIC, THERE IS AN ENFORCEMENT CHALLENGE.

IN TERMS OF RETURN OF INCIDENTAL FINDINGS AND INDIVIDUAL RESEARCH RESULTS, I WOULD JUST SAY THAT THIS IS A VERY HOT BUTTON ISSUE RIGHT NOW. THERE'S A LOT OF WORK BEING DONE WITHIN NIH AND OTHER GROUPS AROUND THIS ISSUE. I ATTEMPTED TO

PROVIDE SOME AREAS OF GENERAL CONSENSUS AND THEN SOME KIND OF REMAINING QUESTIONS.

IN TERMS OF CONSENSUS, MOST PEOPLE WOULD AGREE THAT THERE'S A NEED TO PROVIDE AN OPT-IN OR OPT-OUT OPPORTUNITY FOR PATIENTS SO THAT THEY ARE STATING THEIR PREFERENCE AS TO WHETHER OR NOT THEY WANT TO RECEIVE RESULTS. EVEN WITH THAT BEING SAID, PROVIDING THAT OPT-IN OR OPT-OUT IS MORE DIFFICULT IN A REPOSITORY SETTING BECAUSE YOU MAY NOT KNOW HOW THE SPECIMENS WILL BE USED. SO IT'S DIFFICULT TO DESCRIBE TO THE PARTICIPANT WHAT KINDS OF RESULTS THEY COULD EXPECT TO GET. PATIENTS MAY HAVE PREFERENCES FOR RECEIVING ONE TYPE OF INFORMATION AND NOT ANOTHER. IN A BROAD FUTURE USE KIND OF CONSENT, YOU CAN'T REALLY DESCRIBE TO THEM HOW THAT WILL WORK.

THERE ARE ALSO -- SOME WOULD ARGUE THAT THERE ARE INSTANCES WHERE PATIENTS SHOULD BE TOLD THEIR RESULTS REGARDLESS OF THEIR CHOICE. THIS IS A VERY CONTROVERSIAL CONCEPT, BUT SOME WOULD ARGUE THAT THERE IS A DUTY TO RESCUE. AND SO IF YOU KNOW THAT THERE IS A VERY SERIOUS CLINICAL IMPLICATION RESULT THAT IS ACTIONABLE, THERE MIGHT BE SOME DUTY TO RESCUE AND INFORM THE PATIENT. SO THAT'S SOMETHING VERY CONTROVERSIAL, AND I CITED A PAPER.

YOU CAN GO READ ABOUT THAT.

MOST PEOPLE WOULD ALSO AGREE THERE'S A NEED FOR ESTABLISHED ANALYTICAL VALIDITY BEFORE RETURNING, AND THAT THERE'S A NEED FOR RESULTS TO BE CLINICALLY SIGNIFICANT AND/OR ACTIONABLE. THERE'S DISAGREEMENT AS TO WHETHER CLINICALLY SIGNIFICANT IS ENOUGH OR WHETHER IT MUST ALSO BE ACTIONABLE. AND THE REAL DIFFICULTY HERE IS TO DEFINE ALL THOSE CRITERIA. WHAT IS CLINICALLY SIGNIFICANT? WHAT IS CLINICALLY ACTIONABLE? HOW DO YOU APPLY THOSE TO INDIVIDUAL STUDIES?

ALSO THERE'S A LOT OF DISAGREEMENT ABOUT WHETHER CLIA IS APPLICABLE. MY IMPRESSION IS THAT CMS WOULD SAY YES. IF YOU ARE RETURNING ANALYSIS FOR PATIENT CARE, IT'S APPLICABLE. AND SO IF ONE OF YOUR CRITERIA IS CLINICALLY SIGNIFICANT OR ACTIONABLE, IT'S HARD TO ARGUE THAT YOU'RE NOT RETURNING IT FOR PATIENT CARE.

NOW, I THINK THERE ARE OTHER STUDIES WHERE THEY ARE -- ONE OF THEIR STUDY AIMS IS AROUND RETURN OF RESEARCH RESULTS, AND THEY'RE RETURNING EVERYTHING. IF YOU'RE RETURNING EVERYTHING, YOU REALLY AREN'T RETURNING IT FOR PATIENT CARE NECESSARILY. BUT THIS IS A VERY KIND OF OPEN ISSUE. THERE ARE SOME PEOPLE WHO ARGUE THAT IF YOU RETURN

THE RESULTS AND CLEARLY STATE THEY ARE RESEARCH RESULTS THAT SHOULD NOT BE USED FOR CLINICAL CARE UNTIL REPLICATED IN A CLIA-APPROVED LAB, THAT THAT'S OKAY. BUT THIS IS REALLY KIND OF AN OPEN QUESTION.

IF CLIA IS FOUND TO APPLY, THERE'S A LOT OF DOWNSTREAM QUESTIONS. DO YOU NEED TO REPLICATE IN A CLIA-APPROVED LAB? WHO'S GOING TO PAY FOR THAT TO HAPPEN? WHAT IF YOU DON'T HAVE A SAMPLE TO REPLICATE? ESPECIALLY IN CASE OF TISSUE, SHOULD BANKS HOLD ONE ALIQUOT IN CASE THEY EVER NEED TO REPEAT? AND THEN WHAT IF THERE ISN'T A CLIA-APPROVED LAB FOR WHATEVER TEST?

AND THEN ANOTHER OUTSTANDING QUESTION IS WHAT ABOUT RESULTS WITH REPRODUCTIVE SIGNIFICANCE OR PERSONAL MEANING? SHOULD THOSE BE RETURNED? AND HOW DO YOU DEFINE THOSE TERMS?

A FEW RESOURCES. MY OFFICE SPONSORED A WORKSHOP LAST SUMMER ON THIS TOPIC THAT WAS CONFINED SPECIFICALLY TO RETURN OF RESEARCH RESULTS FOR PARTICIPANTS IN BIOSPECIMEN STUDIES, SO IT'S MORE SPECIFIC TO BIOBANKING, WHICH MIGHT BE OF INTEREST. AND THERE'S ALSO AN NHLBI GROUP THAT HAS A RECENT PUBLICATION. THEY WERE FOCUSING ON RETURN OF GENETIC RESEARCH RESULTS. YOU'LL BE GLAD TO KNOW THE TWO ARE FAIRLY HARMONIZED THOUGH THEY HAVE KIND

OF A DIFFERENT FOCUS, BUT THE BASIC PRINCIPLES ARE VERY SIMILAR.

AND SUSAN WOLF, WHO'S AT UNIVERSITY OF MINNESOTA, HAS A CURRENT NHGRI GRANT ENTITLED "MANAGING INCIDENTAL FINDINGS AND RESEARCH RESULTS IN GENOMIC BIOBANKS AND ARCHIVES." SHE IS SPONSORING AN UPCOMING MEETING IN DC ON THE 19TH AROUND THIS ISSUE.

I DO THINK THERE ARE SOME SPECIFIC CHALLENGES TO RETURN OF INCIDENTAL FINDINGS AND INDIVIDUAL RESEARCH RESULTS FOR BIOBANKS. BIOSPECIMENS, AS I SAID, ARE OFTEN COLLECTED WITH BROAD CONSENT FOR FUTURE RESEARCH USE, AND IT'S THEREFORE VERY DIFFICULT TO PREDICT WHAT TYPES OF RESULTS YOU MIGHT FIND AND TO INFORM PATIENTS.

IF TIERED CONSENT IS USED, THE CONSENT CATEGORIES ARE USUALLY VERY BROAD. AND I THINK IT WOULD BE UNCLEAR TO A PARTICIPANT HOW THEIR CHOICES MAY AFFECT WHAT KINDS OF RESEARCH RESULTS THEY RECEIVED BACK. EVEN IF THE BIOSPECIMEN IS ORIGINALLY COLLECTED FOR A SPECIFIC PROJECT, IT COULD BE USED IN FUTURE RESEARCH. AND, AGAIN, THEN THE PATIENT MAY NOT HAVE BEEN INFORMED ABOUT THOSE KINDS OF RESULTS. AND WE HAVE TO ACKNOWLEDGE THAT. REMNANT BIOSPECIMENS NOT NEEDED FOR CLINICAL

PURPOSES MAY ALSO BE USED FOR RESEARCH IF DETERMINED THE USE DOES NOT CONSTITUTE HUMAN SUBJECTS RESEARCH OR IF A WAIVER OF CONSENT IS GRANTED.

THOSE PEOPLE MAY BE TOTALLY UNAWARE THAT THAT RESEARCH WAS HAPPENING AND WOULD BE SURPRISED OR SHOCKED IF SOMEONE CALLED THEM UP WITH RESEARCH FINDINGS. AND THAT PARTICIPANT WOULD HAVE BEEN UNABLE TO OPT OUT OF RECEIVING UNWANTED INFORMATION.

TO FURTHER KIND OF HIGHLIGHT THIS POINT, I JUST MADE A LITTLE SCHEMATIC OF HOW THIS COULD WORK IN ONE COMMON BIOREPOSITORY MODEL. SO HERE IN THE CENTER WE HAVE OUR BIOREPOSITORY. AND IN SOME CASES THE BIOREPOSITORY MAY BE HOUSED WITHIN ONE ACADEMIC CENTER, FOR EXAMPLE, RECEIVING SPECIMENS FROM ONLY ONE CENTER. IN MANY CASES THE REPOSITORY RECEIVES SAMPLES FROM A VARIETY OF INSTITUTIONS, FROM A VARIETY OF COLLECTION SITES. AND THEN THERE'S THROUGH SOME KIND OF APPROVAL PROCESS, THE SPECIMENS GO OUT TO VARIOUS RESEARCHERS FOR APPROVED PROJECTS.

SO WHAT IF THEN WE HAVE RESEARCHER ONE HAS SOME RESEARCH RESULTS THAT MEETS WHATEVER CRITERIA FOR RETURN? THAT SAMPLE COULD HAVE COME FROM COLLECTION SITE TWO, OR IT COULD HAVE COME FROM THREE DIFFERENT COLLECTION SITES DEPENDING ON WHETHER IS IT JUST A RESULT THAT APPLIES TO ONE

PARTICIPANT OR MAYBE IT'S A SUBCLASS. YOU KNOW, THEY HAVE THIS RESEARCH FINDING THAT SOME PROPORTION OF THEIR SUBJECTS HAVE MUTATION X. AND SO THE SPECIMENS MAY HAVE COME FROM A NUMBER OF COLLECTION SITES.

WHAT DO WE DO? WHO MAKES THE DECISION TO RETURN? IN MANY CASES THE REPOSITORY DOES NOT HAVE THE IDENTIFIERS. THAT'S VERY DEPENDENT ON THE MODEL, BUT THAT'S A COMMON MODEL IS THAT THE REPOSITORY DID NOT HAVE IDENTIFIERS. THEY'RE HOUSED WITHIN THE COLLECTION SITES. SO THE BANK CAN'T RETURN, BUT THE BANK IS KIND OF IN THE MIDDLE. WHAT IF SITES 2, 3, AND 4 DISAGREE ABOUT WHAT TO DO? I THINK THIS COULD BE A VERY COMMON OCCURRENCE. IS IT OKAY THAT DIFFERENT PARTICIPANTS WILL BE RECEIVING DIFFERENT LEVELS OF INFORMATION BASED ON WHERE THEY HAPPENED TO PARTICIPATE? IS THAT OKAY? DO WE WANT THAT TO BE MORE STANDARDIZED? AND WHAT IF THE CONSENTS DIFFER AT SITES 2, 3, AND 4?

SO THESE ARE ALL KIND OF OPERATIONAL ISSUES THAT MAKE IT MORE PROBLEMATIC WHEN YOU HAVE THIS BIOBANKING MODEL AS OPPOSED TO SOMETHING WHERE YOU THE RESEARCHER HAS A DIRECT RELATIONSHIP WITH THE PATIENT. AND I WOULD ALSO SAY THAT I'VE HEARD FROM IRB CHAIRS WITHIN INSTITUTIONS THAT THEY ARE

SOMEWHAT UNCOMFORTABLE IN THIS SITUATION BECAUSE THEY DON'T HAVE ANY CONTROL OR KNOWLEDGE ABOUT RESEARCHER ONE. IS HE DOING HIS RESEARCH CORRECTLY? IS THIS SOMETHING THAT SHOULD BE CONTROLLED? IS THIS SOMETHING THAT SHOULD BE RETURNED? THEY DON'T HAVE ANY DIRECT INTERACTION WITH THAT PERSON. DO THEY WANT TO TAKE ON THE ONUS OF RETURNING THIS DATA THAT THEY ARE NOT AT ALL INVOLVED IN?

AND MY FINAL UNSOLICITED OPINION IS THAT I THINK THERE'S A REAL NEED FOR MORE EMPIRICAL RESEARCH ON ETHICAL, LEGAL, AND SOCIAL ISSUES. IN MY MIND AN IPS CELL REPOSITORY WOULD BE AT THE INTERSECTION OF A LOT OF NEW SCIENTIFIC AND ETHICAL CHALLENGES. AND THERE'S A LOT OF GREAT VALUE IN KNOWING WHAT RESEARCH PARTICIPANTS ACTUALLY UNDERSTAND ABOUT RESEARCH AND WHAT THEIR PREFERENCES ARE. I THINK IN MANY CASES IT'S VERY EASY TO BE PATERNALISTIC AND THINK WE SHOULD DO X. WE SHOULD DO X, PATIENTS WANT Y, BUT OUR PERCEPTIONS MAY NOT REALLY BE ACCURATE. I THINK THERE MIGHT BE A LOT OF OPPORTUNITIES TO FORM COLLABORATIONS WITH ETHICAL RESEARCHERS TO TRY AND ANSWER SOME OF THESE QUESTIONS AS YOU'RE GIVING GRANTS OR CONTRACTS TO COLLECT SAMPLES OR DO ADD-ON STUDIES.

THERE'S BEEN -- IT'S BECOME MORE COMMON

TO, WHEN CONDUCTING A RESEARCH STUDY, ADD ON A SMALLER STUDY WHERE YOU ASK PARTICIPANTS WHAT DID YOU UNDERSTAND ABOUT THAT CONSENT THAT YOU SIGNED? HOW COMFORTABLE WERE YOU? THINGS LIKE THAT. I THINK THAT CAN BE OF REAL VALUE. AND IF IT'S NOT THEN DONE, IT'S HARDER TO DO DOWN THE ROAD. AND I THINK A LOT OF THESE QUESTIONS, IF YOU ADDRESS THEM IN A HYPOTHETICAL MANNER, ARE NOT REALLY THE SAME AS WHEN YOU'RE ASKING ACTUAL PARTICIPANTS WHAT THEIR FEELINGS ARE.

THAT'S ALL I HAVE. I'D BE HAPPY TO TAKE QUESTIONS OR IF YOU WANT TO DO THAT LATER.

CHAIRMAN LO: NICOLE, THANKS VERY MUCH FOR A VERY, VERY THOROUGH AND STIMULATING PRESENTATION. WE'RE GOING TO GO BACK AND DISCUSS EACH OF THESE SPECIFIC TOPICS: CONSENT, RETURN RESULTS, ETC. SO I'M GOING TO SUGGEST THAT ON SPECIFIC SUBSTANTIVE ISSUES WE HOLD AND HAVE THAT FOLDED IN AS PART OF OUR GENERAL DISCUSSION, WHICH IS COMING UP. NOW IF THERE ARE EITHER CLARIFICATION QUESTIONS AS TO WHAT NICOLE SAID OR QUESTIONS ABOUT WHAT CAHUB OR NCI OR NIH IS DOING, WHY DON'T WE COVER THAT NOW, BUT NOT GET INTO SPECIFIC POINTS ABOUT THE SUBSTANCE.

DR. KIESSLING: I HAVE A QUESTION ABOUT THE TERM "BIOBANKS." IS THERE ANYWHERE A LIST OF,

IS THERE A BIOBANK REGISTRY, IS THERE A GENERAL LIST OF WHAT IS A BIOBANK AND WHERE ARE THEY AND WHO ARE THEY?

DR. LOCKHART: THE SHORT ANSWER IS NO NOT REALLY. AND IT ALSO DEPENDS WHAT YOU WOULD CALL A BIOBANK. AND I WILL ALSO SAY THAT THERE'S A LOT OF DIFFERENT TERMS USED, BIOBANK, BIOREPOSITORY. THE NCI HAS ADOPTED BIOSPECIMEN RESOURCE. SO A LOT OF DIFFERENT TERMS. THEY ALL PRETTY MUCH MEAN THE SAME THING.

BUT MANY, INCLUDING THE NCI, WOULD THINK OF A BIOBANK AS INCLUDING A FREEZER OF SPECIMENS IN SOMEONE'S LAB. SO FROM THAT PERSPECTIVE, THAT'S A COLLECTION OF SPECIMENS THAT ARE BEING USED FOR RESEARCH. IS THAT A BIOBANK? IF SO, THERE'S NOT A BIG LIST. MOST OF THE LARGER BIOBANKS ARE INVOLVED IN GROUPS LIKE THE INTERNATIONAL SOCIETY FOR BIOLOGICAL AND ENVIRONMENTAL REPOSITORIES, ISBER. IN TERMS OF LARGE BIOBANKS, YOU CAN PROBABLY FIND THEM. BUT IT DEPENDS ON IF YOU WANT TO EXTEND THAT TO EITHER INDIVIDUAL RESEARCHERS OR EVEN INSTITUTIONAL BIOBANKS.

A LOT OF ACADEMIC CENTERS HAVE SMALL BIOBANKS THAT ARE MAINLY JUST USED FOR THEIR OWN RESEARCH. AND IN SOME CASES THEY HAVE KIND OF A

LUNG BIOBANK THAT MAYBE A LUNG CANCER SURGEON SET UP, AND THERE MIGHT BE ANOTHER BREAST CANCER BIOBANK THAT THE BREAST SURGEON SET UP. SO THERE CAN BE EVEN WITHIN AN INSTITUTION SEVERAL SMALL BIOBANKS THAT MAY SHARE SAMPLES IF YOU DO A COLLABORATION. IT'S NOT TERRIBLY WELL DEFINED.

THIS IS A LARGE PART OF THE PROBLEM IS IF YOU'RE A RESEARCHER, HOW DO YOU FIGURE OUT WHERE TO GET SAMPLES? SOMETIMES YOU HAVE TO KNOW SOMEONE. AND QUALITY CONTROL. ARE ALL THESE PEOPLE, HOW ARE THEY PROCESSING THEIR SAMPLES? HOW ARE THEY PRESERVING THEIR SAMPLES? DO THEY HAVE ANY IDEA WHAT THE QUALITY OF THOSE SAMPLES ARE AND HOW THAT WILL AFFECT DOWNSTREAM RESEARCH? WHEN YOU HAVE SO MANY PEOPLE WORKING IN SILOS OR ISOLATION, IT'S VERY HARD TO HAVE STANDARDS AND TO HAVE QUALITY.

MS. LANSING: I WANT TO JUST MAKE SURE I'M CLEAR ON THIS AND VERY MINDFUL OF WHAT CHRIS BROUGHT UP. IN ALL OF THE GOVERNMENT AGENCIES THAT YOU'RE REPRESENTING --

DR. LOCKHART: THAT I'M NOT REPRESENTING, BUT THAT I'M AWARE OF.

MS. LANSING: THAT YOU'RE DESCRIBING. I KNOW YOU'RE NOT REPRESENTING THEIR POINT OF VIEW, BUT I JUST WANT TO MAKE SURE I UNDERSTAND THIS. IN

ALL OF THE GOVERNMENT AGENCIES, THE PATIENT DOES NOT HAVE THE RIGHT TO ACCESS THEIR OWN MATERIAL?

DR. LOCKHART: DO YOU MEAN IN TERMS OF WITHDRAWAL OR IN TERMS OF RESEARCH RESULTS?

MS. LANSING: RESEARCH RESULTS.

DR. LOCKHART: I WOULD NOT PUT IT THAT STRONGLY, THAT THEY DO NOT HAVE THE RIGHT. I WOULD SAY IT'S NOT GENERALLY COMMON PRACTICE.

MS. LANSING: IT'S MOSTLY ANONYMOUS.

DR. LOCKHART: IT'S NOT USUALLY ANONYMOUS, BUT OFTEN CODED.

MS. LANSING: WHAT CHRIS WAS BRINGING UP, WHICH I THINK IS SUCH A VITAL POINT, WHICH IS I'M GOING TO ADDRESS WHAT, I THINK, LATER, BUT I JUST WANT TO BE SURE THAT IF YOU WERE TO GIVE TISSUE OR CELLS INTO A BANK IN ALL OF THESE VARIOUS REGULATED AGENCIES, YOU WOULD NOT BE ABLE TO KNOW, AS A COMMON PRACTICE, BE ABLE TO KNOW WHAT WAS GOING ON BECAUSE IT WOULD BE ANONYMIZED. IS THAT A GENERAL THING.

UNIDENTIFIED SPEAKER: AT LEAST BLINDED.

CHAIRMAN LO: EVEN IF IT'S NOT ANONYMIZED, YOU WOULDN'T KNOW WHO GOT THE MATERIALS.

MS. LANSING: THAT'S WHAT I'M TALKING ABOUT. AND IS THAT TRUE IN PRIVATE ONES THAT AREN'T GOVERNMENT REGULATED? I GUESS IT WOULDN'T BE, WOULD

IT?

DR. LOCKHART: I THINK THE SAME PRACTICE GENERALLY HOLDS. IN MY LIMITED EXPERIENCE, RETURN OF INDIVIDUAL RESEARCH RESULTS IS GENERALLY RARE CURRENTLY. I THINK THERE IS GOING TO BE A GREATER MOVEMENT TOWARDS THAT ESPECIALLY AS MORE AND MORE DATA IS GENERATED. THERE ARE SOME LOGISTICAL DIFFICULTIES I TALKED ABOUT SOMEWHAT. THE INDIVIDUAL RESEARCHER PROBABLY DOES NOT HAVE THE CODE, FOR THE MOST PART, IN TERMS OF IT'S POSSIBLE TO LINK BACK TO THE PATIENT, BUT THE END RESEARCHER USUALLY CAN'T. AND THERE'S A LOT OF SENSE IN HAVING IT SET UP THAT WAY. WOULD YOU REALLY WANT RESEARCHER X JUST CALLING PEOPLE UP?

MS. LANSING: NO, I WOULDN'T. THAT'S ACTUALLY -- THESE ARE THE ISSUES THAT WE'RE GOING TO GET INTO. AND I THINK WITHOUT -- I LISTENED CAREFULLY TO WHAT YOU'RE SAYING, AND YOU WERE TERRIFIC IN EXPLAINING IT ALL. AND THE COMBINATION OF WHAT YOU WERE SAYING AND WHAT CHRIS SAID HAS GOT MY MIND THINKING OF WAYS TO SOLVE SOME OF THESE PROBLEMS.

DR. LOCKHART: I THINK THERE IS MOVEMENT TOWARDS THINKING ABOUT HOW TO RETURN MORE RESULTS. AND I THINK WE HAVE TO MAKE A DISTINCTION BETWEEN

AGGREGATE AND INDIVIDUAL. THERE COULD BE A LOT OF BENEFIT, AND I THINK A LOT OF THE RESEARCH PARTICIPANTS WOULD BE HAPPY WITH RETURN OF AGGREGATE RESULTS, THAT THEY KNEW THEIR SAMPLE WAS USED IN THIS PAPER. AND MAYBE THEY CAN ACCESS A LAY SUMMARY OF IT, AND THEY KNOW THAT THEIR DONATION BENEFITED SCIENCE. SOME PEOPLE WILL BE HAPPY WITH THAT ALONE. IT DEPENDS. IT DEPENDS WHETHER YOU'RE A HEALTHY VOLUNTEER OR IF YOU ARE A PATIENT WITH A DISEASE. IS IT A COMMON DISEASE? IS IT A RARE DISEASE? IS IT A LETHAL DISEASE? THERE'S A LOT OF DIFFERENT QUESTIONS HERE, AND I THINK THAT'S WHY GETTING COMMUNITY MORE INVOLVED WILL HELP ANSWER SOME OF THESE.

THERE ARE SOME ONGOING STUDIES. ONE OF THEM IS AT THE NIH THROUGH THE NHGRI. LES BESEKER IS DOING A VERY DETAILED SEQUENCE ANALYSIS. AND AS PART OF HIS STUDY, HE'S RETURNING INDIVIDUAL RESEARCH RESULTS. AND ONE OF HIS RESEARCH QUESTIONS IS THE RETURN OF RESULTS, HOW PATIENTS FEEL ABOUT IT, WHAT DO THEY WANT, HOW DO THEY PROCESS IT. AND SO PEOPLE ARE STARTING TO TRY AND ADDRESS THIS.

MS. LANSING: WITHOUT GETTING INTO THE DETAILS, BECAUSE I KNOW WE'RE GOING TO GO THROUGH, PATIENTS CAN HAVE A CHOICE TOO, WHICH IS SOMETHING

THAT I THINK WE HAVE TO TALK ABOUT HERE. YOU DON'T HAVE TO GET THE RESULTS. YOU CAN GET THE RESULTS. THEY CAN BE AGGREGATED. THEY CANNOT BE AGGREGATED. THEY CAN MAKE DECISIONS.

CHAIRMAN LO: SHERRY, JUST TO FOLLOW UP ON THAT, MOST WRITING ON THIS SUGGESTS THAT IT'S THE OFFER TO RETURN THE INDIVIDUAL RESULTS TO THE PATIENT THAT'S THE KEY QUESTION, OR THE DONOR CAN CHOOSE EITHER TO SAY, YES, I WANT THEM OR, NO, THANK YOU. I CHANGED MY MIND OR DECIDED NOT TO.

OTHER QUESTIONS?

DR. ROBERT TAYLOR: I JUST HAVE A QUICK CLARIFICATION QUESTION. ON YOUR FOURTH SLIDE YOU DESCRIBED THE REPRODUCTIVE USE OF MATERIALS. AS KIND OF A REPRODUCTIVE MEDICINE PERSON, I'M WONDERING ARE WE REALLY TALKING ABOUT PROLIFERATION OR REPLICATION OR PROMULGATION OF THE SAMPLE, OR ARE WE TALKING ABOUT REAL REPRODUCTION THE WAY I THINK ABOUT IT?

DR. LOCKHART: I'M NOT ENOUGH OF AN EXPERT TO ANSWER. I THINK I WOULD JUST SAY THAT WHATEVER YOU'RE DOING IN THAT REALM, YOU NEED TO BE CLEAR ABOUT BECAUSE THE PATIENT IS NOT GOING TO UNDERSTAND THOSE DISTINCTIONS THAT YOU'RE MAKING OR HOW ANY OF THOSE THINGS ARE DIFFERENT. SO IF YOU ARE USING

SAMPLES IN ANY WAY RELATED TO REPRODUCTION, I THINK THAT'S SOMETHING PEOPLE WOULD BE SENSITIVE ABOUT. AND THEY'RE GOING TO START WORRYING ARE YOU CLONING ME? THEY'RE GOING WORRY ABOUT THAT. SO WHATEVER YOU'RE DOING WOULD NEED TO BE CLEAR BECAUSE IF YOU JUST INCLUDE A PHRASE, AND WE MAY ALSO USE YOUR SAMPLES FOR REPRODUCTIVE RESEARCH, I DON'T THINK THAT WOULD BE ENOUGH. PEOPLE WOULD PANIC, THAT YOU'RE EITHER DOING RESEARCH THAT'S RELATED TO ABORTION OR RELATED TO CLONING.

OR MY LARGER POINT IS THAT THESE ARE SO -- THESE QUESTIONS ARE SO COMPLEX, AND I THINK THAT'S SOMETHING MOST PEOPLE ARE VERY WORRIED ABOUT, THAT IT JUST WOULD NEED TO BE CLEAR WHAT PRECISELY YOU WERE PLANNING ON DOING AND HOW THAT WOULD BE CONTROLLED. SO WE ARE GOING TO DO THIS TYPE OF REPRODUCTIVE RESEARCH, BUT IT WILL NEVER BE CLONING. IF THAT'S TRUE, THEN THAT WILL GIVE PATIENTS SOME LEVEL OF COMFORT. I WOULD PRESUME IT IS, BUT PATIENTS DON'T -- THEY DON'T KNOW. THEY'VE NEVER DONE THIS BEFORE. I WILL JUST SAY THAT'S WHERE THIS PROCESS THING REALLY COMES INTO PLAY.

MY HUSBAND AND I WERE RECENTLY RECRUITED FOR A STUDY AT A VERY WELL-RESPECTED ACADEMIC INSTITUTION. HE HAS A CHRONIC DISEASE. WE ARE

VISITING A SPECIALIST. WE WERE APPROACHED FOR A GENETIC STUDY, HIM AS AN AFFECTED INDIVIDUAL AND ME AS A NONAFFECTED. THE CONSENT WAS PRESENTED SIGNATURE SIDE UP FOR US TO JUST SIGN. AND MY HUSBAND KNEW THE GENETICIST, WAS SUPER EXCITED BECAUSE HE HAS A BACKGROUND IN GENETICS. SO HE WAS TALKING TO THE CLINICAL NURSE ABOUT, OH, ARE THEY STUDYING VARIANT X OR VARIANT Y? AND JUST VERY EXCITED. DIDN'T READ THE CONSENT AT ALL, NOT AT ALL.

HE JUST WAITED UNTIL I TOLD HIM ABOUT IT LATER OVER LUNCH, THAT, OH, OUR SAMPLES ARE GOING TO BE IN THIS BIOBANK THAT WE BOTH KNOW. THEY'RE GOING TO BE USED FOR ALL KINDS OF BROAD FUTURE USES. OH, AND THEY MAY MAKE CELL LINES. HE DIDN'T READ IT AT ALL. IT WAS PRESENTED -- I COULDN'T BELIEVE IT WAS PRESENTED SIGNATURE SIDE UP FOR US TO JUST SIGN. WE'RE BOTH SCIENTISTS. WE WERE OKAY WITH IT, BUT I CAN'T IMAGINE THAT THAT PROCESS IS OPTIMAL.

CHAIRMAN LO: OTHER QUESTIONS?

MS. ISASI: I JUST WANTED TO FOLLOW UP QUICKLY ON ANN'S POINT ABOUT WHAT IT MEANS A BIOBANK. AND THE SAME PROBLEM WE HAVE IN THE STEM CELL BANKING CONTEXT. INTERNATIONAL STEM CELL BANKING INITIATIVE IS TRYING TO NOT ONLY ADDRESS THE

TERMINOLOGY, BUT WE HAVE BEEN TRYING TO IDENTIFY WHAT, QUOTE, UNQUOTE, A STEM CELL BANK EXIST. AND THE ISSUE OF INDIVIDUAL LABS CALLING THEMSELVES REPOSITORIES AROUND THE WORLD IS PREVALENT.

DR. KIESSLING: I THINK WHAT'S IMPORTANT TO RECOGNIZE HERE IS THAT THIS IS NOT GOING TO BE A ONE SIZE FITS ALL. SO A BANK OF BLOOD CELL LINE SAMPLES IS GOING TO BE TOTALLY DIFFERENT FROM A BANK OF TISSUE SAMPLES. I DON'T THINK WE'RE GOING TO BE ABLE TO COME UP WITH GUIDELINES FOR ALL OF THEM.

CHAIRMAN LO: AGAIN, HERE I THINK WE'RE REALLY TALKING ABOUT AN IPS CELL BANK. WE'RE NOT TALKING ABOUT THE REPOSITORIES OF THE CELLS WHICH PEOPLE MIGHT USE TO DERIVE IPS CELLS. OUR JOB IS A LITTLE BIT SIMPLER THAN JOBS THAT HUGE BIOBANKS FACE THAT HAVE DIVERSE TYPES OF DEPOSITS IN THEM.

DR. ROBERT TAYLOR: FROZEN SPERM BANKS.

CHAIRMAN LO: PAT AND JEFF, DID YOU HAVE YOUR HAND UP?

MR. SHEEHY: YOU ARE GOING TO TAKE TISSUE SAMPLES. SO IT'S NOT JUST THE LINES. THAT CAME OUT IN THE WORKSHOP. YOU ARE GOING NEED THE RESOURCE TISSUE AS WELL.

CHAIRMAN LO: IN THE CIRM BANK. CIRM IS GOING TO BANK TISSUES FROM WHICH YOU WILL DERIVE

LINES?

(MULTIPLE RESPONSES OF YES.)

CHAIRMAN LO: LET ME JUST PURSUE THIS.

DR. FEIGAL: SO DOES NIH.

CHAIRMAN LO: BUT FOR CIRM, AGAIN, LET'S FOCUS ON CIRM. SO IS CIRM GOING TO ALLOW RESEARCHERS TO WITHDRAW SPECIMENS FOR NON-IPS RELATED RESEARCH?

DR. KIESSLING: WE'RE GOING TO ANSWER THAT, I THINK.

DR. FEIGAL: THAT'S PART OF THE UTILIZATION ISSUE. WHAT'S THE PURPOSE OF THIS BANK, THAT'S PART OF THE ISSUE.

CHAIRMAN LO: ALL RIGHT.

DR. OLSON: I WOULD JUST HIGHLIGHT ONE OTHER POINT TO KEEP IN MIND. AS YOU HEARD FROM WHAT OUR OBJECTIVES ARE WITH THE BANK, IT'S NOT JUST FUTURE. IT'S ALSO FOR SAMPLES THAT HAVE BEEN DERIVED BY RESEARCHERS. SO YOU HAVE TO CONSIDER THE CIRCUMSTANCES UNDER WHICH -- THERE IS A PREEXISTING. NOW, THERE OBVIOUSLY ARE CIRM GUIDELINES FOR DERIVATION OF LINES AND PRESUMABLY THAT COVERS IT. IT'S BOTH FUTURE AND PAST.

CHAIRMAN LO: GREAT.

DR. PATRICK TAYLOR: SO WE ALL START WITH

SIMPLICITY AND WE ALL CARE A LOT. AND THEN WE ALL END UP EMBRACING COMPLEXITY. I'M THINKING VERY MUCH OF THE OBSTACLES FACED BY DONORS AS WERE SO WELL ARTICULATED THIS MORNING. SO WHAT DO YOU THINK WE SHOULD DO TO BALANCE WHAT LOOKED LIKE VERY MUCH COMPETING PRACTICAL CONCERNS AT THE IMPLEMENTATION LEVEL WHEN WE CARE SO MUCH ABOUT TRYING TO DO THINGS RIGHT BY EACH DONOR AND IN THE PROCESS CREATE A SYSTEM OF SUCH PROLIXITY THAT IT BECOMES QUITE CONTINGENT FOR SCIENTIFIC RESEARCHERS AND POTENTIALLY QUITE BURDENSOME. NOT ONLY MANY FACTORIAL, BUT WITH NO STANDARDS AS TO HOW TO ACTUALLY ADDRESS AND WEIGH COMPETING CONCERNS. I THINK THAT'S WHY STILL 200 YEARS, 100 YEARS AFTER PEOPLE STARTED DOING SOME OF THESE THINGS WE'RE STILL TALKING ABOUT CONSENT.

SO WHAT ARE YOUR OWN THOUGHTS ABOUT THAT? HAVING HEARD A REALLY BRILLIANT ARTICULATION OF MANY OF THESE CONCERNS, I'M LEFT WONDERING, OKAY, IF WE PAY ATTENTION TO ALL OF THEM, WE'LL BE DOING SOMETHING THAT EMBRACES A DILEMMA. SO WHAT ARE YOUR THOUGHTS ABOUT DOING THE WHOLE THING RIGHT?

CHAIRMAN LO: RECOGNIZING YOU'RE NOT SPEAKING FOR NCI, NIH, OR ANY PART OF THE FEDERAL GOVERNMENT.

DR. PATRICK TAYLOR: I'M NOT SHIFTING THE PROBLEM TO YOU, ALTHOUGH THAT WOULD BE DELIGHTFUL. IT'S REALLY HEARING SOME REAL THOUGHTS ABOUT HOW TO GRAPPLE WITH THAT FUNDAMENTAL QUESTION.

DR. LOCKHART: I THINK MY ANSWER TO THAT WOULD BE TO TRY AND ASSESS, THROUGH WHATEVER WAYS YOU CAN, WHAT THE PARTICIPANTS REALLY WANT AND HONOR WHAT THEY WANT. SO FOR CIRM, IF YOU'RE PLANNING TO TARGET DEVELOPMENT OF IPS CELL LINES IN PARTICULAR DISEASE AREAS, THAT'S A BIT MORE CONFINED. YOU MIGHT BE ABLE TO WORK WITH THOSE ADVOCACY GROUPS, FIGURE OUT WHAT THEY MAY WANT IN TERMS OF CONSENT, WHAT THEY'RE COMFORTABLE WITH. DO THEY WANT RESULTS?

IF YOU CAN, YOU CAN THINK ABOUT PROVIDING CHOICES. I JUST -- I THINK YOU NEED TO MAKE SURE THOSE CHOICES ARE REAL, THAT YOU CAN DO WHATEVER YOU TELL PEOPLE YOU CAN DO. AND THAT YOU ARE FULLY PREPARED TO HONOR THEM, WHATEVER PROMISES YOU MAKE. SO IF YOU SAY YOU'RE GOING TO RETURN ALL INDIVIDUAL RESEARCH RESULTS, YOU NEED TO BE ABLE TO DO THAT, AND YOU NEED TO MAKE SURE THAT PEOPLE ARE IN AGREEMENT WITH THAT AND SIGNED UP FOR THAT.

CHRIS IS A VERY, VERY EDUCATED PATIENT ADVOCATE. NOT EVERYBODY CAN HANDLE INFORMATION THAT

SHE'S VERY COMFORTABLE HANDLING. SOME PEOPLE MAY NEED A GENETIC COUNSELOR TO HELP THEM WADE THROUGH REAMS OF INFORMATION. SO IF YOU ARE PROMISING TO RETURN THINGS, YOU NEED TO MAKE SURE IT'S DONE RESPONSIBLY. BUT I THINK TRYING TO WORK WITH YOUR PATIENT GROUPS WOULD BE IDEAL.

DR. PATRICK TAYLOR: SO THERE'S TWO DIFFERENT THINGS. ONE IS MAKING SURE WHEN YOU MAKE A PROMISE, YOU KEEP IT. THE OTHER IS MAKING SURE THE CHOICES YOU ACTUALLY OFFER PEOPLE ARE ETHICAL CHOICES AND TAKING INTO ACCOUNT SOME OF THE FACTORS THAT PEOPLE HAVE REFERRED TO, INCLUDING ACTUAL FEASIBILITY.

IT DOES STRIKE ME THAT WE TALK ABOUT CONSENT AS A PROCESS, BUT WE OFTEN TREAT THE CONSENT DEMANDS, QUOTE, UNQUOTE, AS STATIC. IT'S NOT DYNAMIC, NOT SOMETHING THAT COULD CHANGE THROUGH A PROCESS OF CONVERSATION AS IF WHEN WE TALK ABOUT MEETING PATIENT OR DONOR DEMANDS, I'VE BEEN BOTH MYSELF, IT'S SOMEHOW AS A GIVEN THAT WE TAKE AS UNCHANGEABLE THROUGH THE PROCESS OF DIALOGUE. IT MAKES ME WONDER WHETHER IF WE LISTEN MORE CAREFULLY TO KIND OF THE INCLUSION THAT WE'RE TALKING ABOUT, WE MIGHT ACTUALLY END UP WITH MORE REALISTIC AND POSSIBLE CONSENT APPROACHES THAT REFLECT MUTUAL

ADJUSTMENT RATHER THAN A STATIC SET OF DEMANDS.

CHAIRMAN LO: I'M GOING TO GIVE SHERRY THE LAST COMMENT, AND THEN I WANT TO PUSH ON TO OUR FOUR SPECIFIC TOPICS BECAUSE I THINK THAT'S WHERE IT'S GOING TO GET REALLY -- WHERE THE RUBBER IS GOING TO HIT THE ROAD.

MS. LANSING: I THINK THE RUBBER IS GOING TO HIT THE ROAD THERE, BUT I GUESS I CAN'T HELP BUT RESPOND TO YOUR QUESTION. AND TO ME I THINK THIS IS ALL ABOUT THE PATIENT. OFTEN WHAT WE'RE DOING IS ALL ABOUT THE SCIENTISTS, BUT TO ME THIS IS ALL ABOUT THE PATIENT. AND I THINK WE'RE SO FORTUNATE TO HAVE A HIGHLY INTELLIGENT AND ENGAGED PATIENT ADVOCATE, AND I DO KNOW THAT NOT EVERYBODY WHO'S FACING DECISIONS IS THE SAME. BUT TO ME I THINK THAT WE WOULD BE ABLE TO COME UP WITH A LIST OF CHOICES FOR A PATIENT TO MAKE A DECISION ABOUT DO YOU WANT IT ANONYMIZED? DO YOU NOT WANT IT ANONYMIZED? DO YOU WANT THE RESULTS? DO YOU NOT WANT THE RESULTS? DO YOU WANT IT TO BE USED JUST SPECIFICALLY FOR THIS DISEASE? DON'T YOU WANT IT TO BE USED SPECIFICALLY FOR THIS DISEASE?

AND I THINK THAT WITH INFORMED CONSENT IT IS POSSIBLE TO HAVE A MENU THAT ALLOWS THE PATIENT TO PARTICIPATE IN A VERY PERSONAL WAY IN WHAT

INFORMATION THEY WANT. AND I'M AFRAID OF MAKING IT ADVOCACY GROUPS BECAUSE THAT'S ASSUMING EVERYBODY IN AN ADVOCACY GROUP FEELS THE SAME AND THEY DON'T. I REALLY THINK THIS IS LIKE A MENU OF CHOICES THAT PEOPLE HAVE. AND THE THING THAT I THINK THAT YOU SAID, WHICH WAS SO BRILLIANT, WHICH I'VE NEVER THOUGHT ABOUT, WAS, OKAY, YOU CHECK OFF THE BOX AND THAT'S IT.

BUT WHAT I THINK IS ALSO PART OF THIS IS THAT THIS IS A PROCESS FIVE YEARS FROM NOW OR TOMORROW YOU HAVE THE RIGHT TO SAY I CHANGE MY MIND. I DO WANT THE INFORMATION OR I CHANGE MY MIND I DON'T WANT THE INFORMATION.

AND I THINK IT'S ALL LEADING TO THIS PERSONALIZED MEDICINE THAT IS SO TALKED ABOUT IN ALL THE DISEASES AND GIVING PEOPLE THE RIGHT TO HAVE THE INFORMATION THAT THEY DO OR DON'T WANT. AND THERE ARE MANY PEOPLE THAT WON'T WANT IT. GIVING THE CELL, GIVING THEM THE RIGHT TO DECIDE WHERE IT WILL BE USED. I THINK WE CAN DEVISE A MENU, AND I THINK THAT'S WHAT OUR RECOMMENDATIONS SHOULD DEAL WITH IS WHAT KIND OF MENU IT SHOULD BE.

DR. LOCKHART: I WOULD SAY THAT'S CERTAINLY AN APPROACH, AND IT WILL HAVE A LOT OF BENEFIT TO PATIENTS IF YOU CAN ALLOW THEM TO HAVE

THAT CHOICE. I WOULD JUST THINK THROUGH THE OPERATIONAL AND LOGISTIC CONSEQUENCES OF HAVING THOSE MENUS AND BEING ABLE TO MAKE SURE YOU CAN HONOR ALL THOSE CHOICES. EVEN THINGS ABOUT STATISTICAL POWER. IF YOU HAVE ALL THESE DIFFERENT MENUS, AND THEN DO YOU NOT HAVE ENOUGH SAMPLES YOU CAN MAKE CELL LINES OUT OF, OR IS IT VERY, VERY DIFFICULT FOR THE BANK TO FIGURE OUT WHAT SAMPLES THEY CAN GIVE TO WHICH RESEARCHER BECAUSE THERE'S ALL THESE CHOICES. I THINK IT CAN CERTAINLY BE DONE. I JUST THINK YOU NEED TO THINK THROUGH BOTH HOW YOU'RE GOING TO IMPLEMENT IT AND THEN --

MS. LANSING: THIS IS WHAT WE'RE GOING TO TALK ABOUT, BUT THERE'S A MINIMUM LEVEL WHICH YOU START. AND I THINK WE'VE ESTABLISHED THAT. NOW THE QUESTION IS WE KNOW THAT THE MINIMUM LEVEL IS, YES, IT CAN BE USED FOR THIS AND IT CAN'T BE USED FOR THAT, AND WE KNOW THAT BECAUSE THAT'S THE GOVERNMENT GUIDELINES. NOW THE QUESTION IS CAN IT BE USED FOR MORE THAN THAT, AND WHAT IS THE PATIENT'S RIGHT TO GET INFORMATION? THAT'S REALLY TO ME WHAT THE ISSUE SEEMS TO BE.

DR. LOCKHART: AND I WOULD ALSO SAY IF CIRM STARTS STRIKING NEW GROUND IN THIS AREA, I WOULD REALLY ADVOCATE TRYING TO STUDY THAT PROCESS.

I THINK THAT WILL BE REALLY USEFUL IS WHEN YOU MAKE THESE STRIDES TO TRY AND INCLUDE PATIENTS AND RESPECT THEIR CHOICES, DOES IT WORK OUT HOW YOU THOUGHT IT WOULD? ARE THE PATIENTS HAPPY WITH THE CHOICE THEY MADE? DID THEY UNDERSTAND WHEN THEY MADE THAT CHOICE WHAT IT WOULD ENTAIL OR WHAT THEY WOULD RECEIVE? A LOT OF THIS IS NEW GROUND, AND I THINK KIND AS YOU MOVE FORWARD, THAT WILL BE A VERY USEFUL EXERCISE SO THAT YOU CAN IMPROVE YOUR PRACTICES AND ALSO LET OTHERS IN THE COMMUNITY KNOW THIS REALLY WORKED, THIS DIDN'T.

MS. LANSING: AND BE FLEXIBLE IN YOUR PRACTICES AS WELL.

CHAIRMAN LO: OKAY. WITH THAT, THANKS VERY MUCH, NICOLE. WE REALLY APPRECIATE YOU'RE HELPING US. GEOFF IS NOW GOING TO SORT OF GET US TO THE TREADMILL HERE AND REALLY HIT THE SPECIFIC ISSUES, STARTING WITH CONSENT.

DR. LOMAX: I'D REALLY LIKE TO REACH BACK FIVE MINUTES IN THE CONVERSATION TO THE POINT PAT OLSON JUST MADE ABOUT WE ACTUALLY DO HAVE STOCKS OF MATERIALS THAT WE'RE DEALING WITH. AND SO LET ME JUST GO BACK ONE SLIDE. I'VE TRIED TO SORT OF SIMPLIFY, BUT GET A LITTLE MORE SPECIFIC. THIS IS SPECIFICALLY ON THE RANGE OF CONSENTS FOR CELLS AND

TISSUES WHICH WE KNOW ARE OUT THERE. AND I'VE TRIED TO COME UP WITH SORT OF THREE SUBJECTIVE CATEGORIES. ONE I'M CALLING -- ONE I'M SORT OF INDICATING THERE'S OPTIMAL CONSENT. BY OPTIMAL IT MEANS THAT THESE WOULD BE PROSPECTIVE COLLECTIONS FOR WHICH YOU KNOW YOU'RE COLLECTING MATERIALS INTENDED TO GO INTO THE FUTURE BANK.

SO, FOR EXAMPLE, IN SOHEL'S SLIDE, THE EXAMPLE OF MAYBE A CASE CONTROL STUDY WHERE YOU'RE WORKING WITH A DISEASE POPULATION. THAT'S A FAIRLY -- AT LEAST A CASE CONTROL COLLECTION WHERE YOU'RE WORKING WITH A PARTICULAR DISEASE. YOU CAN REALLY GO, I THINK, IN AT THAT POINT AND REALLY GET OPTIMAL CONSENT. I THINK THAT'S SORT OF THE LEAST SORT OF CHALLENGING AREA FROM A PERSPECTIVE OF HOW DO WE MOVE FORWARD BECAUSE THERE'S A FAIRLY CLEAR PATHWAY THERE.

IN ADDITION, I THINK WHERE A LOT OF MATERIALS EXIST NOW THAT ARE SORT OF RELEVANT TO WHAT ELLEN DESCRIBED IN TERMS OF THE UPCOMING CIRM COLLABORATION, WE HAVE VERY COMPREHENSIVE CONSENT THAT'S CONSISTENT WITH OUR EXISTING REGULATIONS, WHICH WE HAVE A VERY COMPREHENSIVE SET OF PROCEDURES FOR COLLECTING THOSE MATERIALS. I WOULD LIKE TO CLASSIFY THAT CONSENT AS VERY THOROUGH, BUT IT MAY

NOT HAVE EVERY POSSIBLE USE. AND WHETHER THAT'S A PROBLEM OR NOT I DON'T KNOW, BUT I'D LIKE TO PUT IT IN THIS CATEGORY OF COMPREHENSIVE. I THINK AS AN INSTITUTE WE'VE MADE SURE AND FOLLOWED UP THAT MATERIALS ARE AT THAT LEVEL.

THEN I THINK I WOULD IMAGINE THIS IS PROBABLY MORE THE EXCEPTIONAL CATEGORY. SO THE CATEGORY THAT THERE MAY BE SOME NEED FOR, BUT WOULDN'T BE SORT OF PREDOMINANT MATERIALS IN THE BANK OR CELLS WHERE THERE MIGHT BE LIMITED CONSENT, OR AS WE HEARD IN A PREVIOUS PRESENTATION, JUST MATERIALS THAT COME THROUGH PATHWAYS WHERE YOU JUST DON'T REALLY NECESSARILY GET CONSENT, FOR EXAMPLE, MEDICAL WASTE, BUT THEY MAY HAVE EXTRAORDINARY SCIENTIFIC SIGNIFICANCE AT LEAST AS A CONTROL SAMPLE, OR HISTORICALLY THEY'VE JUST BEEN IN SCIENCE SO LONG, THE WEALTH OF INFORMATION WHICH YOU DON'T WANT TO TAKE OFF THE TABLE IF YOU'RE STUDYING A PARTICULAR DISEASE.

AND WE WANTED TO EMPHASIZE THAT OUR REGULATIONS DO AUTHORIZE THE USE OF SORT OF ANONYMIZED CELLS THAT DON'T HAVE CONSENT. THE WAY WE SET IT UP, AND, AGAIN, THIS GOES BACK TO BERNIE'S POINT ABOUT TRYING TO RAISE THE BAR WHERE WE TOUCH -- WHERE OUR FUNDS TOUCH THINGS VERSUS

SUPPORTING THE SCIENCES. WE SAY IF YOU'RE DOING THOSE COLLECTIONS UNDER A CIRM PROTOCOL WITH CIRM FUNDING, YOU HAVE TO GET CONSENT, AND THIS IS SORT OF THE LEVEL YOU NEED TO BE AT, BUT WE'RE NOT GOING TO EXCLUDE THE USE OF MATERIALS THAT HAVE COME THROUGH THESE OTHER PATHWAYS.

AND I THINK THAT'S THE BALANCE WE STRUCK IN TERMS OF TRYING TO ACHIEVE A CERTAIN LEVEL WITH OUR FUNDING, BUT NOT EXCLUDING MATERIALS FROM THE RESEARCH STREAM. SO WITH THAT SAID, I'VE TRIED TO -- I THINK IT WOULD BE PRODUCTIVE TO SORT OF THINK THROUGH SOME OF THESE CATEGORIES AND SORT OF USING KIND OF THE STOPLIGHT ANALOGY WHERE I THINK IT WOULD BE KIND OF SMOOTH SAILING WITH FUTURE COLLECTIONS. OUR COMPREHENSIVE CELLS THAT WE'RE POTENTIALLY GOING TO BE SHIPPING OVER TO THIS REPOSITORY IN THE NEAR FUTURE ARE PROBABLY ON SOLID GROUND, BUT ARE THERE THINGS WE NEED TO THINK ABOUT.

AND, AGAIN, THE SORT OF MATERIALS THAT COME OUT WITH MORE LIMITED CONSENT AND DISCLOSURE, AGAIN, HOW DO WE WANT TO THINK ABOUT THOSE MATERIALS? UNDER WHAT CONDITIONS WOULD WE BE COMFORTABLE WITH THEM BEING SORT OF INCORPORATED INTO SOME SORT OF CIRM-FUNDED REPOSITORY OR DISTRIBUTION INITIATIVE?

I THINK THAT WAS THE -- AGAIN, THIS IS USING THE SAME SORT OF COLOR CODING. TRIED TO SORT OF, AGAIN, EMPHASIZE THE STATUS OF THE MATERIALS, SOME OF THE ETHICAL CONSIDERATIONS, AND THEN THINKING ABOUT THE POLICY RECOMMENDATIONS. SO I HOPE THAT'S A HELPFUL FRAMEWORK FOR MOVING THE CONSENT DISCUSSION IN A MANNER THAT I THINK IS MOST APPLICABLE TO THE CIRM SITUATION AND OBVIOUSLY THERE COULD BE THINGS MISSING AS WELL.

CHAIRMAN LO: SO I WOULD SUGGEST, BECAUSE THIS IS AN IMPORTANT AND COMPLICATED TOPIC, WE SORT OF TRY AND TAKE IT IN CHUNKS OR PIECES. LET'S ASSUME FOR THE MOMENT -- LET'S FIRST DECIDE DO WE WANT TO FOLLOW GEOFF'S, MAYBE YOU COULD BACK UP ONE SLIDE ON THIS, THREE DIFFERENT SITUATIONS OF CONSENT. FIRST IS WHERE YOU'RE HAVING A NEW COLLECTION OF MATERIALS SPECIFICALLY PLANNING TO DERIVE AN IPSC LINE. AND SO YOU HAVE AN OPPORTUNITY -- ACTUALLY YOU HAVE TO INTERACT WITH THE DONOR TO GET THE SAMPLE AND HAVE AN OPPORTUNITY TO TALK WITH THEM AS ONE SITUATION AND THEN THE OTHER TWO.

AND MAYBE WE SHOULD TAKE THEM ONE AT A TIME. I WOULD SUGGEST WE TALK ABOUT THE GREEN LEVEL FIRST JUST SO WE CAN SAY IF WE COULD DO IT IN THE

BEST WAY WE COULD, BECAUSE WE'VE IDENTIFIED THE DONOR OR PATIENT, WE HAVE A CHANCE TO TALK TO THEM BEFORE WE GET THAT SKIN BIOPSY, WHAT WOULD THAT CONSENT PROCESS LOOK LIKE? AND THEN THE OTHER TWO WE MAY NOT BE ABLE TO DO EVERYTHING WE WOULD WANT IN THE GREEN SITUATION.

SO NOW, GEOFF, YOU CAN GO TO THE NEXT SLIDE. AS I LOOK ACROSS THE TOP LINE, THE GREEN LINE, SO WE CERTAINLY HAVE AN OPPORTUNITY TO TALK TO THEM ABOUT WHAT BIOBANKING IS ALL ABOUT, WHAT IPS DERIVATION IS ABOUT. WE HAVE A CHANCE TO TALK TO THEM ABOUT THINGS THAT WE CAN EXPECT RESEARCHERS TO DO, WHICH MAY NOT BE SOMETHING THAT A LOT OF PEOPLE UNDERSTAND, SOME PEOPLE MAY NOT UNDERSTAND AND MAY HAVE QUESTIONS, SUCH AS, FOR EXAMPLE, WHOLE GENOME SEQUENCING. THAT'S SORT OF ONE SET OF ISSUES.

AND THEN WE ALSO HAVE THE OPPORTUNITY TO ASK THEM A SERIES OF OTHER QUESTIONS LIKE IF IN THE FUTURE SOMETHING COMES UP THAT WE HAVEN'T COVERED BUT SEEMS REALLY CONTROVERSIAL AND DIFFICULT, DO WE HAVE YOUR PERMISSION TO GET BACK TO TALK TO YOU AGAIN. WE CAN ALSO THERE, FOLLOWING SHERRY'S SUGGESTION, ASK QUESTIONS ABOUT PREFERENCES FOR RETURN OF RESULTS, BUT WE SHOULD DEFER THAT TILL WE DECIDE LATER ON TODAY.

WHY DON'T WE START WITH THE GREEN LEVEL. AND JUST WHAT DO PEOPLE THINK SHOULD BE IN THE OPTIMAL CONSENT PROCESS WHERE THE DONOR'S SITTING RIGHT IN FRONT OF US AND WE CAN TALK?

DR. FEIGAL: I DO THINK YOU NEED TO DEFINE, EVEN THOUGH WE HAVE THOUGHTS ABOUT WHAT'S A BIOBANK, WE NEED TO HAVE SOME DEFINITION. ARE WE TALKING ABOUT A RESOURCE THAT'S GOING TO BE MADE PUBLICLY AVAILABLE? ARE WE TALKING ABOUT SOMEBODY SITTING IN A LAB? I THINK IT WOULD BE HELPFUL TO GET SOME SENSE OF THAT.

CHAIRMAN LO: I WAS TRYING TO ADDRESS WHAT I TOOK TO BE THE CHARGE FROM CIRM LEADERSHIP, WHICH IS IN THE CIRM PROPOSAL FOR AN IPSC BIOBANK --

DR. FEIGAL: SO A PUBLICLY AVAILABLE RESOURCE.

CHAIRMAN LO: GOD BLESS NIH, BUT WE'RE NOT GOING TO SOLVE THEIR PROBLEMS TODAY.

DR. FEIGAL: I ALSO WANTED TO GET AROUND SORT OF THE AD HOC THE RESEARCHER MAY BE DERIVING THINGS.

CHAIRMAN LO: NO. THIS IS SOMETHING THAT CIRM IS GOING TO BE FUNDING AND HAVING A BIG SAY.

DR. ROBERT TAYLOR: AND THIS IS PAST TISSUE?

CHAIRMAN LO: RIGHT NOW THE GREEN LINE IS NEW TISSUE GOING FORWARD. THE OTHER TWO ARE THE PREVIOUS TISSUE.

DR. ROBERT TAYLOR: I GUESS WHAT I'M WONDERING IS WE CAN KIND OF INTELLECTUALLY THINK ABOUT IT AS AN IPS BANK THAT DOESN'T STORE FRAGMENTS OF SOMEBODY'S SKIN AND DOESN'T STORE -- IT'S ALL KINDS OF POST FACTO ONCE THESE CELLS HAVE BEEN GENERATED.

CHAIRMAN LO: NO. I STAND CORRECTED.

DR. ROBERT TAYLOR: YOU GUYS HAVE A BIGGER VIEW THAN THAT. IT REALLY GETS INTO TISSUE BANKING IN GENERAL.

CHAIRMAN LO: WELL, MY UNDERSTANDING -- THIS IS IMPORTANT TO BE CLEAR ON. IT'S TISSUE BANKING SO THAT WE CAN GO BACK AND REDERIVE IPSC LINES IF WE NEED TO. IT'S NOT NECESSARILY TISSUE BANKING FOR A CANCER RESEARCHER TO SAY, HEY, I'VE GOT THIS NEAT STUDY.

DR. ROBERT TAYLOR: IS THAT FOR SURE? IT SOUNDS TO ME LIKE IT IS A TISSUE BANK, A TISSUE BANK YOU CAN GO BACK TO FOR ANYTHING YOU WANTED TO DO WITH TISSUE. AND IT WOULD BE NAIVE TO SORT OF THINK LESS OF IT THAN THAT, I THINK.

DR. OLSON: I BELIEVE THE IDEA WOULD BE IT

IS AN IPS BIOBANK WHICH WOULD INCLUDE THE TISSUE OF ORIGIN FOR THE IPSC LINE, AND THEY WOULD BE LIMITED PRESUMABLY TO THAT. I DON'T KNOW THAT WE'VE GOTTEN INTO BLOOD SAMPLES. I DON'T THINK SO.

CHAIRMAN LO: YOU MAY BE ABLE TO DERIVE IPS CELLS FROM BLOOD. I THINK LET'S TRY AND FOCUS ON SOMETHING THAT LOOKS LIKE WHAT CIRM IS REALLY INTERESTED IN. IF WE CAN'T SOLVE THAT, THEN IT DOES NO GOOD TO TALK ABOUT ALL THESE OTHER THINGS. LET'S TRY AND DO THAT AND SEE WHERE WE ARE.

MR. SHEEHY: I JUST HAD A QUESTION. SO THIS ONLY APPLIES TO THIS BANKING PROPOSAL? WHAT IF WE HAD PEOPLE CREATING LINES THROUGH RESEARCH? AND PRESUMABLY ONE ASPECT OF THIS BANKING PLAN IS TO BE KIND OF A BRING ALL OF OUR DIFFERENT CREATED LINES TOGETHER. SO REALLY, YOU KNOW, I KNOW YOU WANT TO MINIMIZE THE SCOPE TO THIS ONE SINGLE USE TO CREATE A BANK, BUT ACTUALLY THIS WILL -- AND CERTAINLY IT DOESN'T MAKE ANY SENSE TO SAY IF YOU CREATE A LINE FOR OUR BANK, WE HAVE THESE RULES. BUT IF YOU CREATE A LINE FOR RESEARCH, WE HAVE A DIFFERENT SET OF RULES USING OUR MONEY.

AND I THINK AT THE END OF THE DAY, ALL THESE ARE GOING TO BE PART OF ONE COLLECTIVE GROUP. AS I READ THE PROPOSAL, PART OF IT IS SPECIFIC

BANKING INITIATIVES AND THE OTHER, WHICH CAME OUT IN THE WORKSHOP, IS TO COLLECT ALL THESE TOGETHER.

I DO THINK THE SOURCE TISSUE IS NOT A SMALL PIECE OF THIS. PEOPLE WILL WANT TO DO STUFF WITH THE SOURCE TISSUE, AND YOU HAVE TO BANK THE SOURCE TISSUE BECAUSE THE LINES ARE NOT IMMORTAL.

CHAIRMAN LO: SO LET ME TRY --

MR. SHEEHY: I HATE TO MAKE IT MORE COMPLICATED.

CHAIRMAN LO: LET'S TRY AND SOLVE A SIMPLER PROBLEM FIRST, AND THEN WE CAN GET MORE COMPLICATED. AND THE SIMPLE PROBLEM, THE FIRST SIMPLE PROBLEM IS IF CIRM IS GOING TO PUT FORTH A PROPOSAL TO ESTABLISH AN IPSC BIOBANK, INCLUDING ORIGINAL SOMATIC CELL MATERIALS TO REDERIVE LINES, IF NEED BE, WHAT WOULD WE SAY ABOUT -- AND WE'RE GOING TO HAVE NEW MATERIALS COLLECTED FOR THAT PURPOSE GOING TO THE BANK. WHAT WOULD WE WANT THE CONSENT PROCESS TO LOOK LIKE? THAT'S, I TAKE IT, GEOFF'S GREEN LINE.

THE YELLOW THING, GEOFF, IS YOUR SECOND THING IS THERE ARE LINES THAT, FOR EXAMPLE, CIRM RESEARCHERS HAVE ALREADY DERIVED WITH WHAT THE STANDARDS WERE WHEN THEY DERIVED THE LINES. AND DO WE HAVE ANY CONCERNS ABOUT THE FACT THAT THEY DIDN'T

MENTION A BIOBANK, FOR EXAMPLE, IN THE ORIGINAL CONSENT? DO WE HAVE ANY CONCERNS THEY DIDN'T MENTION SOME DOWNSTREAM USES OF IPSC'S OR GENOMIC SEQUENCING? SO THAT'S THE CONSENT WAS DONE IN THE PAST, WE MAY NOT BE ABLE TO RECONTACT THE DONOR, THE LINE IS ALREADY THERE, AND WE'D LIKE TO INCLUDE THEM IN THE BANK, AND MAYBE SOME OF THE ORIGINAL TISSUE IF THAT'S LYING AROUND.

DR. FEIGAL: I THINK THAT WILL GET AT JEFF'S QUESTION.

CHAIRMAN LO: THAT WILL GET AT JEFF'S QUESTION.

AND THE THIRD, I THINK, ARE LINES THAT, AGAIN, ARE ALREADY IN EXISTENCE OR MAYBE WERE FUNDED BY SOME OTHER MECHANISM, NEW LINES, WHERE THERE MAY NOT HAVE BEEN ANY CONSENT AT ALL. FOR EXAMPLE, THEY MAY HAVE BEEN DERIVED UNDER THE FEDERAL EXCEPTION FOR DEIDENTIFIED MATERIALS NOT BEING RESEARCH, THAT THEY JUST TOOK SAMPLES, DEIDENTIFIED THE EXISTING LEFT-OVER CLINICAL SPECIMENS, DEIDENTIFIED THEM AND SAID, HEY, WE CAN DERIVE. SO I JUST WANT TO TRY NOT DO EVERYTHING AT ONCE BECAUSE I THINK THAT'S TOO COMPLICATED. MY SENSE IS IT GETS MORE COMPLICATED AS WE GO FROM GREEN TO YELLOW TO PINK.

DR. PATRICK TAYLOR: THIS IS INTENDED AS A

HELPFUL QUESTION, AND ACTUALLY HOPEFULLY TO SUGGEST THAT MAYBE, DESPITE THAT TREND, IN ONE WAY IT MIGHT BE LESS COMPLICATED. IS IT ACCURATE THAT FOR THE PINK AND THE YELLOW WE'RE NOT TALKING ABOUT ASSOCIATED CLINICAL DATA TO THAT SAME DEGREE THAT GREEN MAY INVOLVE? SO THAT THE PINK MAY REALLY JUST BE SPECIMENS AND NOT IDENTIFIABLE TO PATIENT INFORMATION IN ANY FORM. THOROUGHLY IDENTIFIED, DEIDENTIFIED EXCEPT THEY SAID DNA WAS THE IDENTIFIER. SAME PERHAPS FOR THE YELLOW.

DR. LOMAX: THAT IS -- THAT'S ACCURATE. I WOULD AGREE WITH THAT. THE ONLY COMMENT, THE ONLY QUOTE I WILL MAKE IS THAT I'VE HEARD THAT PEOPLE AT TIMES SAY IF YOU INTEND TO DO WHOLE GENOME SEQUENCING, THERE IS NO SUCH THING AS ANONYMITY. SO TO WHAT EXTENT YOU BELIEVE THAT, THAT WOULD BE THE ONLY CAVEAT.

DR. PATRICK TAYLOR: EVEN THE PIONEERS OF SAYING EVERYTHING IS IDENTIFIABLE NEVER SAID THAT EXCEPT THERE'S ALWAYS SOME ACCESS TO SOMETHING THAT'S REQUIRED WHICH HAS THE DNA STUFF IN SOME FORM. WHEREAS, THE GREEN MAY WELL INVOLVE SOME REAL ATTENTION TO THE KIND OF THINGS OUR KIND DONOR SPOKE ABOUT. HER EFFORTS TO KEEP THE MEDICAL RECORD OF THE FAMILY CURRENT AND AVAILABLE MAY HAVE SOME

COUNTERPART IN THE GREEN STUFF GOING FORWARD. I HOPE THAT'S HELPFUL. WE MAY ACTUALLY HAVE SOME REASON FOR THINKING THROUGH THE APPLICATION HERE OF SOME OF THE THINGS YOU, BERNIE, AND OTHERS HAVE PIONEERED WITH RESPECT TO PAST SPECIMENS SIMPLY BECAUSE THEY DON'T RAISE THE SAME CONFIDENTIALITY ISSUES AND SO ON. THANKS.

MS. HEMPEL: I WANTED TO MENTION JUST IN LISTENING TO NICOLE AND THIS CONVERSATION ABOUT CONSENT IS JUST HOW YOU PLAN TO GET THE CONSENT. ARE YOU PLANNING TO SIT DOWN WITH PEOPLE IN PERSON AND GO OVER THE CONSENTS? GENERALLY MY EXPERIENCE WITH CONSENT FORMS, AND I'VE SIGNED LIKE HUNDREDS OF THESE CONSENT FORMS NOW, IS THAT IT ENDS UP IN A PIECE OF PAPER LIKE WHAT NICOLE WAS TALKING ABOUT. AND THESE CONSENT FORMS ARE REALLY COMPLICATED, AND IT GOES BACK TO WHAT SHERRY WAS TALKING ABOUT. THE CONSENT FORMS ARE WRITTEN -- I CAN SEND YOU A BUNCH OF THEM. THEY'RE WRITTEN BY LAWYERS AND PEOPLE DO NOT UNDERSTAND THE CONSENT FORMS. I'VE GONE THROUGH THE CONSENT FORMS. I DON'T UNDERSTAND THEM. I DON'T THINK THE AVERAGE PERSON WHO'S GOING TO BE PARTICIPATING IN THIS, I THINK THAT'S YOUR CHALLENGE IS HOW DO YOU GET THE CONSENT FROM PEOPLE AND THEY ACTUALLY KNOW WHAT THEY'RE CONSENTING TO.

SO THAT WAS THIS QUESTION THAT I HAD WAS JUST HOW YOU PLAN TO GET THE CONSENT. AND IF IT'S GOING TO JUST BE A PIECE OF PAPER, I'M THINKING WHAT MATERIALS COULD YOU PROVIDE TO PEOPLE SO THAT THEY COULD UNDERSTAND THE LANGUAGE BEHIND ALL OF THE COMPLICATIONS OF IPS CELLS BECAUSE I THINK THE AVERAGE PERSON, THEY DON'T KNOW.

CHAIRMAN LO: LET ME AGAIN, I'M TRYING TO STRUCTURE THE DISCUSSION SO WE CAN START KNOCKING OFF SOME ISSUES. THAT'S A HUGE POINT IN MY OWN VIEW, AND I THINK I SPEAK FOR A LOT ON THE COMMITTEE. NO, CONSENT IS NOT A PIECE OF PAPER. IT'S A DISCUSSION. IT'S A PROCESS.

WHAT I'D LIKE TO FOCUS ON FIRST IS WHAT DO WE NEED TO DISCUSS? WHAT ARE THE TOPICS? WHAT ARE THE ISSUES WE NEED TO DISCUSS AS PART OF THIS GREEN LEVEL CONSENT? AND IS THERE AGREEMENT ON WHAT THOSE THINGS SHOULD BE? AFTER WE SETTLE THAT, THEN WE CAN TALK. I THINK THERE'S A WHOLE LOT OF WORK TO BE DONE HOW TO MAKE THAT WORK IN PRACTICE IN TERMS OF INFORMATION ON MATERIALS, WHO DOES THE CONSENT PROCESS, HOW LONG IS IT GOING TO TAKE, DO YOU CHECK FOR UNDERSTANDING, OPPORTUNITY TO ASK QUESTIONS, GO HOME AND THINK ABOUT IT.

LET'S FIRST TALK ABOUT WHAT SHOULD THE

TOPICS BE THAT WE ARE RECOMMENDING BE INCLUDED IN THAT GREEN LEVEL?

DR. KIESSLING: THERE HAVE BEEN A COUPLE OF THINGS THAT HAVEN'T BEEN MENTIONED YET THAT ARE ABSOLUTELY KEY TO THIS. ONE IS THESE PEOPLE HAVE TO BE CONSENTED FOR INFECTIOUS DISEASE TESTING. AND THAT'S A PROCESS ALL BY ITSELF. THAT HAS TO BE LIKE NO. 1. YOU'VE GOT TO DECIDE WITH THIS PERSON ARE THEY WILLING TO HAVE A BROAD PANEL OF INFECTIOUS DISEASE TESTING. THAT'S STEP ONE.

IN STEP TWO WE HAVE TO DECIDE DO WE WANT THESE PEOPLE TO BE PSYCHOLOGICALLY TESTED. STANDARDS FOR, FOR INSTANCE, EGG DONATION, PARTICULARLY FOR THE HUMAN -- THE EGG DONATION PROGRAM THAT WE WORKED OUT IS ALL THE DONORS WENT THROUGH SOME KIND OF PSYCHOLOGICAL ASSESSMENT SO THAT YOU CAN HAVE SOME IDEA AS TO WHAT THEY ACTUALLY ARE GOING TO UNDERSTAND ABOUT WHAT YOU TALK ABOUT. AND THIS CAN BE A VERY SHORT PROCESS. THERE'S SOME VERY STANDARDIZED TESTS THAT CAN BE DONE.

I THINK WHAT WE KNOW ABOUT THE INDIVIDUAL HAS TO START AT THE VERY BEGINNING, AND THEN YOU CAN DECIDE WHAT EXACTLY YOU WANT THE INDIVIDUAL TO KNOW ABOUT WHAT'S GOING TO HAPPEN WITH THEIR TISSUES.

CHAIRMAN LO: I'M GOING TO WORK DOWN THE

RIGHT AND THEN WORK DOWN THE LEFT.

DR. ROBERTS: FOR ME A BIG ISSUE WAS ONE THAT NICOLE MENTIONED, WHICH IS MAKING SURE THAT THE DONORS UNDERSTAND WHETHER OR NOT THEIR TISSUE AND DERIVED STEM CELL LINES WILL BE USED TO STUDY OTHER THINGS, OTHER DISEASES. SO WHAT DISTINGUISHES, AND I THINK THIS IS PART OF WHAT YOU WERE SAYING, WHAT DISTINGUISHES THE TOP, WHICH MAY ACTUALLY MAKE IT MORE COMPLICATED, THE GREEN LINE, THE CURRENT DONORS BEING RECRUITED, IS THAT THESE THEN WILL -- SINCE BEING RECRUITED BY DISEASE, THESE ARE PEOPLE WHO HAVE THE DISEASE OR THEIR CHILDREN HAVE THE DISEASE AND THEY'RE PROBABLY PARTICIPATING BECAUSE THEY WANT TO FIND A CURE FOR THEIR DISEASE. AND THEY MAY VIEW THIS VERY DIFFERENTLY IF WHAT'S GOING TO HAPPEN IS THEIR TISSUE IS BEING USED TO CURE SOME OTHER DISEASE.

DR. KIESSLING: YOU THINK THEY NEED TO BE PSYCHOLOGICALLY ASSESSED?

DR. ROBERTS: WELL, I'D LIKE WANT TO KNOW EXACTLY WHAT THAT MEANS FOR THE PSYCHOLOGICAL ASSESSMENT.

DR. KIESSLING: THERE'S SOME STANDARDS.

DR. ROBERTS: I THINK IT IS IMPORTANT TO MAKE SURE THAT THEY UNDERSTAND WHAT IS IN THE

CONSENT FORM.

DR. PATRICK TAYLOR: WORKING FROM SOME OF THE THINGS THAT HAVE BEEN SAID THIS MORNING, I THINK IT IS REALLY USEFUL, BERNIE, TO DO WHAT YOU WERE FOCUSING ON, WHICH IS, FIRST OF ALL, TO DISTINGUISH INTERVENTIONAL USES AND STUDIES. IN MY OWN EXPERIENCE THE TIMES OF CONSENT REALLY SHOULD BE LONG AND DETAILED, FOR EXAMPLE, WHEN IT SPELLS OUT A PATHWAY OF OFFICE VISITS AND ADMINISTRATION OF TEST DRUGS AND ALL KINDS OF THINGS, SO A FAMILY CAN GO BACK AND SAY, OKAY, IS THIS WHAT'S GOING TO BE HAPPENING TO MY CHILD. HERE'S WHAT IT ALL INVOLVES. THAT SHOULD BE A LONG AND DETAILED CONSENT LIKE WHAT'S REALLY GOING TO BE HAPPENING. BUT IF THIS IS REALLY FOCUSED ON BASIC SCIENCE WORK, I THINK THAT DOES SIMPLIFY MANY THINGS, AND IT'S AN IMPORTANT FOCUS.

THE SECOND THING IS I THINK IT ALSO HELPS ADDRESS ANN'S QUESTION BECAUSE WHILE IF A CONSENT IS VERY, VERY COMPLEX OR INVOLVES A WHOLE LOT OF UNFORESEEN DANGERS, I CAN SEE HOW THAT COMPREHENSIVE TESTING MIGHT BE VERY IMPORTANT. HERE IT MIGHT END UP FUNCTIONING AS AN OBSTACLE TO DONORS WHO ARE REALLY JUST TRYING TO MAKE A BASIC SCIENCE DONATION. SO I THINK YOUR FOCUS IS REALLY HELPFUL.

THE SECOND THING, I GUESS, IS THERE'S BEEN A REAL EMPHASIS ON EMPIRICAL THINGS. WHAT DO DONORS REALLY CARE ABOUT? I THINK WHAT WE'VE HEARD AND PROBABLY MANY OF US HAVE HEARD IS THAT THE UNCERTAINTY OF KNOWLEDGE GENERATION IS NO BIG SURPRISE TO DONORS WHO FACE THE UNCERTAINTY OF A CHILD'S PROGRESS THROUGH LIFE. WE ALL ACTUALLY ARE USED TO THAT. AND SO SAYING THAT PEOPLE HAVE TO GRAPPLE WITH SPECIFIC CERTAINTIES ABOUT EVERYTHING IN SCIENCE IS NOT REALLY WHERE IT'S AT. BUT FINDING OUT EMPIRICALLY THE THINGS THEY WOULD OBJECT TO IS REALLY IMPORTANT. SO THERE'S PROBABLY SOME WORK TO BE DONE IN A SIMPLIFIED AND MORE UNIFORM CONSENT THAT DOES SPOT ON SOME ISSUES. I THINK THAT IS A USEFUL DIRECTION.

CHAIRMAN LO: LET ME GO THROUGH ONCE.

MR. SHEEHY: I HAD THE SAME POINT HE DID. I THINK WHAT WE'RE REALLY TALKING ABOUT IS REDOING CONSENT FOR IPS DONATION. WE MAY BE THINKING WE'RE TALKING ABOUT A BANK, BUT THIS IS GOING TO HAVE BROAD IMPACT. AND I NOTICE HOW MUCH EVERYONE'S OPINIONS ABOUT THIS HAVE BEEN INFLUENCED BY HEARING FROM SOMEONE WHO'S ACTUALLY PARTICIPATED IN THE PROCESS. I THINK THERE'S A REAL NEED TO GETTING SOME SORT OF EMPIRICAL DATA IN ORDER TO START

TALKING ABOUT THIS. WE'RE KIND OF PULLING THINGS OUT OF OUR HEAD AS WE'RE TRYING TO CONSIDER THIS WITHOUT ACTUALLY HAVING GONE THROUGH THE EXPERIENCE OF DOING A DONATION.

WE'VE HEARD FROM ONE INDIVIDUAL WHO'S RAISED AN ENORMOUS NUMBER OF ISSUES. AND I THINK THAT BEFORE WE START THINKING ABOUT IDEALLY WHAT WE'D LIKE TO HAVE IN A CONSENT FORM, WE HAVE PEOPLE WHO HAVE BEEN DONATING FOR THE LAST TWO, THREE, FOUR YEARS FOR IPS. AND IS THERE SOME WAY -- AT LEAST WITHIN CALIFORNIA, IT WOULD BE A USEFUL EXERCISE TO COLLECT SOME DATA, ACTUALLY BOTH QUANTITATIVE AND QUALITATIVE DATA, TO ACTUALLY FIND OUT ABOUT THEIR EXPERIENCE. BEFORE WE START REALLY MAKING RULES OR GIVING GUIDELINES IN THIS, WE SHOULD REALLY TRY TO FIND OUT WHAT PEOPLE THINK. THAT WOULD BE MY SUGGESTION. I KNOW THAT THAT IS NOT QUITE AS SIMPLE.

DR. ROBERT TAYLOR: AND I WAS JUST GOING TO MAKE THE COMMENT THAT I THINK WE OUGHT TO KNOW WHAT WE'RE UP AGAINST TOO. NICOLE, MAYBE YOU CAN ADDRESS THIS. I KNOW WITHIN MY OWN INSTITUTION, THERE ARE KIND OF CANCER-ORIENTED COMPANIES -- I COULD NAME A COUPLE IF IT WERE REQUESTED -- THAT ARE COLLECTING TISSUE SAMPLES AS CLINICAL TEST SAMPLES,

SAY, A CHUNK OF BREAST CANCER FOR STEROID RECEPTOR MEASUREMENTS. THEY'RE BANKING THOSE TISSUES. THEY'RE GENERATING CELL LINES, I WOULD IMAGINE, FROM THOSE TISSUES. THEY'RE DOING ALL KINDS OF STUFF THAT NEVER WAS CONSENTED. THIS ALL WENT UNDER THE RADAR BECAUSE THESE WERE, QUOTE, CLINICAL SAMPLES THAT ARE GOING TO THESE COMPANIES.

SO IN THE PRIVATE SECTOR THIS KIND OF THING -- THERE ARE THESE TISSUE BANKS THAT ARE HAPPENING. FRANKLY, I THINK PATIENTS ARE PAYING FOR THE OPPORTUNITY TO CONTRIBUTE SAMPLES TO THOSE. SO THAT'S HAPPENING AT KIND OF ONE LEVEL WITH REALLY NO REGULATION WHATSOEVER, AND WE'RE TALKING ABOUT ALL THESE LAYERS OF THINGS. SO I KIND OF AGREE WITH JEFF THAT IT WOULD BE HELPFUL TO SORT OF STEP BACK AND KIND OF ASSESS WHERE ARE WE TODAY. MAYBE YOU KNOW MORE ABOUT THIS KIND OF THING THROUGH THE NCI, BUT I THINK THAT THERE'S -- I DON'T KNOW. WE'RE GOING TO HAVE, I THINK, A WHOLE SERIES OF DIFFERENT STANDARDS IN THE FIELD THAT ARE GOING TO BE PRETTY BIZARRE TO TRY TO DEAL WITH ETHICALLY.

MS. FEIT: I AGREE. IT SOUNDS LIKE A MINE FIELD. YOU OPEN ONE DOOR AND TEN OTHERS OPEN. AND I THINK WE'RE GOING TO BE BUTTING UP AGAINST A LOT OF OTHER STANDARDS, SOME THAT MAY HAVE BEEN WRITTEN

SO MANY YEARS AGO, THAT THEY REALLY DON'T APPLY. AND THAT'S WHY UNDER THE RADAR BEHAVIOR STARTS WHEN YOU DON'T HAVE CURRENT POLICIES AND STANDARDS TO GUIDE PEOPLE IN THEIR PRACTICES AND WHAT THEY'RE DOING WHEN PEOPLE MOVE AHEAD.

SO I THINK FOLLOWING JEFF'S RECOMMENDATION MAY BE THE RIGHT WAY TO BEGIN DOWN THIS PATH BECAUSE WE MAY, AGAIN -- AS AN INSTITUTE WE BLAZED TRAILS ON NEW FRONTIERS OF STEM CELL RESEARCH AND SETTING STANDARDS AND DOING THINGS, AND THIS MAY BE ANOTHER AREA WHERE WE'RE GOING TO DO THAT. WE'RE GOING TO BE REWRITING SOME NEW STANDARDS AND SOME NEW DIRECTIONS FOR RESEARCH.

DR. KAMP: THANKS. I GUESS I HAVE A COUPLE OF ISSUES THAT, FIRST OF ALL, THE RED, YELLOW, GREEN, AND CALLING GREEN SORT OF OPTIMAL AND IMPLYING THAT RECONSENT IS THE OPTIMAL APPROACH AND A MORE COMPREHENSIVE APPROACH ISN'T OPTIMAL. I THINK THAT PRESUMES THAT WE KNOW WHAT PATIENTS AND DONORS WILL WANT. I THINK THERE ARE COMPELLING REASONS THAT SOME PATIENTS WILL WANT TO BE INVOLVED IN THE PROCESS, RECONSENTED, AND OTHERS REALLY WILL WANT TO CONTRIBUTE TO THE RESEARCH, BUT BE ANONYMOUS IN THE PROCESS.

SO I THINK WE HAVE TO BE A LITTLE CAREFUL

IN WHAT WE DESCRIBE AS OPTIMAL. ISN'T IT MORE FUTURE MOVING FORWARD CONSENT PROCESSES VERSUS EXISTING? ARE WE PRESUMING THAT ALL EXISTING CONSENT PROCESSES ARE POOR OR SUBOPTIMAL? I DON'T KNOW THAT. I THINK WE NEED TO BE DATA DRIVEN, BUT WE DON'T HAVE THAT ANSWER.

MS. LANSING: I KNOW I'M MISSING SOMETHING IN ALL OF THIS BECAUSE USUALLY I'M THE MOST CONSERVATIVE OF EVERYBODY HERE. AND HERE I FEEL LIKE I'M -- IT WASN'T JUST BECAUSE OF WHAT CHRIS SAID. I THINK IT'S JUST FROM THE YEARS OF BEING A PATIENT ADVOCATE MYSELF IN THE CANCER COMMUNITY IN PARTICULAR, BUT JUST WATCHING EVERYTHING. AND I GUESS TO ME I'M SORT OF REPEATING WHAT I SAID OPTIMAL. TO ME INFORMED CONSENT IS ALL ABOUT EMPOWERING THE PATIENT TO MAKE INFORMED CHOICES. AND I DO BELIEVE THAT THE CHOICES HAVE TO BE DISCUSSED. I THINK WE HAD THAT INITIALLY IN OUR INITIAL DISCUSSIONS. SO IT CAN'T JUST BE A LEGAL DOCUMENT. THAT WOULD NOT BE RIGHT. IT CAN BE SIMPLIFIED WITH THE DISCUSSION WHERE YOU CHECK BOXES WHATEVER.

I'M AFRAID I DON'T BELIEVE IN A PSYCHOLOGICAL EVALUATION BECAUSE I THINK THAT WILL REALLY FRIGHTEN PEOPLE OFF. THAT'S LIKE SOMETHING

THAT I THINK YOU WOULD SAY WHAT DOES THAT MEAN? YOU ARE GOING TO TELL -- SO EVEN THOUGH IT'S VERY REGIMENTED, I'M AFRAID THAT VERY WORD WOULD FRIGHTEN PEOPLE.

TO ME, I'M REPEATING WHAT I SAID, TO HAVE THE CHOICE THAT THE DATA REMAIN ANONYMOUS, THAT YOU AND ONLY YOU HAVE THE ABILITY TO GET THE DATA IF YOU WISH, OR THAT THE DATA CAN BECOME PUBLIC, THAT DOESN'T REQUIRE, IN MY OPINION -- IT'S NOT SO HARD TO UNDERSTAND.

SECOND, THAT YOUR TISSUE OR YOUR CELLS CAN BE USED JUST FOR THE SPECIFIC NARROW RESEARCH THAT YOU CARE ABOUT OR CAN BE USED IN ANY WAY THAT SCIENCE DETERMINES FOR ALL DISEASES. WE KNOW IT CAN'T BE USED FOR CLONING BECAUSE THAT'S AGAINST OUR LAW.

AND THEN RECONTACT, TO ME, IS THAT THAT'S YOUR RESPONSIBILITY. AND IF YOU CHOSE THAT IT'S ANONYMIZED, THEY CAN'T FIND IT. SO I JUST -- I KNOW I'M MISSING SOMETHING, AND I KNOW I'M JUST NOT GETTING THIS, BUT IT DOESN'T SEEM LIKE A PANDORA'S BOX. I KNOW I'M MISSING THIS. I'M JUST TELLING YOU THIS. AND FROM A PERSON WHO HAD TROUBLE PRONOUNCING PLURIPOTENT, IT'S NOT SURPRISING THAT I'M NOT UNDERSTANDING SOME OF THIS. I JUST HAVE TO KNOW

WHAT I'M MISSING BECAUSE IT SEEMS TO ME SO CLEAR, AND I DON'T CONSIDER IT OPTIMAL, YELLOW, OR RED. I JUST CONSIDER IT THAT YOU HAVE THESE CHOICES.

DR. LOMAX: CAN I MAKE JUST ONE CLARIFICATION ON THE CATEGORIES? AND PLEASE DON'T VIEW THIS AS SORT OF OPTIMAL WITH A CAPITAL O. IT WASN'T INTENDED TO BE SORT OF THE METAPHYSICAL IDEAL. THE ATTEMPT HERE WAS, AND IT WAS BASED ON THE PREVIOUS PART OF THE PRESENTATION, AFTER REVIEW OF THE MOST CONTEMPORARY GUIDELINES AND RECOMMENDATIONS, IT WAS TRYING TO SORT OF SAY IF OUR GOAL WERE AND WE BUY INTO THOSE, TO GET A HUNDRED PERCENT FIT OR A PERFECT FIT, THEN THAT WAS THE GREEN, AND THE YELLOW REALLY IS VERY GOOD.

AGAIN, THE BENCHMARK HERE WAS THE POLICY GUIDANCE AND REGULATORY GUIDANCE THAT IS SORT OF UP TO DATE. SO I JUST WANT TO MAKE SURE I'M NOT TRYING TO SORT OF IMPOSE SOMETHING THAT IT WASN'T MEANT TO BE. THIS IS MORE THE POLICY EVALUATION. AND I KNOW THE COLORING THING IS A BIT CUTE AND PEOPLE CAN REACT TO IT DIFFERENTLY, BUT THAT WAS THE ATTEMPT THERE. THAT WAS THE BENCHMARK THROUGH WHICH THIS EVALUATION WAS DEVELOPED.

CHAIRMAN LO: I WOULD SUGGEST -- I THINK COLORS ARE OKAY. MY FAMILY ACCUSES ME OF HAVING NO

COLOR SENSE, SO IT DOESN'T MATTER TO ME. PEOPLE ARE SENSITIVE TO COLORS. I SUGGEST WE TALK ABOUT THE FIRST ONE AS CONSENT GOING FORWARD, PROSPECTIVE.

DR. FEIGAL: DON'T THINK OF IT AS OPTIMAL. JUST THINK OF IT'S AN OPPORTUNITY, IT'S PROSPECTIVE. THE OTHER IS ALREADY EXISTING.

CHAIRMAN LO: SO LET ME TRY AND SAY SOMETHING ABOUT WHAT I HEARD THE GROUP SAY. A NUMBER OF YOU REALLY SAID WE REALLY HAVE TO UNDERSTAND WHAT DONORS CARE ABOUT, AND THAT'S AN EMPIRICAL QUESTION. AND WE OUGHT TO TAKE ADVANTAGE OF THE CHANCE TO GATHER EMPIRICAL INFORMATION. AND I WOULD JUST ADD TO THAT THAT THERE ACTUALLY HAVE BEEN A LOT OF OTHER STUDIES, EMPIRICAL STUDIES, DONE IN OTHER SETTINGS, PARTICULARLY IN GENETICS RESEARCH SETTINGS. SOME OF THE THEMES THAT COME OUT ARE, FIRST, DONORS REALLY WANT TO BE ASKED. EVEN IF THEY WOULD AGREE TO YOU CAN DO WHATEVER YOU WANT TO THE MATERIAL, THEY WANT TO BE ASKED FOR THE OPTION. THAT'S CONSISTENT.

PEOPLE HAVE BEEN ASKED ABOUT THE VALUE OF CHECK BOXES IN A SO-CALLED TIERED CONSENT FORM. SO WILL YOU DONATE FOR THIS PARTICULAR STUDY ON PARKINSON'S DISEASE? WILL YOU ALSO ALLOW IT TO BE STUDIED FOR OTHER SERIOUS NEUROLOGICAL DISEASES,

OTHER DISEASES?

THE BIG DIFFERENCE, IT SEEMS TO ME, BETWEEN IPS CELLS AND OTHER TYPES OF REPOSITORIES IS THAT IPS CELLS REPLENISH THEMSELVES. SO THAT IF I GIVE SOMEONE AN ALIQUOT OF CELLS TO STUDY SOMETHING TOTALLY DIFFERENT THAN PARKINSON'S DISEASE, IT DOESN'T NECESSARILY COMPROMISE THE ABILITY OF PARKINSON'S RESEARCHERS TO DO THE RESEARCH. WHEREAS, IF I HAVE JUST A LIMITED AMOUNT OF TISSUE OR BLOOD SAMPLE THAT'S FINE, EVERY TIME I GIVE SOME OF IT AWAY, IT MEANS IN THE FUTURE I MAY NOT BE ABLE TO USE IT.

AGAIN, WHERE PEOPLE HAVE BEEN ASKED, AND AGAIN IT'S THE REAL QUESTION, IF YOU ASK, THEY MIGHT TELL YOU SOMETHING DIFFERENT THAN IF YOU DO IT WITHOUT ASKING. IF YOU ASK, THE VAST MAJORITY OF PEOPLE SAY, OH, YEAH. IF IT CAN HELP SOMEONE WITH ANOTHER DISEASE, ABSOLUTELY GO AHEAD. NOW, THEY MAY -- I THINK IT'S QUITE LIKELY, BUT IT'S AN EMPIRICAL QUESTION, GIVEN THAT THE RESEARCH ABILITY TO STUDY THE DISEASE I WAS MOST CONCERNED WITH IS NOT COMPROMISED BY GIVING IT TO OTHER PEOPLE TO STUDY OTHER DISEASES.

MS. LANSING: THAT'S A WAY OF ASKING THE QUESTION THOUGH. I'M SAYING THAT THE RESEARCH,

THERE WILL BE ENOUGH CELLS TO STUDY, AND WHATEVER WAY TO EXPLAIN IT TO A LAY PERSON, AND IF THERE ARE EXTRA CELLS, RATHER THAN SAYING THAT THEY MULTIPLY...

CHAIRMAN LO: AND THE OTHER THING I WOULD SUGGEST IS THAT WE ALWAYS USE THE -- A LOT OF YOU HAVE SAID THAT PEOPLE VARY. AND WE HEARD CHRIS, WHO'S A VERY ARTICULATE, THOUGHTFUL PERSON WHO KNOWS A LOT ABOUT THIS, THERE ARE OTHER DONORS WHO JUST SAY, HERE, TAKE MY SPECIMEN. I DON'T REALLY WANT TO BE INVOLVED ALL THE TIME. BUT I THINK IT'S OFFERING OPTIONS. SO THAT IF YOU WANT THE OPTION OF BEING IDENTIFIED, OF BEING RECONTACTED, IF YOU DECIDE THAT'S SOMETHING YOU'RE AGREEING TO DO, WHICH YOU MAY OR MAY NOT AS A RESEARCH INSTITUTION, OFFERING THAT AS AN OPTION AND LEAVING IT UP TO PEOPLE TO SAY, YES, I DO OR, NO, THANK YOU. THE GENERAL TENDENCY IS AS LONG AS YOU DON'T OVERWHELM THEM WITH TOO MANY OPTIONS AND YOU PRESENT OPTIONS IN A WAY THAT PEOPLE UNDERSTAND, PEOPLE APPRECIATE THE OPTION.

WE'VE DONE THIS AT UCSF, SAID TO PEOPLE WOULD YOU LIKE THE OPTION OF BEING RECONTACTED IN THE FUTURE ABOUT RESEARCH THAT WE CAN'T PREDICT NOW, THAT WE CAN ANTICIPATE SOME RESEARCH SUBJECTS MIGHT

HAVE CONCERNS ABOUT BEING INVOLVED WITH, PEOPLE ARE SPLIT. SOME PEOPLE ARE WILLING. YOU TOLD ME THERE'S SOME OTHER OVERSIGHT PROCESS WHICH IS NOT ANYTHING GOES. I'M GOING TO HAVE TO TRUST YOU FOLKS TO WORK IT OUT, THAT WHAT'S DONE IS REASONABLE AND THAT'S FINE. OTHER PEOPLE SAY NO. IT'S, AGAIN, ALLOWING FOR THE COMPLEXITY.

LET ME JUST GO BACK TO THE EMPIRICAL THING. IS ONE OF THE THINGS, THE SENSE OF WHAT I WAS HEARING, THAT WE WOULD LIKE THIS TO BE DATA DRIVEN, EMPIRICALLY BASED, AND TO BOTH LOOK AT -- I THINK WE COULD ASK GEOFF TO REVIEW THE LITERATURE ON THIS, WHICH IS QUITE EXTENSIVE. THERE'S SOME NICE REVIEWS. ALSO TO TAKE ADVANTAGE OF CIRM-FUNDED RESEARCH TO DO -- MAYBE FUND SOME ADD-ON STUDIES ON WHICH WE CAN BASE THIS.

AND I THINK THE OTHER THING IS WE NEED TO TAKE PEOPLE AND SORT OF EXPLAIN IN DETAIL WHAT ALL THIS MIGHT INVOLVE AND THEN ASK THEM, NOW THAT WE'VE EXPLAINED IT TO YOU, WOULD YOU WANT TO BE ASKED THIS, THIS, AND THAT.

DR. PATRICK TAYLOR: TO ME THERE'S A PRINCIPLE THAT WE COULD STATE THAT WOULD HELP GUIDE US TOWARDS SIMPLICITY AND UNIFORMITY. AND THAT'S TO GIVE DONORS, ASSURE DONORS HAVE EMPOWERING CHOICES

ABOUT THE THINGS THEY CARE ABOUT. AND SO THE CATEGORIES OF CHOICE, REALLY EMPOWERING ONES VERSUS THE OTHER ONES, ARE REALLY IMPORTANT.

SO ON THE POINT OF STUDIES, IT SEEMS TO ME THAT HOW STUDIES ARE FRAMED, IT WOULD BE GREAT TO DO STUDIES, BUT WE HAVE TO BE VERY CAREFUL IN FRAMING THEM. FOR EXAMPLE, GOING BACK TO THE TERMS USED THIS MORNING, IF WE ASK PEOPLE TO DO STUDIES ABOUT WHAT DONORS THINK ABOUT ACTIONABILITY, WHICH REALLY ISN'T A DONOR TERM, AND OBVIOUSLY, AS WE'VE SEEN, CAN BE SOME ASTOUNDING THINGS, AND WE'LL END UP WITH WEIRD RESULTS WHICH SIMPLY REFLECT THE PAST VIEWS OF HOW CLINICIANS AND LAWYERS AND SCIENTISTS HAVE CATEGORIZED THEM. SO THERE'S ALMOST SOME PREVIOUS WORK IN UNDERSTANDING WHAT ARE THE CATEGORIES OF CONSENT THE DONORS THEMSELVES CREATE. WHAT WOULD THEY OBJECT TO? WHAT WOULD THEY WISH TO HAVE AS EMPOWERING? AND MAKING THAT THE SUBJECT FOR EMPIRICAL RESEARCH.

DR. ROBERTS: AFTER YOUR POINT, BERNIE, ABOUT THE LINES BEING REGENERATING SO THAT IT'S NOT AS IF YOU DONATE FOR ONE RESEARCH ON ONE DISEASE, IT'S COMPROMISED IF THERE'S RESEARCH DONE ON ANOTHER DISEASE. BUT I GUESS THAT I WANT TO REFRAME MY CONCERN, WHICH IS THAT IN THE CONSENT FORM DONORS

ARE TOLD REALISTICALLY WHAT IS LIKELY TO COME OUT OF THIS RESEARCH. IN OTHER WORDS, I GUESS I STILL HAVE THE SENSE THAT SINCE THE DONORS ARE GOING TO BE SELECTED BY DISEASE, SO WHAT I'VE READ IS IT'S FIVE DONORS PER DISEASE, FOR EXAMPLE, THAT THE RECRUITMENT IS BASED ON A DISEASE. AND SO THEY MAY BE DONATING BECAUSE THEY BELIEVE THAT THE RESEARCH IS GOING TO LEAD TO A CURE FOR THIS DISEASE.

AND THAT JUST -- I THINK IT JUST HAS TO BE CLEAR TO THE DONORS WHETHER THIS IS RESEARCH THAT'S GOING TO BE DONE, BASIC SCIENCE RESEARCH THAT IS GOING TO GENERALLY LOOK INTO AN UNDERSTANDING OF THE DISEASE AS OPPOSED TO RESEARCH THAT IS GOING -- THAT THEIR LINES ARE GOING TO BE USED TO CURE THEM. THAT SEEMS LIKE A DIFFERENCE THAT WOULD MAKE A DIFFERENCE TO THE DONOR. SO JUST THAT EXPLAINING --

CHAIRMAN LO: AND AGAIN --

DR. ROBERTS: -- CLEARLY WHAT IS GOING TO BE DONE WITH THEIR TISSUE.

CHAIRMAN LO: AGAIN, I THINK WE HAVE TO GO BACK TO THE SCIENTIFIC PROPOSAL. MY UNDERSTANDING WAS THAT IT'S PRIMARILY TO UNDERSTAND THE PATHOPHYSIOLOGY OF DISEASE, TO IDENTIFY NEW THERAPEUTIC TARGETS, AND TO SCREEN POTENTIAL THERAPIES, USUALLY SMALL MOLECULES, AND TO EVALUATE

WHETHER CANDIDATE THERAPIES ARE EFFECTIVE OR NOT IN THE LABORATORY MODEL. THAT'S, I THINK, THE PRIMARY INTENT.

WHAT I HEARD IS THAT, YOU KNOW, TRANSPLANTATION THERAPIES IS WHAT WE'RE HEADED FOR IN A THE LONG RUN; BUT THAT THESE LINES, ALTHOUGH WE'RE NOT CLOSING THAT OFF, WE'RE PRIMARILY TRYING TO DERIVE THEM AND BANK THEM TO FACILITATE THE PATHOPHYSIOLOGY, DRUG DISCOVERY, AND DRUG TESTING. IS THAT ACCURATE? I THINK YOUR POINT'S TOTALLY RIGHT. YOU CAN'T SORT OF GIVE A MIXED MESSAGE THAT --

DR. ROBERTS: RIGHT. I THINK BOTH OF US DIDN'T QUITE UNDERSTAND THAT, SO I'M THINKING THAT A DONOR MAY NOT UNDERSTAND UNLESS IT'S EXPLAINED CLEARLY.

DR. OLSON: I DO WANT TO MAKE ONE CLARIFICATION. USING LINES FOR DRUG DISCOVERY HAS THE POTENTIAL TO IDENTIFY COMPOUNDS WHICH POTENTIALLY CAN BECOME THERAPEUTICS. SO THERE IS THAT POSSIBILITY.

CHAIRMAN LO: IT'S NOT THAT THE LINES -- THAT THE CELLS I DONATE ARE --

DR. OLSON: THE LINES THEMSELVES WOULD NOT GO INTO PEOPLE.

DR. ROBERT TAYLOR: THEY COULD POTENTIALLY. WHY NOT ADD THAT POTENTIAL?

MR. SHEEHY: JUST LIKE WE'VE SEEN WITH SOME CANCER THERAPIES, IT MAY WORK FOR THAT DONOR, DONOR X, BUT DONOR Y THAT SCREEN MAY NOT WORK. SO WE KNOW THAT WITH CANCER THERAPIES, THAT CERTAIN CANCER THERAPIES WORK ON PEOPLE THAT HAVE CERTAIN GENETIC BACKGROUNDS. SO, YOU KNOW, HAVING THAT INFORMATION IN A DRUG SCREENING CONTEXT COULD BE VERY IMPORTANT TO KNOW THAT THIS PARTICULAR COMPOUND HAD A HIT FOR YOU. RIGHT. IT MAY NOT HAVE A HIT FOR EVERY SINGLE PATIENT. WHEN YOU TALK DRUG DEVELOPMENT, WE'RE GOING TO SCREEN ALL THESE COMPOUNDS AND COME UP WITH A SINGLE MOLECULE THAT WORKS FOR EVERYBODY.

WHERE WE'RE GOING IN CANCER THERAPEUTICS IS THAT WE'RE ACTUALLY TARGETING WITH MORE PERSONALIZED. THAT INFORMATION FOR A DONOR COULD BE VERY IMPORTANT, AND COMING BACK TO THEM WITH THAT INFORMATION, I WOULD WANT TO KNOW IF --

CHAIRMAN LO: DOROTHY RAISED A REALLY IMPORTANT QUESTION. WHAT IS LIKELY TO HAPPEN? SO I THINK WE REALLY -- IT SOUNDS LIKE WE'RE NOT CLEAR ON THE DIFFERENCE BETWEEN YOUR CELLS WILL LEAD TO RESEARCH THAT MAY HELP IDENTIFY PROMISING TREATMENTS

FOR YOUR CONDITION, BUT THE CELLS THEMSELVES, RIGHT NOW WE DON'T THINK IT'S A PRIMARY GOAL OF THE BANKING TO USE THOSE PARTICULAR CELLS AS THERAPY. THEY MAY HELP IDENTIFY NEW CANDIDATE DRUGS, AS JEFF SAID, MAY HELP IDENTIFY THE KINDS OF PEOPLE A GIVEN THERAPY MAY WORK FOR AND NOT WORK FOR. BUT IN TERMS OF THIS IDEA THAT MY CELLS WILL BECOME THE TREATMENT FOR ME OR MY FAMILY, THAT'S REALLY WAY -- WE'D ALL LIKE TO GET THERE, BUT I THINK IT WOULD PROBABLY NOT BE ACCURATE TO HOLD THAT OUT TO PEOPLE AS A PRIMARY REASON FOR DONATING.

DR. KAMP: COULD I SAY IT'S PROBABLY -- I THINK IT'S ABSOLUTELY CORRECT. IT SHOULDN'T BE A PRIMARY REASON FOR DONATING GIVEN THE CURRENT STATE OF SCIENCE, BUT I ALSO THINK IT WOULD BE A FUNDAMENTAL MISTAKE TO EXCLUDE THAT POSSIBILITY BECAUSE THERE MAY BE CELL LINES THAT ARE DERIVED WITH CURRENT TECHNOLOGIES THAT MAY SURPRISE US AND MAY BE USED FOR THERAPY. AND PLUS YOU'RE GOING TO BE ESTABLISHING A HIGH QUALITY, CONTROLLED BANK THAT WILL HAVE THE RESOURCES TO BE SURE TO TEST THE LINES. SO TO AUTOMATICALLY EXCLUDE THAT POSSIBILITY, I THINK, IS A MISTAKE.

CHAIRMAN LO: WE FACE THIS IN OTHER TYPES OF RESEARCH. AND HOW YOU FRAME IT IN THE DISCUSSION

WITH THE DONOR IS CRUCIAL. IT SEEMS TO ME THERE'S A PRIMARY GOAL, INTENTION OF WHAT YOU'RE PLANNING TO DO WITH THE BANK. AND I THINK TIM SAID IT VERY WELL. YOU DON'T WANT TO EXCLUDE THE POSSIBILITY. SO I THINK YOU HAVE TO SAY WE HOPE THAT IN THE FUTURE IT WILL BE POSSIBLE TO DEVELOP CELLULAR-BASED THERAPIES. THERE IS A -- WE DON'T WANT TO EXCLUDE THE POSSIBILITY THAT YOUR VERY CELLS MAY BE USED TO HELP TREAT A PERSON, NOT JUST TO SCREEN DISEASE. BUT ON THE OTHER HAND, THAT'S NOT THE PRIMARY REASON WE'RE DOING THAT.

I THINK IT'S HOW YOU FRAME IT, AND I THINK THAT'S A LOT OF WHAT WE'RE TALKING ABOUT. WHEN I SAT ON THE RECOMBINANT DNA ADVISORY COMMITTEE, WE SAW CONSENT FORM AFTER CONSENT FORM THAT REALLY TALKED ABOUT PHASE I DOSE FINDING STUDIES AS CURES, AS TREATMENT, WHEN REALLY THE GOAL WAS TO ASSESS DOSAGE AND TOLERABILITY.

NOW, YOU CAN EXCLUDE THE POSSIBILITY THAT THERE THEY MAY BE A THERAPY, BUT I THINK YOU DON'T WANT TO OVERSELL THAT. SO I THINK CRAFTING THAT, AND I THINK THIS -- TO GO BACK TO WHAT A NUMBER OF YOU SAID BEFORE, I THINK IT WOULD REALLY BE WONDERFUL TO SORT OF HAVE A LOT OF PATIENT AND ADVOCACY GROUP DISCUSSIONS. THIS IS WHAT WE'RE

TRYING TO COMMUNICATE. IF WE SAY IT THIS WAY, DOES THAT MESSAGE GET ACROSS? WELL, IT MAY GET ACROSS TO ME, BUT IT WOULDN'T GET ACROSS TO PEOPLE LIKE THIS OTHER PERSON IN MY GROUP. BECAUSE I THINK FOR US TO SIT AROUND AND TRY -- I THINK WE'RE CLEAR ON WHAT WE'RE TRYING TO DO. I THINK ONE OF THE THINGS I'M HEARING IS TO MAKE IT ACTUALLY WORK IN PRACTICE, WE HAVE TO REALLY DO SOME EMPIRICAL WORK.

DR. TROUNSON: SO, BERNIE, I THINK FOR THE POINT OF VIEW OF CELL THERAPIES, IT'S MOST UNLIKELY THESE CELLS WOULD BE APPROPRIATE UNDER FDA. SO WE WOULD PROBABLY WANT TO DERIVE CELLS IN A VERY SPECIAL WAY. AND I THINK GOING FORWARD THERE WILL BE DEVELOPMENTS THAT WILL GO BEYOND THIS RESEARCH IN THE WAY YOU NEED TO DERIVE CELLS. THEY PROBABLY HAVE TO COME FROM A SPECIAL SOURCE, AND THEY HAVE TO DEMONSTRATE THAT THEY'RE NOT -- THEY DON'T HAVE MAJOR MUTATIONS THAT YOU MIGHT GET IN SKIN CELLS ON THE SURFACE AND SO ON. SO I THINK IT'S MOST UNLIKELY THESE CELLS WOULD BE APPROPRIATE FOR CELL THERAPIES. AND THEY WOULDN'T BE DERIVED IN A WAY WHICH WOULD BE CONSISTENT WITH THE WAY THE FDA WOULD REALLY WANT THEM TO BE USED.

CHAIRMAN LO: BECAUSE THEY'RE NOT GMP QUALITY LINES.

DR. TROUNSON: RIGHT.

DR. LOCKHART: I WOULD JUST REALLY ECHO A LOT OF WHAT YOU JUST SAID, BERNIE. I THINK YOU'RE GOING TO HAVE TO WALK A VERY FINE LINE AND TRY TO AVOID THERAPEUTIC MISCONCEPTION, THAT PEOPLE WILL BE PARTICIPATING BECAUSE THEY THINK THAT THIS MORE REMOTE CHANCE -- THAT BASICALLY THEIR DONATION WILL HELP THEM IN THE FUTURE. AND SO I AGREE THIS IS GOING TO NEED TO BE A VERY CAREFULLY THOUGHT OUT DESCRIPTION OF HOW THEIR CELLS MAY BE USED AND WHAT BENEFIT THAT WILL BE TO THEM OR OTHERS WITH THEIR DISEASE.

I WOULD ALSO ECHO THAT I THINK THIS MIGHT BE AN INSTANCE WHERE FIELD TESTING THESE CONSENT DOCUMENTS IN SOME WAY WILL HELP YOU GET A FEEL FOR ARE THOSE FINE POINTS UNDERSTOOD, OR DO PATIENTS OR ADVOCATES WHO READ THE FORM THINK, OH, NO. THIS IS ABSOLUTELY GOING TO HELP ME, AND THIS IS GOING TO BE MY CURE. AND IF I JUST WAIT A YEAR, THE CELLS WILL BE READY. I THINK THEY CAN PROVIDE A LOT OF REALLY IMPORTANT INPUT.

TO ONE OF DOROTHY'S EARLIER POINTS ABOUT RECRUITMENT BY DISEASE, I THINK SOMETHING THAT NEEDS TO BE THOUGHT OUT IN PARTICULAR HERE IS YOU DON'T RUN THE RISK OF DEPLETION LIKE YOU DO WITH

BIOSPECIMENS, THE CELLS WILL SELF-REPLICATE, YOU ALSO HAVE THE ABILITY TO STUDY A WIDE RANGE OF THINGS, AND THAT WILL BE IMPORTANT FOR PATIENTS TO UNDERSTAND, THAT THERE MIGHT BE OTHER KINDS OF OBJECTIONABLE TO INDIVIDUAL TYPES OF RESEARCH THAT A PATIENT MAY NOT ANTICIPATE.

SO MAYBE SOMEONE WILL WANT TO TAKE THE CELLS, DERIVE THEM INTO NEURONS, AND STUDY MENTAL HEALTH DISORDERS. THE PATIENT WOULD NEVER THINK OF THAT NECESSARILY IF THEY'RE A HEART DISEASE PATIENT OR SOMETHING. THEY DON'T HAVE ANY KIND OF BRAIN CONDITION. THEY MAYBE WOULDN'T EVEN THINK ABOUT THAT POTENTIAL USE. SO JUST LETTING PEOPLE KNOW THAT THERE'S A WIDE, WIDE RANGE OF POTENTIAL USES. THEIR OBJECTION MAY NOT BE THAT IT WOULD HARM OR TAKE AWAY FROM OR DETRACT RESEARCH IN THEIR OWN DISEASE TYPE, BUT MORE THAT THERE'S A VERY BROAD POSSIBILITY OF USES THAT COULD HAPPEN.

DR. KIESSLING: I'D LIKE TO MAKE A SUGGESTION THAT WE GO ABOUT THIS A SLIGHTLY DIFFERENT WAY. BECAUSE I THINK WHAT WE NEED TO DO FOR THESE LONG-TERM LINES AND FOR THE BANK THAT YOU'RE TRYING TO DEVELOP IS UNDERSTAND THAT CONSENTING SOMEBODY TO DONATE TISSUE IS A PROCESS. IT'S NOT A DOCUMENT. IT'S NOT LANGUAGE IN A PIECE

OF PAPER. IT'S A PROCESS. AND I THINK IF WE RECOGNIZE THAT THE PROCESS FOR RECRUITING NORMAL HUMAN SUBJECTS INTO A WELL-DEFINED RESEARCH PROTOCOL IS VERY DIFFERENT OR MAY BE VERY DIFFERENT FROM INTERACTING WITH A GROUP PEOPLE WHO ARE SICK AND WHO HAVE A DISEASE CONDITION THAT THEY'RE TRYING TO DEAL WITH.

I DON'T THINK YOU WANT THE PROCESS TO BE DIFFERENT, BUT I THINK YOU NEED TO REALIZE THAT PEOPLE'S RESPONSES TO WHAT YOU ARE DOING IS DIFFERENT IF YOU ARE A NORMAL HEALTHY SUBJECT VERSUS HAVING SOME TERRIBLE DISEASE. I THINK WE NEED TO COME UP WITH STEPS IN A PROCESS, WHAT'S GOING TO BE STEP ONE, UNDERSTANDING THAT SOME PEOPLE ARE GOING TO BE NORMAL AND SOME PEOPLE ARE GOING TO BE DISEASED, AND THEN WHAT IS STEP TWO.

AND I KIND OF WANT TO CLARIFY THE THOUGHT I HAD ABOUT THE PSYCHOLOGICAL ASSESSMENT BECAUSE THE ONLY WAY TO UNDERSTAND THAT SOMEBODY REALLY UNDERSTANDS THE PROCESS IS TO HAVE SOMEBODY WHO'S NOT AN INTIMATE PART OF THE RESEARCH TEAM TALK TO THIS PERSON FOR A FEW MINUTES. IS THIS PERSON DONATING TISSUES BECAUSE THEY THINK IT'S THE ONLY WAY THEY'RE GOING TO GET CARE. THERE'S SOME VERY SCARY THINGS ABOUT SAYING NO TO A RESEARCHER WHO

WANTS TO STUDY YOUR DISEASE. SO THE ONLY WAY TO REALLY ASSESS THAT IS TO HAVE SOMEONE WHO IS PSYCHOLOGICALLY TRAINED WHO'S NOT PART OF THE TEAM TALK TO THIS PERSON, MAKE SURE THAT THEIR MOTIVES, THAT THEY UNDERSTAND THEIR MOTIVES, AND THAT THEY UNDERSTAND WHAT THEY'RE DOING.

BUT I THINK WHAT WE WANT TO DO HERE IS WHAT IS STEP ONE OF THE PROCESS OF ORGANIZING TISSUES FOR THIS BANK?

CHAIRMAN LO: I HEARD THAT ONE STEP PEOPLE SAID IS TO GATHER EMPIRICAL INFORMATION ON WHAT'S IMPORTANT TO PEOPLE. AND THAT INCLUDES, TO ME, I WOULD SUGGEST, BOTH WHAT'S ALREADY BEEN PUBLISHED BECAUSE PEOPLE HAVE DONE A LOT OF THIS, AND OPPORTUNITIES TO ACTUALLY ASK MORE DIRECTED QUESTIONS WITH REGARD TO IPS RESEARCH.

WE HAVE A LIST OF -- THERE'S ALWAYS THIS INTERACTION. YOU SORT OF DON'T GO WITH A TOTALLY BLANK SLATE. YOU WANT TO HEAR WHAT PEOPLE ARE CONCERNED ABOUT AFTER THEY UNDERSTOOD WHAT THE ENDEAVOR IS ALL ABOUT. YOU ALSO HAVE IDEAS, ISSUES THAT HAVE POPPED UP WITH OTHER BIOBANKS WITH OTHER RESEARCH AND IN THE LITERATURE. AND SOME OF THOSE INCLUDE RECONTACT, STUDY OTHER DISEASES NOT JUST YOUR OWN, WHOLE GENOME SEQUENCING, AND WE'LL GET TO

SOME OTHERS LATER IN THE DISCUSSION.

SO I THINK AM I HEARING THAT THE SUGGESTION SO FAR IS TO TRY AND IDENTIFY ON AN EMPIRICAL BASIS HOW IMPORTANT THESE ISSUES ARE LIKELY TO BE IN THIS IPSC CONTEXT. AND ALSO WHAT IS KNOWN ABOUT WAYS OF PRESENTING INFORMATION AND OPTIONS THAT WORKS AND DOESN'T?

DR. FEIGAL: I JUST WANT THE GROUP TO THINK OF SOME OF THE BIG ISSUES THAT WE'RE GRAPPLING WITH. WE ARE GOING TO HAVE THE OPPORTUNITY IN THE VERY NEAR TERM IF WE -- FOR EXAMPLE, THE CIRM IS PUTTING TOGETHER THE CONCEPT FOR THIS LARGE BANK IDEA. BUT IN JUNE WE'RE GOING TO HAVE THE WINDOW OF OPPORTUNITY IN WORKING WITH NINDS IF THE ICOC APPROVES US MOVING FORWARD. SO COMING VERY QUICKLY WE'RE GOING TO HAVE AN OPPORTUNITY TO WORK ON THIS IPS CELL REPOSITORY IDEA. AND SO PART OF IT IS TO GET OUR THOUGHTS CRYSTALLIZED, MAY NOT BE PERFECT, BUT THINK ABOUT WHAT ARE THE BIG ISSUES THAT WE WANT TO ASK BECAUSE YOU'RE TALKING ABOUT, JEFF, GOING BACK AND GETTING QUANTITATIVE AND QUANTITATIVE INFORMATION FROM PEOPLE WHO HAVE ALREADY DONATED.

I'M SORT OF QUESTIONING DO WE NEED CONSENT TO DO THAT. BUT THE BIGGER ISSUE IS WHAT QUESTIONS DO WE WANT TO ASK THEM? THEY'VE ALL RECEIVED

PROBABLY A VARIETY OF DIFFERENT TYPES OF CONSENT FORMS. SO I THINK THE METHODOLOGY IN TERMS OF WHAT IS IT WE WANT TO ASK THEM IS GOING TO BE IMPORTANT, AND IT PROBABLY DEPENDS ON WHAT PROCESS THEY WENT THROUGH IN TERMS OF HOW THEY'RE GOING TO RESPOND TO OUR QUESTIONS.

I JUST THINK WE NEED TO -- WE'RE GOING TO HAVE SOME NEAR TERM OPPORTUNITIES. SO ON A PRAGMATIC BASIS, NICOLE GAVE A VERY, I THINK, ARTICULATE DESCRIPTION OF EXPERIENCE WITH BIOSPECIMENS IN A RANGE OF THINGS, NOT SPECIFICALLY IPS. HARDER IS THIS THING, ARE THERE THINGS WE HAVE LEARNED ABOUT HOW THINGS HAVE BEEN DONE BEFORE, AND IS THERE SOMETHING VERY UNIQUE ABOUT THE IPS REPOSITORY THAT WILL REQUIRE SOME TAILORED TYPE OF CONSENT? BECAUSE I THINK AT THE END OF THE DAY, WE ALL WANT INFORMED CONSENT TO BE DIFFERENT. WE ALL SEE THAT THERE'S PROBLEMS WITH THE WAY IT'S DONE RIGHT NOW.

BUT I'M TRYING TO THINK PRAGMATICALLY IN TERMS OF IN A COUPLE OF MONTHS, WE'RE GOING TO HAVE AN OPPORTUNITY TO MOVE FORWARD. WHAT DOES THIS GROUP THINK IS THE RIGHT WAY TO CRYSTALLIZE THEIR THOUGHTS AROUND THE ISSUE?

CHAIRMAN LO: AGAIN, I THINK SOME OF IT IS

SCOPE. I THINK THAT THIS PANEL PROBABLY IS BEST SUITED TO THINK ABOUT IPSC REPOSITORIES RATHER THAN REPOSITORIES IN GENERAL. AS I'VE HEARD THE DISCUSSION TODAY, A LOT OF WHAT WE'RE SAYING IS NEGATIVE, THAT WE THINK A LOT OF CONSENT NOW IS JUST BEING OFFERED A CONSENT FORM, NOT REALLY UNDERSTANDING, NOT HAVING A CHANCE TO HAVE IT EXPLAINED TO YOU, AND THAT WE THINK WHAT IS KNOWN ABOUT OR WHAT IS EASILY KNOWABLE. WELL, WHAT'S IMPORTANT TO PEOPLE SHOULD DRIVE REDESIGN OF THE CONSENT PROCESS.

IT STRIKES ME IF WE'VE HAD PROBLEMS ON THIS BOARD UNDERSTANDING SOME OF THE ISSUES, WE OUGHT TO AT LEAST SUGGEST THAT MAYBE THIS IS SOMETHING THAT DESERVES SPECIAL ATTENTION. SO THE PURPOSE OF THE IPSC DERIVATION AND THE BANKING, THE ISSUE OF DONORS' UNDERSTANDING OF BOTH THE BENEFIT OF ALLOWING YOUR RESEARCH TO BE -- YOUR CELLS TO BE USED FOR OTHER TYPES OF RESEARCH RATHER THAN JUST RESTRICTING IT. WE HAVEN'T YET TALKED A WHOLE LOT ABOUT WHOLE GENOME SEQUENCING, BUT I KNOW NIH AND OTHERS ARE STRUGGLING WITH WHAT IS APPROPRIATE CONSENT FOR WHOLE GENOME SEQUENCING WHERE YOU GET EVERY BASE PAIR IN YOUR BODY VERSUS GENOMEWIDE ASSOCIATION STUDIES WHERE YOU GET 500,000 SNPS

VERSUS TARGETED GENETIC SEQUENCING OF AN AREA OF INTEREST OR LOOKING FOR A SPECIFIC GENE.

BECAUSE I THINK THE CONCERN IS THAT THE WHOLE GENOME SEQUENCING RENDERS THAT SAMPLE IDENTIFIABLE, AT LEAST IN THEORY, IN A WAY THAT THOSE OTHER TYPES OF ANALYSIS MAY NOT. SO THE WHOLE REGULATORY EDIFICE OF DEIDENTIFIED SAMPLES BEING SINGLED OUT UNDER THE COMMON RULE MAY COLLAPSE IF WHOLE GENOME SEQUENCING RENDERS AN ANONYMIZED SAMPLE IDENTIFIABLE.

AND THEN I THINK THIS RECONTACT ISSUE, AND I THINK THE OTHER THING IS ALLOWING FOR, WHAT I'VE HEARD, ALLOWING FOR THE VARIATION IN PEOPLE'S BOTH DESIRE TO HAVE INFORMATION AND THE DEGREE OF INTERACTION THEY WANT.

DR. TROUNSON: WE'RE ENTERING A TOTALLY NEW AGE OF COMMUNICATION. AND I WONDER IF WE OUGHT TO THINK ABOUT THAT A LITTLE MORE. I LIKE THE IDEA THAT PATRICK BROUGHT UP, THAT YOU HAVE CHOICES. WE'RE IN A TIME WHERE THIS COULD BE IN REAL-TIME. IF THERE WAS SOME NEW DEVELOPMENT WHERE YOU THOUGHT MAYBE YOUR CELLS COULD BE USEFUL, WHY WOULDN'T YOU WANT TO NECESSARILY BE ABLE TO CHANGE IT? THESE DAYS THESE COMMUNICATION SYSTEMS ALLOW YOU TO DO THAT, AND MAYBE YOU OUGHT TO BE CONTACTED ON A

REGULAR BASIS TO GET THE FEEL FOR WHAT'S HAPPENING WITH YOUR MATERIAL.

IT'S NOT THAT DIFFICULT. THESE COMMUNICATIONS CAN HAPPEN RELATIVELY EASILY, AND MAYBE THEY SHOULD BE PART OF THE STRUCTURE OF THE BANK, THAT IT DOES DO THE VERY BEST IT CAN TO KEEP IN TOUCH WITH PEOPLE AND ALLOW PEOPLE TO SORT OF PUT COMMENTS IN A WAY INTO THEIR FILE THAT COULD BE ACTUALLY CHANGED IN TIME. BECAUSE WE'RE IN A TIME THAT CHANGE IS HAPPENING SO RAPIDLY, AND IT'S TOTALLY UNPREDICTABLE WHERE THINGS MIGHT GO, SO YOU MAY CHANGE YOUR MIND AND YOU MAY FEEL THAT YOU WANT TO HAVE MUCH MORE INFORMATION WHERE YOU DIDN'T WANT BEFORE AND SO ON. WHY NOT HAVE THAT IN THIS DAY AND AGE? WHY NOT GIVE PEOPLE THAT OPPORTUNITY IN REAL-TIME TO BE MORE ENGAGED? IF THEY DON'T WANT TO BE, THEN THAT'S FINE. IF THEY DO, THEN I THINK THERE'S SOME MERIT IN THINKING ABOUT IT.

DR. PATRICK TAYLOR: I JUST WANT TO SAY I THINK THAT'S A GREAT COMMENT. IT JUST OCCURRED TO ME WE ALL REALIZE THAT ON A BASIC HUMAN LEVEL, WE HAVE TO WORK WITH RELATIONSHIPS AND MAKE THEM TRUSTING ONES. SOMETIMES WE SORT OF FORGET THAT, AND IT'S EASY TO THINK THAT MAYBE PEOPLE WHO JUST GIVE THEIR SAMPLES DON'T REQUIRE THAT INVESTMENT.

SO I THINK YOU'VE JUST EXPRESSED IN VERY PRACTICAL, SIMPLE, CONCRETE, DOABLE TERMS HOW TO MAINTAIN A RELATIONSHIP WITH DONORS IN A WAY THAT WOULD PROBABLY MAKE CIRM A COMPLETE LEADER.

CHAIRMAN LO: OFFER TO MAINTAIN A RELATIONSHIP WITH THOSE DONORS.

DR. PATRICK TAYLOR: VERY SIMPLE.

DR. LOCKHART: I DON'T KNOW IF YOU'RE GOING TO HAVE AN ANSWER FOR THIS. I DON'T KNOW HOW FAR YOU ARE IN YOUR PLANNING. DOES CIRM PLAN ON HOLDING IDENTIFIERS FOR THESE PATIENTS?

DR. LOMAX: CIRM WOULDN'T NECESSARILY BE THE ENTITY THAT WOULD EVEN BE EQUIPPED. WE DON'T HAVE THE ABILITY TO BE A -- WHAT WOULD BE REQUIRED, WE WOULDN'T DO THAT. IT WOULD BE A DELEGATED AUTHORITY.

CHAIRMAN LO: AS YOU KNOW, THERE ARE A LOT OF MODELS IN BIOBANKS WHERE THE BIOBANK ITSELF IS, WHATEVER YOU WANT TO ALL IT, THE TRUSTED INTERMEDIARY, THE GUARDIAN, THE STEWARD WHERE THEY HAVE ACCESS, THE BIOBANK HAS ACCESS TO THE IDENTIFIERS. SO, FOR EXAMPLE, THEY CAN MATCH NEW CLINICAL DATA AND NEW FINDINGS FROM ONE RESEARCH LAB AND ANNOTATE THE LINE. BUT THEY PRESUMABLY WOULD BE GIVING OUT THOSE LINES IN A DEIDENTIFIED FORMAT IN

THE OLD HIPAA SENSE TO RESEARCHERS.

NOW, CHRIS RAISED THE QUESTION OF HOW ABOUT INDIVIDUAL DONORS WHO WANT TO BE IDENTIFIED TO EVERYBODY? SHOULD WE OFFER THAT OPTION? BUT BY AND LARGE THE IDEA HAS BEEN, PARTLY BECAUSE IT JUST MAKES EASIER TO DO THE RESEARCH, THAT THE EXTENT THAT IRB'S AND HIPAA PRIVACY BOARDS ARE FOLLOWING A DEFINITION OF AN OVERSIGHT FRAMEWORK THAT ALLOWS DEIDENTIFIED RESEARCH TO BE APPROVED MUCH FASTER. THERE ARE ADVANTAGES IN TERMS OF NOT HOLDING BACK RESEARCH TO NOT GIVING RESEARCHERS IDENTIFIABLE INFORMATION BECAUSE THEN EACH IRB HAS TO REVIEW IT AS A FULL PROPOSAL.

DR. LOCKHART: SO MY POINT HERE WAS THAT, TO ALAN'S POINT, IF YOU ARE GOING TO DO THAT LEVEL OF CONTACT AND RETURN OF INFORMATION AND HAVE A MUCH MORE INTERACTIVE PROCESS, THEN THE BANK MAYBE WOULD NEED TO HAVE ACCESS TO IDENTIFIERS, WHICH A LOT OF BANKS DON'T OR THEY DON'T WANT THEM BECAUSE THEY DON'T WANT THAT REGULATORY BURDEN. AND IT'S VERY MUCH SOMETHING YOU ARE GOING TO HAVE TO THINK ABOUT HOW IS IT GOING TO BE RUN. IT HAS TO BE IN THE BUDGET. JUST REALLY LOGISTICAL OPERATIONAL THINGS BECAUSE IT IS A NEW MODEL. I WOULD RECOMMEND YOU LOOK AT OR TALK TO ISAAC KOHANE OUT OF MIT.

CHAIRMAN LO: BETH ISRAEL CHILDREN'S.

DR. PATRICK TAYLOR: I'M A COAUTHOR ON THOSE PAPERS. ACTUALLY YOU DON'T NEED IDENTIFIERS; YOU NEED LINKS. UNDER ONE OF OUR MODELS WE ACTUALLY USED DNA TO TELL US THE LINK.

CHAIRMAN LO: BUT YOU NEED HIGH SECURITY. SO WE ARE -- WE'VE SPENT A VERY LIVELY AND, I THINK, HELPFUL, PRODUCTIVE MORNING. LUNCH IS SCHEDULED LIKE ALMOST RIGHT NOW IN A COUPLE OF MINUTES. BUT WE SHOULD PAUSE FOR A MINUTE AND ASK FOR PUBLIC COMMENT FROM THE PEOPLE WHO HAVE BEEN IN THE AUDIENCE, WHETHER ANY OF YOU WOULD LIKE TO MAKE A PUBLIC COMMENT. STEVE. AND FOR THE PURPOSE, OF THE RECORD, JUST IDENTIFY YOURSELF.

DR. PECKMAN: I'M STEVE PECKMAN FROM UCLA. AND I REALLY APPRECIATE THIS VERY INTELLIGENT AND DYNAMIC DISCUSSION. I'D LIKE TO START OFF WITH A QUESTION TO THE GROUP THOUGH, WHICH IS A QUESTION THAT SHOULD INFORM AND BE IN THE BACKGROUND OF EVERYTHING THAT'S DISCUSSED ABOUT THIS TOPIC, WHICH IS WHAT MAKES AN IPSC BANK DIFFERENT THAN ANY OTHER TISSUE BANK, OR ARE WE ENGAGED IN STEM CELL EXCEPTIONALISM AGAIN? WHICH IS SOMETHING THAT THIS GROUP AND THAT CIRM AS AN ENTITY HAS TRIED TO AVOID.

AND THAT IF THERE IS NO DIFFERENCE, THEN

IS THERE A REASON TO GO BACK AND REHASH THE REQUIREMENTS FOR INFORMED CONSENT AND REGULATORY OVERSIGHT OVER THIS TYPE OF BANK AS OPPOSED TO ANY OTHER BANK? SO I THINK THAT SHOULD BE A FUNDAMENTAL QUESTION THAT CONSTANTLY INFORMS YOUR DISCUSSION AND ANY IDEAS FOR IMPLEMENTING GUIDANCE OR REGULATION.

I THINK IT'S VERY IMPORTANT THAT IF WE WANT TO HAVE EVIDENCE-BASED RESEARCH, THAT IT NEEDS TO BE GUIDED BY EVIDENCE-BASED POLICY. AND SO I WOULD TOTALLY ENDORSE THE IDEA OF A LITERATURE REVIEW OF THE POLICYMAKING THAT HAS GONE ON BEFORE AND THE RESEARCH ON DONORS THAT HAS GONE ON BEFORE WHICH, AS BERNIE SAID, IS QUITE EXTENSIVE IN THE LITERATURE AND LET THAT INFORM YOUR DISCUSSION MOVING FORWARD.

I THINK IT'S ALSO IMPORTANT TO UNDERSTAND AND TO KEEP IN THE FOREFRONT OF YOUR MIND WILL YOU BE CREATING GUIDANCE OR RULES FOR THE CREATION -- FOR THE DONATION OF PRIMARY CELLS THAT WOULD BE USED TO CREATE IPS CELLS THAT OBSTRUCTS THE DONOR AND OBSTRUCTS RESEARCH? THAT IS NOT CONSISTENT WITH OUR CURRENT STANDARDS AND WITH THE STANDARDS THAT HAVE BEEN DEVELOPED OVER TIME TO PROTECT THE RIGHTS AND WELFARE OF DONORS NO MATTER HOW IMPERFECT THOSE MAY BE.

ANOTHER POINT I THINK THAT NEEDS TO BE THOUGHT THROUGH AND NEEDS TO BE THOUGHTFUL IS THAT IN THE SCOPE OF THE PROPOSED CIRM BANK, NOT ALL DONORS ARE PATIENTS. THERE'S A WHOLE CATEGORY OF CONTROLLED DONORS THAT ARE GOING TO BE INVOLVED THAT WILL NOT HAVE A DISEASE THAT THEY KNOW ABOUT OR ANY DISEASE AT ALL. AND THERE MAY BE DIFFERENT ISSUES IMPACTING THEIR DONATION AS SOMEONE WHO HAS A DISEASE.

AND FINALLY, I'D LIKE TO TOUCH ON A POINT THAT'S GOING TO BE VERY COMPLICATED AND SHOULD NOT BE OVERSIMPLIFIED, HAS TRIED TO BE TACKLED BY MANY COMMITTEES, INCLUDING THE NATIONAL BIOETHICS ADVISORY COMMISSION THAT BERNIE WAS A VERY IMPORTANT MEMBER OF, WHICH IS WHAT TO DO WITH RESEARCH FINDINGS. I WANT TO REMIND YOU ALL, BECAUSE I KNOW YOU'RE ALL VERY KNOWLEDGEABLE ABOUT THIS, THAT RESEARCH DATA ARE NOT CLINICAL DATA. THERE'S A REASON WHY IT'S RESEARCH DATA. WE DON'T KNOW WHAT IT MEANS. AND TO SAY THAT WE HAVE AN OBLIGATION TO PROVIDE PATIENTS OR CONTROLLED DONORS WITH DATA THAT WE CAN'T CONFIRM, THAT WE DO NOT UNDERSTAND, AND WE DON'T KNOW THE IMPLICATIONS OF CAN CREATE FAR GREATER RISKS THAN NOT GIVING THEM THE DATA.

AND THIS IS A VERY SERIOUS ETHICAL ISSUE,

THAT IF YOU ARE GOING TO THINK ABOUT REVISING BANKING AND DISTRIBUTING GUIDELINES AND REGULATIONS THAT IS FUNDAMENTAL, AND I'LL GIVE YOU AN EXAMPLE. WHEN THE BRCA1 GENE WAS FIRST DISCOVERED, THERE WAS GREAT FEAR AMONG WOMEN, ESPECIALLY ASHKENAZI JEWS FOR WHICH THE ORIGINAL GENETIC IDEAS WERE -- DONOR CELLS CAME FROM, OF PREDISPOSITION TO BREAST CANCER. NOW, THERE ARE A COUPLE OF WAYS TO TRY TO ADDRESS A PREDISPOSITION TO BREAST CANCER, AND ONE IS PROPHYLACTIC MASTECTOMY AND THE OTHER IS PROPHYLACTIC CHEMOTHERAPY.

I CAN TELL YOU THAT AS A MEMBER OF AN IRB AT THE TIME THAT WE SAW MANY RESEARCH PROJECTS UPON THE FIRST PUBLICATION OF THE IDENTIFICATION OF THE BRCA1 GENE TO GO INTO BREAST CANCER COMMUNITIES AND START TO GET WOMEN TO ENROLL IN RESEARCH THAT OFFERED THEM THE OPTION OF PROPHYLACTIC MASTECTOMY.

WHAT A LOT OF PEOPLE HAVE FORGOTTEN IS THAT THERE'S A LOT OF FALSE POSITIVE AND FALSE NEGATIVE IN THESE GENETIC TESTINGS. DO WE WANT WOMEN TO BE CARVING UP THEIR BODIES BASED ON AN UNCONFIRMED GENETIC ANALYSIS OF A POTENTIAL DISEASE THAT THEY MAY NOT EVER GET? AND SO WHEN WE TALK ABOUT A RIGHT OF A PATIENT TO DATA, I THINK WE NEED TO BE CONCERNED AS PEOPLE WHO ARE INTERESTED IN

ETHICS AND MAKING RULES THAT WE IDENTIFY WHAT THOSE DATA ARE AND THAT WE'RE VERY SENSITIVE TO THE LEVEL OF DATA THAT CAN CAUSE HARM TO A PERSON WITHOUT ANY POTENTIAL BENEFIT GIVEN TO THEM OUT OF CONTEXT AND WITHOUT CONFIRMATION.

SO I STRONGLY URGE YOU TO CONSIDER TWO CONCEPTS. THE CLINICAL VALIDITY OF THE DATA AND THE CLINICAL UTILITY OF THE DATA BEFORE WE START MANDATING RETURN OF UNCONFIRMED RESEARCH RESULTS, THESE ARE NOT CLINICALLY VALIDATED DATA, TO PEOPLE WHO ARE GRAPPLING WITH DISEASE EITHER INDIVIDUALLY OR WITHIN THEIR FAMILIES. THANK YOU.

CHAIRMAN LO: THANKS, STEVE. ANY OTHER COMMENTS FROM MEMBERS OF THE PUBLIC? DO WE KNOW THAT LUNCH IS ACTUALLY HERE? SO I'M GOING TO LET US GO TO LUNCH BECAUSE WE DESERVE IT. WE NEED A BREAK AFTER THIS VERY LIVELY MORNING.

I WANT TO SORT OF JUST ANTICIPATE, PUT IN YOUR SORT OF SUBCONSCIOUS WHILE YOU'RE EATING, TWO ISSUES THAT WE HAVEN'T DEALT WITH OR SEVERAL ISSUES. ONE IS THE ISSUE OF RECONSENT FROM CHILDREN WHOSE SPECIMENS WERE OBTAINED UNDER PARENTAL PERMISSION WHO NOW ARE TURNING 18, ISSUE OF TRYING TO RECONTACT THEM AND CONSENT THEM.

SECOND ISSUE, STEVE RAISED THE QUESTION OF

WHAT'S DIFFERENT ABOUT STEM CELL RESEARCH. ANOTHER ISSUE IS WHAT'S DIFFERENT ABOUT WHOLE GENOME SEQUENCING AND SHOULD THAT BE HIGHLIGHTED AS SOMETHING TO REALLY CONSIDER HAVING AN EXTENSIVE DISCUSSION.

FINALLY, I WANT TO POSE A QUESTION. IF WE'RE STUDYING DISEASES AND WE'RE ASKING FOR FIVE DONORS TO DONATE MATERIALS FOR CELLS, DONATING FOR IPS RESEARCH, UNLESS IT'S AN EXTREMELY, EXTREMELY RARE DISEASE, THERE WILL BE A LOT MORE DONORS FOR IPS DERIVATION THAN FOR HUMAN EMBRYONIC STEM CELL DERIVATION, AND CERTAINLY THAN WOMEN DONATING OOCYTES FOR RESEARCH PURPOSES WITHOUT ANY COMPENSATION BEYOND OUT-OF-POCKET EXPENSES. WHY NOT SIMPLY ENCOURAGE RESEARCHERS TO SELECT DONORS WHO ARE ELIGIBLE IN TERMS OF DISEASE OR CONTROL WHO AGREE TO RESEARCH ON OTHER DISEASES AND CONDITIONS? DOESN'T MEAN ALL RESEARCH, BUT WHO DON'T WANT TO RESTRICT IT ONLY TO THEIR CONDITION OR TO THEIR ORGAN SYSTEM. THAT WOULD MAXIMIZE THE SCIENTIFIC USEFULNESS OF THE LINES, AND YOU WOULD STILL MAKE SURE THAT THEY UNDERSTOOD WHAT THEIR SAMPLES MIGHT BE USED FOR, HOW THEY WOULD BE SHARED, AND SO FORTH, AND WHAT MIGHT BE OFFERED. THOSE ARE THINGS TO THINK ABOUT.

OTHERWISE, I THINK WE DESERVE A BREAK AND LUNCH. THOSE OF YOU WHO WANT TO GO OUTSIDE, IT TURNS OUT IF YOU GO BACK, THERE'S A SWIMMING POOL WITH A LITTLE SORT OF OUTDOORS LOUNGE, WHICH IS A LOT BETTER. THE OTHER PLACE THEY DIRECTED US TO IS A SMOKING AREA RIGHT IN FRONT OF THE HOTEL ON WILSHIRE AVENUE.

(A RECESS WAS TAKEN.)

CHAIRMAN LO: OKAY. WHY DON'T WE TRY AND RECONVENE. WE HAVE A LOT OF OTHER THINGS WE WANTED TO TALK ABOUT. I'M GOING TO SUGGEST THAT, BECAUSE WE HAD FOUR BIG TOPICS OF WHICH CONSENT WAS ONLY ONE, THAT WE NOT TRY AND RESOLVE EVERY ISSUE ABOUT CONSENT. BUT LET ME TRY TO SUMMARIZE WHAT I HEARD AND WHERE I THINK WE ACTUALLY HAVE A FAIR AMOUNT OF AGREEMENT. THERE'S THINGS THAT WE'RE JUST GOING TO HAVE TO CARRY OVER. AND I'M GOING TO, AS I ALWAYS DO, RELY HEAVILY ON GEOFF TO KIND OF DO FOLLOW-UP AND PUT THIS THING TO SPECIFIC LANGUAGE.

SO I THINK WE ALL AGREE THAT CONSENT, IT'S NOT A DOCUMENT, IT'S NOT A SIGNATURE ON A FORM, BUT WE NEED TO FOCUS ON WHAT PEOPLE, DONORS, NEED TO KNOW TO MAKE INFORMED VOLUNTARY DECISIONS. I THINK WE WANT TO MAKE THIS EVIDENCE BASED. I THINK THERE'S A CLEAR IDEA THAT I'M GOING TO ASK GEOFF TO

DO A CRITICAL LITERATURE REVIEW ON WHAT'S KNOWN ABOUT WHAT DONORS THINK OF THE CONSENT PROCESS, WHAT THEY WANT TO DISCUSS, WHAT THEY CARE ABOUT. AND WE MAY WANT TO THINK OF DOING ADDITIONAL EMPIRICAL STUDIES BASED ON THE CIRM EXPERIENCE WITH WHAT WE FUNDED. I DON'T KNOW IF THAT'S FEASIBLE, THERE'S FUNDING, AND SO FORTH.

MS. LANSING: JUST AS A CIRM MEMBER, SO MY OPINION IS ON THE RECORD, I THINK THERE'S ENOUGH LITERATURE OUT THERE FOR US TO GET THE INFORMATION THAT WE NEED. THE BRCA GENE HAS TONS OF STUFF THAT IT'S BEEN DOING ON A LOT OF THIS. I JUST DON'T THINK WE HAVE THE MONEY, NOR SHOULD WE USE THE MONEY TO DO MORE STUDIES. THAT'S JUST MY OPINION. I'M NOT REPRESENTING CIRM.

CHAIRMAN LO: WE'LL PUT A QUESTION MARK. AND WE WANT TO FOCUS ON GIVING DONORS OPTIONS BECAUSE WE UNDERSTAND THERE'S GOING TO BE A RANGE OF DESIRES, PREFERENCES, CHOICES THAT PEOPLE MAKE. SO ON THE NEXT SLIDE, I JUST WANT TO REMIND US THAT WE'VE ACTUALLY DONE A FAIR AMOUNT ON INFORMED CONSENT. WE ACTUALLY HAVE REGULATIONS ON STANDARDS OF CONSENT FOR DONORS WHO FOR FRESH PROCUREMENT, NEW PROCUREMENT FOR IPSC, AND BASICALLY IT'S THEY HAVE TO CONSENT SPECIFICALLY FOR THE DERIVATION. AND SO

I GUESS IT WOULD BE CONSISTENT WITH THAT TO SAY THEY SHOULD ALSO CONSENT FOR INCLUSION IN THE BANK.

AND WE ALSO HAVE STANDARDS FOR CONSENT FOR DONORS THAT ALLOW USE OF DEIDENTIFYING EXISTING MATERIALS TO DERIVE NEW IPS CELL LINES. ANN RAISED AN INTERESTING POINT ABOUT SHOULD WE BE TRYING TO EVALUATE WHAT DO THE DONORS COMPREHEND? WE HAVE A PRECEDENT THAT IN OUR CONSENT FOR OOCYTE DONATION, WHICH IS MUCH MORE COMPLICATED, MUCH MORE CONCERNS ABOUT MISUNDERSTANDING, WE HAD SOME REQUIREMENT THERE BE SOME ASSESSMENT, BUT NOT A PROSCRIPTIVE ONE. SO THAT'S SOMETHING THAT'S A PRECEDENT.

SO IN THE NEXT SLIDE, REAL QUESTIONS, I THINK WE HAVEN'T REALLY GOTTEN TO, BUT WHICH I THINK WILL PERHAPS COME OF THE LITERATURE REVIEW, WHAT TOPICS SHOULD BE ADDRESSED? WHAT OPTIONS SHOULD WE OFFER DONORS? FIRST, IT SEEMS TO ME WE HAVE TO EXPLAIN THE NATURE OF THE BIOBANK. WE PROBABLY SHOULD EXPLAIN WHOLE GENOME SEQUENCING. I SHOULD PUT IN THERE AND DIDN'T PERMISSION TO USE THE LINES FOR RESEARCH ON OTHER CONDITIONS THAN THE ONE THEY WERE ORIGINALLY RECRUITED OR SELECTED FOR. DO THEY WANT AN ONGOING IDENTIFIED RELATIONSHIP WITH THE RESEARCHER WHO DERIVED THE LINE OR THE BANK?

WE DID NOT DISCUSS RECONSENT FOR MINORS.

I THINK IN THE INTEREST OF TIME, WE'LL HAVE TO TRY AND COME BACK TO THAT LATER. AND RESULTS TO DONORS WE ARE GOING TO GET TO A LITTLE BIT FURTHER DOWN THE AGENDA.

SO I THINK WE ACTUALLY HAD A LOT OF DISCUSSION. I THINK I'M GOING TO REALLY ASK GEOFF TO WORK WITH US TO SORT OF DRAW TOGETHER A LITERATURE REVIEW THAT LET'S US KNOW WHAT THE STATE OF THE EMPIRICAL STUDIES ARE ON THE TYPES OF ISSUES THAT SHOULD BE DISCUSSED.

MS. ISASI: AN ISSUE THAT WE HAVE NOT ADDRESSED, YOU HAVE NOT ADDRESSED IS THE INTERNATIONAL SHARING OF THE LINES. AND HOW THIS COULD BE AN ISSUE OF CONCERN OR NOT FROM DONORS IN TERMS OF CONTROL. SOME EMPIRICAL STUDIES DONE IN THE UK AND OTHER COUNTRIES AND ONE THAT WE JUST DID WITH GEOFF ON NURSES WHO SEEK CONSENT, IT WAS IN THE CONTEXT OF EMBRYONIC STEM CELL RESEARCH, BUT IT'S APPLICABLE IS THAT DONORS WERE CONCERNED ABOUT WHO WILL GET THEIR MATERIALS OUTSIDE THEIR JURISDICTION AND THAT RELATED TO THE LEVEL OF OVERSIGHT, SECONDARY USES, INCLUDING`REPRODUCTIVE USES.

SO JUST ANOTHER DIMENSION THAT WE CAN ADD, AND YOU HAVE POLICIES IN PLACE AND STANDARDS IN PLACE TO ASSESS LINES OF FOREIGN ORIGIN; BUT IN THE

CONTEXT OF INFORMED CONSENT, THE POTENTIAL FOR A BIOBANK TO DISTRIBUTE OUTSIDE YOUR OWN JURISDICTION SHOULD BE TAKEN INTO ACCOUNT.

CHAIRMAN LO: RIGHT. THERE'S A WHOLE SET OF ISSUES. SO I GUESS AS I THINK ABOUT THIS, IT STRIKES ME IF YOU ARE GOING TO -- IF CIRM IS GOING TO INVEST IN A BIOBANK, WHICH IS A HUGE INVESTMENT, AS I WOULD UNDERSTAND IT, THE LINES SHOULD BE MAXIMALLY SCIENTIFICALLY USEFUL, SHOULD HAVE MAXIMUM SCIENTIFIC USEFULNESS. IT JUST STRIKES ME THAT YOU SHOULD RECRUIT FIVE DONORS WHO GIVE INFORMED VOLUNTARY CONSENT TO ALLOW THEIR LINES TO HAVE MAXIMAL SCIENTIFIC UTILITY, WHICH WOULD MEAN WHOLE GENOME SEQUENCING, ALLOWING IT TO BE USED FOR RESEARCH ON OTHER TOPICS, TO BE SHARED BROADLY WITH OTHER RESEARCHERS, AND ALSO, I THINK, BE SHARED WITH FOR-PROFIT COMPANIES WHO MAY BE TRYING TO DEVELOP A PRODUCT THAT'S ORIENTED TOWARDS NEW TESTING AND NEW THERAPIES.

IT JUST STRIKES ME THAT IF PEOPLE DON'T WANT TO AGREE TO ALL THAT AFTER BEING INFORMED, THAT'S THEIR RIGHT. THAT'S FINE. BUT I THINK IT MAY NOT BE THE MOST PRUDENT USE OF CIRM RESOURCES TO PUT THE MONEY INTO DERIVING LINES FROM THEM WITH ALL THE RESTRICTIONS.

DR. KIESSLING: ONE OF THE THINGS YOU HAVEN'T TALKED ABOUT ARE EXCLUSION CRITERIA.

CHAIRMAN LO: FOR?

DR. KIESSLING: WHO WOULD BE PEOPLE THAT YOU WOULD NOT ACCEPT TISSUES FROM, AND YOU JUST TOUCHED ON THAT.

CHAIRMAN LO: WELL, I THINK ONE CLEARLY IS PEOPLE WHO AREN'T ABLE TO GIVE INFORMED AND VOLUNTARY CONSENT OR WHOSE PARENTS, I GUESS, AREN'T GOING TO GIVE PERMISSION. BUT I THINK -- SO THIS IS NOT AN ETHICAL -- WELL, MAYBE IT IS ETHICAL. IT'S PRUDENCE. I THINK WE NEED TO SORT OF ASK GEOFF TO THINK ABOUT AS HE WRITES THIS UP WHETHER THIS IS SOMETHING THAT WE SHOULD AT LEAST RAISE FOR CIRM.

DR. ROBERT TAYLOR: IF YOU'RE GOING TO GO THAT FAR AND REALLY IDEALIZE, OPTIMIZE THE SOURCE OF THOSE CELLS, WHY NOT ASK THAT THEY BE GMP DERIVED? AT THIS POINT IF YOU ARE GOING TO REALLY TUNE IT, WHY GO THREE-QUARTERS OF THE WAY DOWN THE FIELD WHEN YOU CAN GO ALL THE WAY DOWN THE FIELD AS WE UNDERSTAND IT TODAY?

CHAIRMAN LO: I DON'T KNOW HOW EXPENSIVE IT WOULD BE TO DERIVE GMP LINES AS OPPOSED TO LAB QUALITY RESEARCH LINES. MY UNDERSTANDING IS IT'S A BIG -- TIM, HAVE YOU DONE GMP LINES?

DR. KAMP: I'M JUST WONDERING IF WE'RE -- IF WE REALLY NEED TO THINK ABOUT THIS RIGHT NOW BECAUSE THOSE ARE -- I'M NOT SURE WE'RE THE RIGHT PEOPLE TO DECIDE WHAT WILL BE IN THE BANK. YOU COULD MAKE ANOTHER ARGUMENT THAT YOU DON'T WANT TO HAVE FIVE LINES FOR EACH DISEASE ONLY, BUT YOU WANT TO REALLY GET DIVERSITY OF LINES. SO HAVING A BROADER SAMPLE IN THE BANK TO ACCESS MAY BE VALUABLE TOO. I DON'T KNOW IF WE NEED TO DO THAT.

CHAIRMAN LO: THAT'S NOT THE PURVIEW OF THIS COMMITTEE. I THINK THE SCIENCE ADVISORY COMMITTEE. MY ONLY THOUGHT WAS THAT WHATEVER GOES IN THERE SHOULD HAVE THE FEWEST RESTRICTIONS ON OTHER RESEARCH USES TO MAKE THEM MAXIMALLY USEFUL TO WHOEVER MIGHT BE ABLE TO BENEFIT.

DR. LOMAX: BERNIE, I WOULD ADD THAT THAT IS ACTUALLY CONSISTENT WITH OUR ESTABLISHED POLICY, THAT WE GET AT THAT IN A RELATED WAY, WHICH IS WE INDICATE THAT THE RESEARCH THAT A DONOR MAY OFFER -- MAY INDICATE CERTAIN RESTRICTIONS ON THE USE OF DONATED MATERIALS, BUT THEN THE INVESTIGATOR OR THE DERIVER IS NOT OBLIGATED TO TAKE THOSE MATERIALS. SO WE'VE SENT A CLEAR SIGNAL THAT WE RECOGNIZE THE VALUE OF A FLEXIBLE SORT OF CONSENT AND DON'T WANT TO BOX PEOPLE IN TO HAVING TO THEN MANAGE

RESTRICTIONS BECAUSE THAT'S SOMETHING THAT'S ALMOST IMPOSSIBLE TO DO FOR SOME OF THESE GRANTEES.

CHAIRMAN LO: I THINK WE WANT TO RESPECT THE VARIABILITY DONORS HAVE IN TERMS OF WHAT'S IMPORTANT TO THEM AND WHAT THEY VALUE AND WHAT THEY ARE OBJECTING TO. BUT I DON'T THINK WE SHOULD SAY THAT A DONOR HAS KIND OF A RIGHT TO BE A CIRM-FUNDED RESEARCH SUBJECT SUBJECT TO THEIR OWN CONDITIONS. I THINK CIRM AND CIRM RESEARCHERS MAY SAY THERE ARE OTHER CONSIDERATIONS AS TO SELECTION CRITERIA FOR WHAT WE WANT PEOPLE TO AGREE TO.

SO LET ME SUGGEST I WOULD LIKE TO MOVE ON TO THE SECOND OF OUR FOUR TOPICS, WHICH IS WITHDRAWAL OF SUBJECTS FROM RESEARCH. WHILE GEOFF IS LINING UP HIS SLIDES, LET ME JUST SAY IN THE COMMON RULE WHICH GOVERNS HUMAN SUBJECTS RESEARCH, RESEARCH PARTICIPANTS HAVE THE RIGHT TO WITHDRAW FROM RESEARCH AT ANY TIME IF IT'S FEASIBLE WITHOUT PREJUDICE TO THEIR ONGOING MEDICAL CARE. SO WE HAVE TO, AS A MATTER OF RESPECTING PATIENT PREFERENCES, PATIENT AUTONOMY, SAY THAT EVEN THOUGH YOU DONATED, YOU CAN CHANGE YOUR MIND AND SAY. BUT WHAT THAT ACTUALLY MEANS IN THE CONTEXT OF AN IPS BANK, PARTICULARLY WHEN NOT JUST OTHER RESEARCHERS WILL BE USING THOSE CELLS, BUT THEY WILL BE TAKING THOSE

CELL LINES AND DRIVING THEM TO SPECIALIZED -- FROM PLURIPOTENT LINES TO MORE SPECIALIZED LINES.

I WAS TALKING TO TIM OVER LUNCH, AND TIM IS VERY, VERY -- TIM'S LAB IS DOING A LOT OF CUTTING EDGE RESEARCH ON DERIVING CARDIOMYOCYTES FOR DRUG SCREENING, FOR EXAMPLE. AND, YOU KNOW, ONCE THE LINE THAT WAS DONATED TO DERIVE AN IPS LINE IS THEN USED TO DERIVE A SPECIALIZED CELL LINE BEING USED BY OTHER RESEARCHERS, IF I AS A DONOR WITHDRAW FROM RESEARCH, DOES THAT MEAN THAT THOSE SPECIALIZED LINES NEED TO BE WITHDRAWN? THAT'S WHAT I THINK GEOFF IS GOING TO HELP TEE UP OUR DISCUSSION.

DR. LOMAX: WHAT I'LL DO IS RUN THROUGH A SET OF CARTOONS THAT ARE ANALOGOUS OR THAT ARE IDENTICAL TO THE TABLE YOU HEARD IN THE MORNING PRESENTATION.

CHAIRMAN LO: THIS IS ON PAGE 6 OF OUR HANDOUT.

DR. LOMAX: I'M JUST TRYING TO, AGAIN, ESTABLISH A SET OF CATEGORIES OR BINS. AND ALSO TO REMIND YOU IN YOUR FOLDER THERE'S SORT OF A NARRATIVE TWO-PAGE FOR EACH OF THESE CATEGORIES AS WELL, JUST TO SORT OF KEEP CLEAR THE CATEGORIES.

SO THE IDEA HERE IS THAT YOU HAVE A DONOR, AND THIS IS REALLY TAKING OFF OF WHAT SOLEL

DESCRIBED AS SORT OF THE VISION WOULD BE YOU HAVE THE INDIVIDUAL, SOME LINKAGE TO MEDICAL INFORMATION, WHICH MAY BE INDIRECT, I.E., MEDICAL RECORDS BEING PINGED BY SOME SORT OF BANKING AUTHORITY OR RESOURCE, SO THE MEDICAL INFORMATION REALLY IS A SORT OF SEPARATE CATEGORY. YOU HAVE THE DONOR. AND UNDER THE HYPOTHESIS THAT THAT INFORMATION WILL ALL GO INTO BOTH A CELL AND DATA REPOSITORY BECAUSE WE'RE NOW TALKING BOTH BIOLOGICAL INFORMATION AND NONBIOGRAPHICAL INFORMATION. WE'VE LEFT A LITTLE DNA PIECE IN THERE TO REMIND US OF THE GENOME SEQUENCING ISSUES THAT KEEP EMERGING.

THAT SORT OF LAYS OUT THE RELATIONSHIP. EVERYTHING ON THE LEFT SIDE OF THAT BOX IN THE MIDDLE LAYS OUT THE RELATIONSHIP WITH EITHER THE DONOR OR INFORMATION ABOUT THE DONOR, WHICH IS ALL VERY RELEVANT UNDER THE COMMON RULE. THE RIGHT SIDE IS LOOKING, THEN, AT THE DISTRIBUTION OR DISTRIBUTED CELLS, POINTING OUT SAMPLES THAT COULD BE ANONYMOUSLY DISTRIBUTED, WHAT HAVE YOU. YOU MIGHT HAVE A DISTRIBUTION -- AND I'VE ALSO SORT OF TRIED TO SET THE EXAMPLE YOU COULD HAVE A PRIMARY DISTRIBUTION TO A LAB THAT IS USING THE CELLS TO DO SOME ADDITIONAL WORK. THEY TRANSFORM THEM AND SUBSEQUENTLY DISTRIBUTE THEM AGAIN. SO THE IDEA IS

THAT DISTRIBUTION COULD BE A PROCESS THAT INVOLVES MULTIPLE PARTIES.

AGAIN, JUST TO KIND OF GIVE US A PICTORIAL FRAMEWORK, WE WANT TO -- AGAIN, THIS IS SORT OF TO REHASH WHAT WE ALREADY HEARD IS THAT, FIRST OF ALL, AN INDIVIDUAL ALWAYS HAS THE RIGHT TO STOP CONTACT. WITHDRAW OPTION 1 WAS SORT OF RECOMMENDED. IT'S JUST A REQUIREMENT OF LAW. IF SOMEONE NO LONGER ONCE WANTS TO BE ENGAGED BY A RESEARCHER UNDER THE COMMON RULE, AND WE OPERATE UNDER THE COMMON RULE, THEN THAT NEEDS TO CEASE.

IN ADDITION, THE TRANSMISSION OF THEIR IDENTIFIABLE INFORMATION TO ANY SORT OF DATA SOURCE, THEY HAVE THE OPTION. THEY CAN SAY, WELL, DON'T CONTACT ME, BUT MY DATA CAN FLOW. BUT THEY ALSO CAN SAY I DON'T WANT ANY CONTACT OR ANY OF MY MEDICAL INFORMATION MOVING FORWARD INTO THE REPOSITORY. AGAIN, THAT'S AN ESTABLISHED LEGAL RIGHT. SO INDIVIDUALS COULD BE INFORMED THAT THAT'S AN OPTION, AND THAT'S THE RIGHT THING TO DO.

AND FINALLY, THE OTHER OPTION THAT THE INDIVIDUAL HAS IS THEY CAN SORT OF DISAPPEAR FROM THE PICTURE COMPLETELY BECAUSE EVEN IN THIS CONTINGENCY, YOU COULD HAVE INFORMATION ABOUT THE DONOR. YOU'RE STOPPING THE NEW FLOW OF INFORMATION

INTO THE REPOSITORY, BUT YOU STILL HAVE EXISTING INFORMATION WHICH IS ASSOCIATED WITH THE INDIVIDUAL. AND THE INDIVIDUAL STILL HAS THE RIGHT TO SAY I WANT TO DISAPPEAR FROM THE PICTURE. DOES THAT MAKE SENSE?

SO THAT'S SORT OF DEFAULT CONDITIONS. OBVIOUSLY, AGAIN, THE WAY YOU SORT OF ADDRESS THIS IS IN THE INITIAL CONSENT, YOU REALLY WANT TO TRY TO USE THE CONSENT PROCESS AS THE WAY OF CAPTURING PEOPLE THAT HOPEFULLY WOULDN'T END UP IN THIS CIRCUMSTANCE BASED ON THE VISION OF THE BANK.

THE AREA WHERE WE HEARD -- WHERE THERE'S SOME DISCUSSION AND UNCERTAINTY IS ONCE YOU'VE GOT MATERIALS THAT HAVE BEEN IN THE BANK, AND JUST LET'S ASSUME THESE MATERIALS HAVE THEN BEEN TRANSFORMED, SO IT'S NOT MY SKIN CELL ANYMORE. IT'S AN IPS CELL THAT'S UNDERGONE SOME TRANSFORMATION. WHILE MY MATERIAL WAS SORT OF THE BUILDING BLOCK FOR IT, IT'S ARGUABLY SOMETHING DIFFERENT THAN PRIMARY MATERIAL FROM ME. WHERE I THINK THE DEBATE BECOMES IS, FIRST OF ALL, WOULD THE REPOSITORY HAVE TO THEN STOP STORING THAT MATERIAL, WOULD HAVE TO SORT OF GET RID OF IT? AND WOULD THE REPOSITORY HAVE TO STOP DISTRIBUTING THE MATERIAL? OR I GUESS AN EXTREME CASE, I HAVEN'T EVEN PUT IT ON HERE YET, AND THEN

BEYOND THAT IT'S ALMOST IMPOSSIBLE ONCE THE MATERIAL IS OUT THERE IN SOME PRIMARY PLACE, SOME OTHER RESEARCHER -- YOU CAN'T SORT OF DRAW THAT STUFF BACK IN, SO AT A CERTAIN LEVEL THAT MATERIAL IS OUT THERE.

AN INTERESTING QUESTION FOR US IS AT THE POINT SOMEONE WITHDRAWS, WOULD WE BE COMFORTABLE OR NOT WITH THESE CONDITIONS, WHICH, AGAIN, WERE, I THINK, WE HEARD THIS MORNING THERE'S DEBATE AND IT'S UNSETTLED IS, FIRST OF ALL, WOULD IT ACCEPTABLE TO TELL THE REPOSITORY SOMEONE CAN WITHDRAW, BUT YOU CAN CONTINUE TO DISTRIBUTE THE IPS CELLS. YOU MAY WANT TO STOP -- YOU SHOULD STOP DISTRIBUTING -- USING THEIR TISSUE, BUT ANYTHING THAT'S BEEN TRANSFORMED AND IMMORTALIZED CAN CONTINUE. OR IS THERE SOME COMPELLING REASON TO SAY, NO, NO FURTHER DISTRIBUTION?

SO ONE ARGUMENT, FOR EXAMPLE, OR ONE SORT OF POINT THAT WAS RAISED, WHAT IF THAT INDIVIDUAL COULD MAKE THE CASE, IN MY SPECIFIC CASE, IT'S SUCH AN UNUSUAL CIRCUMSTANCE, BY CONTINUING TO DISTRIBUTE MY MATERIAL, THERE MAY BE SOME HARM TO ME OR MY FAMILY BECAUSE OF SOME GENETIC CONDITION.

YOU CAN ALSO THINK OF IT IN TERMS OF IN GENERAL THERE WOULD BE A CONTINUED DISTRIBUTION OF

MATERIAL UNLESS THERE WAS SOME EXTRAORDINARY CIRCUMSTANCE IN WHICH YOU WOULD -- I'M TRYING TO SORT OF SUGGEST THERE'S A RANGE OF OPTIONS. THESE ARE THE AREAS WHERE THERE IS, I THINK, BOTH IN TERMS OF PUBLIC POLICY AND THE LITERATURE, THINGS ARE UNSETTLED. IT'S SPECIFICALLY THE TRANSFORMED MATERIALS. SO THAT'S WHERE I THOUGHT IT WAS, AGAIN, USEFUL TO GET SOME THINKING AND SOME DISCUSSION GOING WITH THE GROUP THAT'S SORT OF CHARGED WITH THINKING ABOUT THESE SORTS OF THINGS.

CHAIRMAN LO: GEOFF, IF I COULD ASK YOU TO BACK UP JUST A MINUTE. I WANT TO MAKE SURE I CLARIFY HERE. SO THE WITHDRAWAL OF SPECIMENS, IT SEEMS TO ME THERE'S REALLY -- ARE THERE NOT TWO CASES? THERE'S FOUR WITHDRAWAL OF THE PRIMARY SPECIMENS. I DON'T KNOW WHAT THAT MEANS, THE FROZEN SEGMENT OF MY SKIN BIOPSY AS OPPOSED TO THE FIBROBLASTS THAT WERE DERIVED FROM IT AS OPPOSED TO THE IPS LINE THAT WAS DEPOSITED IN THE CELL BANK?

DR. LOMAX: AS I UNDERSTAND THE DISCUSSION, AND, STEVE, I'D BE HAPPY TO CHIME IN HERE BECAUSE PART OF THIS COMES OUT OF DISCUSSIONS WITH FOLKS LIKE STEVE WHO HAVE A BIT MORE OF A DIRECT TOUCH WITH THIS, IS THAT THERE'S CERTAIN MATERIALS THAT ARE IN A SORT OF NATURAL STATE FROM

THE DONOR, WHICH ARE THE BLOOD, THE PHYSICAL SKIN. SO THOSE SPECIMENS, MY SENSE IS THERE'S A STRONG VIEW THAT THOSE CAN BE -- THAT DONORS COULD HAVE THE OPPORTUNITY TO SORT OF SAY STOP USING THOSE MATERIALS. BUT THEN ONCE THEY'VE GONE THROUGH SOME PROCESS, SOME TRANSFORMATIVE PROCESS WHERE THEY'RE NO LONGER -- I'M NOT IN THE POSITION WHERE I'VE SORT OF BEEN DRAWING THOSE LINES, BUT THERE IS A SENSE THAT THERE'S SOME LINE THERE. I DON'T KNOW HOW BRIGHT THAT LINE IS.

DR. FEIGAL: TO ME THAT SEEMS LIKE THE UNIQUE PART OF THE IPS REPOSITORY AS OPPOSED TO THE STATIC I DONATED A TISSUE, I DONATED BLOOD SAMPLE. THAT MIGHT BE SOMETHING FOR THE COMMITTEE TO TAKE INTO ACCOUNT AS YOU'RE THINKING ABOUT WITHDRAWING AND INFORMED CONSENTS AND THOSE UNIQUE ASPECTS.

CHAIRMAN LO: BUT THERE ARE OTHER TISSUE SAMPLES THAT ARE DONATED AND THEN THEY'RE MANIPULATED IN THE SENSE THEY'RE IMMORTALIZED TO A CANCER CELL, FOR EXAMPLE. YOU COULD MAKE THE ARGUMENT, WELL, IT'S NO LONGER WHAT CAME OUT OF THE DONOR. IT'S SOMETHING THAT A RESEARCHER IN GOOD FAITH PUT A LOT OF EFFORT INTO TRANSFORMING. AND NOW TO SORT OF TAKE AWAY ALL THAT MAY OR MAY NOT BE ETHICALLY DIFFERENT THAN TAKING AWAY WHAT'S

REMAINING OF THE ORIGINAL BIOPSY.

DR. FEIGAL: NO. I WAS JUST REFERRING TO THE STATIC TISSUE WHERE THEY'RE NOT BEING MADE INTO CELL LINES.

CHAIRMAN LO: JUST IT'S FROZEN IN LIQUID NITROGEN.

GEOFF, IF YOU GO TO YOUR NEXT SLIDE, THERE'S YET ANOTHER EXTREME, I GUESS, OPTION 6, WHICH IS TO TRY AND ERADICATE ALL THE MATERIALS DERIVED FROM THE ORIGINAL DONATION SITTING IN ALL THE LABS AROUND THE COUNTRY.

DR. LOMAX: IF YOU LOOK AT POLICIES ON BIOBANKING, ALMOST EVERYTHING WE LOOKED AT THAT'S NOT AN OPTION. PEOPLE, THEY INDICATE IN THE CONSENT AS PART OF THE CONSENT WHEN THEY GO THROUGH THOSE STAGES OF WITHDRAWAL THAT IT SIMPLY WON'T BE AN OPTION TO RECOLLECT. I SORT OF PUT IT OUT THERE TO ILLUSTRATE ALL THE EXAMPLES. IF YOU TAKE LIKE THE BIOBANK -- THERE'S A BIG PROJECT IN THE UK WHERE THEY DID THAT, AND THEY WERE VERY EXPLICIT THAT THEY CANNOT BRING BACK DISTRIBUTED SAMPLES.

CHAIRMAN LO: YOU ALSO OBVIOUSLY CANNOT ERADICATE ANYTHING THAT'S BEEN ANONYMIZED BECAUSE YOU DON'T KNOW WHERE IT IS OR WHO HAS IT.

DR. LOMAX: CORRECT.

DR. PATRICK TAYLOR: JUST A COUPLE FAST THINGS. THIS ISN'T THE ONLY PLACE THIS ISSUE OF DIFFERENTIATION AND DERIVATIVES AND SO ON COMES UP. ONE, OF COURSE, IS IN SCRO JURISDICTION, THE EXTENT TO WHICH IT HAS TO BE ASSERTED OVER DERIVATIVES. ANOTHER IS IN INTELLECTUAL PROPERTY WHERE IT'S COMMON TO ACTUALLY DISTINGUISH BETWEEN THINGS THAT SIMPLY ARE THE SAME THING AND MODIFICATIONS OF THOSE DERIVATIVES. THAT'S IMPORTANT BECAUSE TO THE EXTENT THAT PEOPLE ARE TRANSFERRING THINGS FOR RESEARCH SPONSORED BY OTHERS, THE ABILITY TO RECAPTURE IS GOING TO BE LIMITED BY THOSE INVESTMENTS.

ANOTHER PLACE IT COMES UP IS WHETHER THAT AFFECTS ME ENOUGH. MY POINT IS THERE HAS TO BE, I THINK, SOME ALIGNMENT BETWEEN THESE VARIOUS VIEWS AND WHATEVER RECAPTURE OBLIGATION ANY BANK IMPOSES ON ITSELF.

THE OTHER ASPECT IS I'M REMINDED OF A SO-CALLED CORRIGENDUM OR SOMETHING LIKE THAT IN *NATURE* ABOUT YEAR AND A HALF AGO WHERE THEY OBJECTED STRENUOUSLY TO THE FACT THAT THEY WERE FORCED TO ACTUALLY PUBLISH A PAPER THAT TURNED OUT NOT TO BE REPLICABLE. AND THE REASON FOR THAT IS THAT THE INVESTIGATORS HADN'T DISCLOSED THERE WERE LIMITS IN THE INFORMED CONSENT, THEY DIDN'T KNOW THEY EXISTED,

WHICH PREVENTED ACCESS BY OTHERS LATER ON TO SAMPLES WHICH WERE ACTUALLY IN A REPOSITORY.

SO TO THE EXTENT CIRM OR ITS DELEGEE WOULD ACTUALLY WANT TO MAINTAIN IN A BANK SAMPLES THAT WERE USED FOR RESEARCH AND ACTUALLY BE THE REPOSITORY OF CHOICE AS OPPOSED TO CAUSING THE ADMINISTRATIVE DUPLICATION OF SOME OTHER REPOSITORY, THEN THE NEED TO ACTUALLY MAINTAIN THEM PRECISELY TO ALLOW PAPERS TO BE PUBLISHED IS QUITE IMPORTANT.

I THINK MY OWN SENSE IS THE THOUGHT THAT REGULATIONS MIGHT BE INTERPRETED TO REQUIRE SOME KIND OF TRACK-DOWN OF EVERYTHING IS A NOVEL INTERPRETATION. IT'S NOT THE HISTORIC INTERPRETATION. IT MAY HAVE DEVELOPING SENSIBILITIES TO COMMEND IT, BUT IT IS NOT THE LEGAL MANDATE.

DR. LOMAX: IF YOU NOTICE, THE TRACK-DOWN DOESN'T EVEN SHOW UP ON THIS LIST. AGAIN, IT'S SORT OF PUT OUT TO ILLUSTRATE THAT THERE'S NO WAY TO DO IT FOR ALL THE REASONS. IT GETS SEPARATED OFTEN FROM THE IDENTIFIERS. AND, AGAIN, THEY'RE DISTRIBUTED AT THAT POINT. THE ONLY OPTION WOULD BE IF THERE WAS SOMEBODY DOING SOMETHING THAT VIOLATED A CONTRACT OR AN MTA, BUT THAT'S TYPICALLY NOT THE CASE.

DR. PARTICK TAYLOR: IN HIPAA, FOR EXAMPLE, THERE'S A RELIANCE, A RECOGNITION THAT THE ABILITY TO STOP USING STOPS SHORT, STOPS WHERE OTHERS HAVE RELIED. THAT DEFINITION OF HAVE RELIANCE HAS NEVER TURNED ON IT BEING RELIANCE ON SOME DISTANT THIRD PARTY ALONE. SO TO THE EXTENT THAT THERE ARE SOME RATIONALES WITH LEGITIMATE JUSTIFICATIONS THAT POINT TO RELIANCE, INCLUDING BY, FOR EXAMPLE, CITIZENS OF THE STATE OF CALIFORNIA MAKING AN INVESTMENT, SEEMS LIKE THERE'S GOT TO BE SOME LIMITING PRINCIPLE HERE. WE ARE ALL CHANGING ROLES HERE. I NORMALLY HAVE A DIFFERENT ON THIS ISSUE TOO.

MS. LANSING: HERE'S SORT OF WHAT MY THINKING IS AT THE MOMENT. I FIND THIS ALL SO INTERESTING BECAUSE -- AND IT IS WHAT WE SAID. WE STARTED THIS SIX YEARS AGO, SOMETHING LIKE THAT, AND SCIENCE IS MOVING AHEAD. AND WE SAID WE'D BE FLEXIBLE. WE'D LOOK AT THE PROCESS AND WE'D LOOK AT THE REALITY, WHATEVER. AND WHEREAS I THINK MY BASIS IN THE BEGINNING WITH INFORMED CONSENT WAS ALL ABOUT EMPOWERING THE PATIENT, I HAVE A SLIGHTLY DIFFERENT VIEW ON THIS. AND ON THIS I BELIEVE THAT SCIENCE MUST BE PROTECTED, AND THE SCIENTIST MUST PROTECTED.

SO IN BROAD STROKES, LAY STROKES, WHERE

I'M COMING OUT AT THE MOMENT IS WHEN WE -- WE'VE ALREADY HAD THIS INFORMED CONSENT CHOICES, AND WE'VE REALLY EXPLAINED IT VERY WELL, AND WE MADE SURE THAT THEY UNDERSTAND IT. AND MY FEELING IS THAT ONCE YOU SIGN OFF, AND I KNOW THERE ARE SOME RULES WHERE YOU CAN TAKE CERTAIN THINGS BACK, WHICH IS BASICALLY BEFORE -- AGAIN, I'M DOING THIS IN VERY LAY TERMS -- BEFORE IT'S BEEN CHANGED AND BEFORE THE EXPERIMENTS HAVE STARTED. I WOULD STICK WITH THAT BECAUSE ONCE YOU START TELLING A PATIENT, GEE, I DON'T LIKE WHAT YOU'RE DOING WITH MY CELL. YOU TURNED IT INTO THIS AND YOU TURNED IT INTO THAT. THAT'S REALLY MESSING WITH SCIENCE. AND I REALLY BELIEVE THAT AT THAT POINT WE CAN DO GREAT HARM TO THE RESEARCH THAT WOULD BENEFIT YOUR CHILDREN AND THAT WOULD BENEFIT THE PATIENTS THAT WE'RE TRYING SO HARD TO REPRESENT.

SO I THINK ONCE YOU'VE SIGNED, WITHDRAWAL SHOULD BE UNDER THE VERY LIMITED WAY THAT IT ALREADY EXISTS BECAUSE OTHERWISE I THINK IT REALLY WILL HARM RESEARCH.

DR. LOMAX: THAT WOULD BE A LEVEL 3 HERE. YOU ALWAYS HAVE THAT RIGHT.

MS. LANSING: AND I REALLY WOULD NOT EXTEND IT MUCH BEYOND THAT.

DR. KIESSLING: IT'S ACTUALLY NOT CLEAR TO

ME. I CAN'T THINK OF AN EXAMPLE IN WHICH I KNOW THAT PEOPLE HAVE THE RIGHT TO WITHDRAW TISSUE THEY'VE DONATED FOR RESEARCH.

DR. ROBERT TAYLOR: I'VE HAD THAT.

DR. KIESSLING: IS THERE AN EXAMPLE FOR THAT?

DR. ROBERT TAYLOR: PEOPLE CAN -- THEY CAN REQUEST SAMPLES THAT THEY'VE GIVEN, BLOOD SAMPLES, TISSUE SAMPLES, TO BE SORT OF REMOVED FROM THE SPECIMEN BANK, TISSUE BANK, AND THAT'S WRITTEN INTO MOST OF THE IRB'S THAT I'VE USED.

DR. KIESSLING: THAT COMES UNDER THE WITHDRAWAL FROM THE RESEARCH PHRASE.

DR. ROBERT TAYLOR: WITHDRAW FROM THE RESEARCH. SO I WOULD SAY THAT IN MY EXPERIENCE, THE MORE COMMON THING IS SOMEBODY JUST KIND OF DISAPPEARS. THEY KIND OF PASSIVELY SLIP OFF INTO THE SUNSET. THEY DON'T PROVIDE ANY MORE DATA. YOU CAN'T FOLLOW UP. I DON'T SEE ANY MORAL OBLIGATION TO NOT CONTINUE USING THEIR SAMPLES WITH THE INFORMATION YOU HAVE GOING FORWARD.

DR. LOMAX: IT'S SORT OF THE PRINCIPLE OF SORT OF, FOR EXAMPLE, IT'S IN THE NIH GUIDELINES AS WELL, THAT PRIOR TO HUMAN EMBRYONIC STEM CELL LINE DERIVATION, THERE IS SORT OF YOU CAN TRY TO REQUEST

OUT.

DR. KIESSLING: THAT'S TIME LIMITED.

DR. LOMAX: IT'S TIME LIMITED. THAT'S RIGHT. EXACTLY.

DR. KIESSLING: IT'S SORT OF LIKE THE LEMON LAW WHEN YOU BUY A CAR.

DR. ROBERT TAYLOR: THIS IS A POTENTIAL. AND I'VE HAD PEOPLE CALL BACK YEARS LATER, AND I'VE HAD TO GO DIGGING AROUND THE FREEZER TO FIND A CHUNK OF FROZEN TISSUE THAT I WAS SUPPOSED TO THROW AWAY, AND IT'S A LITTLE BIT OF A HASSLE AND FRUSTRATING TO DO THAT. BUT I WOULD SAY THAT PEOPLE THAT REALLY ACTIVELY DECIDE TO WITHDRAW THEIR SAMPLE, LIKE, I DON'T BELIEVE THAT THIS IS SORT OF ETHICALLY APPROPRIATE NOW OR I DON'T LIKE WHERE THIS RESEARCH IS GOING, I FEEL THAT WE HAVE AN OBLIGATION TO TRY TO ADDRESS THAT AND TO CORRECT IT THE WAY THAT INDIVIDUAL DONOR WANTED.

IT SEEMS TO ME THAT RATHER THAN SOME KIND OF A BIOCHEMICAL VIRAL TRANSFORMATION, THAT IT'S MAYBE BETTER TO DRAW THE LINE OF DEMARCATION AT THE POINT OF ANONYMIZATION OF THE SAMPLE. TO ME ETHICALLY THAT'S CLEANER THAN SOMETHING THAT WE MIGHT HAVE DONE IN THE LABORATORY. ONCE A SPECIMEN BECOMES -- IT'S NO LONGER REALLY READILY TRACEABLE

TO THE DONOR, THEN IT CAN MAYBE MOVE FORWARD IN PERPETUITY AS A0493.9 OR SOMETHING. BUT THAT IF IT'S DIRECTLY IDENTIFIABLE WITH THAT PERSON AND THEY WANT IT PULLED OUT, IT SEEMS TO ME IT'S KIND OF OUR OBLIGATION TO SORT OF PULL IT OFF THE SHELF.

DR. ROBERTS: COULD I JUST ASK ABOUT THAT? I'M JUST TRYING TO UNDERSTAND WHAT IS THE MORAL PRINCIPLE. IS IT THAT THE LINES ARE NOT IDENTIFIABLE ANYMORE, AND SO WHAT YOU'RE PROTECTING IS THE PATIENT PRIVACY? OR IS IT THAT THE PATIENT SHOULD HAVE CONTROL OVER WHAT IS DONE WITH HIS OR HER SAMPLES OR WHAT'S DERIVED FROM THE SAMPLES? BECAUSE, WELL, IF THAT'S -- THEN THAT'S A COMPLETELY DIFFERENT ANSWER THAN WHAT WE'VE BEEN SAYING.

MS. LANSING: I DON'T BELIEVE IN THAT. ASKING WHAT THE ISSUE WAS.

DR. ROBERT TAYLOR: THERE'S A FEASIBILITY KIND OF COMPONENT TO IT AS WELL, BUT MAYBE THAT DOESN'T PROBABLY REACH A LEVEL OF MORAL SORT OF STANDARD THAT THE REST OF IT DOES. BUT THE TRUTH IS IS THAT GOING BACK AND FINDING SOME OF THESE THINGS CAN BE QUITE CHALLENGING, COSTLY, AND --

MS. LANSING: BUT IF YOU CAN FIND THEM AND RESEARCH HAS ALREADY STARTED ON THEM, THEN YOU ARE REALLY STOPPING SCIENCE FROM MOVING. AND I DON'T

THINK THIS IS GOING TO HAPPEN VERY OFTEN, BUT IT COULD HAPPEN IN A TERRIBLE TIME WHEN SOMEONE IS CLOSE TO A BREAKTHROUGH AND SOMEONE COULD SAY, WELL, I DON'T LIKE WHAT'S BEING DONE ON MY CELL LINES. THEY COULD HAVE MISINFORMATION, WHATEVER. I THINK IF THAT FIRST STEP -- IT'S FUNNY BECAUSE AT FIRST I WAS ALL ABOUT EMPOWERING THE PATIENT. NOW ON THIS PARTICULAR ISSUE, I'M ALL ABOUT WHAT'S BEST FOR THE SCIENTIFIC RESEARCH THAT DISEMPOWERED PATIENT HAS ALREADY SIGNED OFF ON.

AND I WANT TO JUST ADD ONE OTHER THING. YOU SAID WHAT IF YOU FIND THAT THERE'S DISEASE IN CERTAIN LINES, WHATEVER, AND THAT IT COULD BE HARMFUL TO PATIENTS TO BE USING THOSE LINES. I HAVE TO ASSUME THE SCIENTISTS WOULDN'T USE THEM WHEN THEY FOUND THAT. I DON'T THINK THEY WOULD WILLFULLY INFECT SOMEBODY WITH A DISEASE. SO I FEEL THAT THAT I WOULD TRUST THE SCIENTISTS WITH.

I JUST DON'T WANT -- IN LAY TERMS I JUST DON'T WANT SOMEONE SAYING, WELL, GOD. I JUST FOUND OUT THAT YOU'RE DOING THIS RESEARCH. I DID SIGN OFF FOR ALL DISEASES AND YOU'RE DOING THIS RESEARCH, AND I REALLY DON'T WANT YOU TO DO RESEARCH ON THAT PARTICULAR DISEASE. AND YOU'VE GONE WAY DOWN THE LINE AND NOW YOU DON'T HAVE ANY MORE LINES, YOU'VE

DONE ALL SORTS OF STUFF TO IT, AND YOU HAVE TO STOP.

DR. ROBERTS: IS THERE A DISTINCTION BETWEEN THE TISSUE AND THE LINES?

DR. KIESSLING: THAT'S WHAT ROB IS SAYING.

DR. ROBERTS: THAT'S WHAT ROB'S SAYING, BUT HIS DISTINCTION WAS BASED ON IDENTIFICATION, WHICH IS NOT THE PRINCIPLE THAT SHERRY IS TALKING ABOUT. SO --

MS. LANSING: I RESPECT WHAT YOU'RE SAYING. I'M LIKE GOING FROM ONE EXTREME TO THE OTHER.

DR. ROBERTS: SHERRY, WOULD YOU SAY THAT THE DONOR DOESN'T HAVE A RIGHT TO WITHDRAW EITHER THE TISSUE OR THE LINE?

MS. LANSING: ONLY IN THE VERY -- ONES THAT ARE ALREADY SET UP. I'M NOT TRYING TO CHANGE THAT, WHAT'S ALREADY SET UP BY LAW.

DR. ROBERT TAYLOR: I THINK SHERRY AND I AGREE. IT'S JUST I'M KIND OF TRYING TO COME UP WITH A MORE DEFENSIBLE PRINCIPLE.

DR. ROBERTS: I JUST WANT TO HEAR WHAT THE PRINCIPLE IS.

CHAIRMAN LO: THERE'S SEVERAL PRINCIPLES AND THEY PULL YOU IN DIFFERENT DIRECTIONS. ONE PRINCIPLE IS RESPECT FOR PERSONS, RESPECT FOR THE

AUTONOMY OF THE DONORS. WE SAY WE'RE FOLLOWING THEIR INFORMED AND VOLUNTARY PREFERENCES, THAT THEY'VE CHANGED THEIR MIND. THAT LINE OF THINKING SAYS WE SHOULD RESPECT THEIR LATEST DECISION, NOT THE ONE THAT -- PEOPLE DO CHANGE.

PAT, I THINK, ARTICULATED ANOTHER PRINCIPLE, WHICH IS JUSTIFIABLE RELIANCE, THAT YOU PROMISED SOMETHING. SOMEONE ELSE IN GOOD FAITH RELIED ON THAT AND DID A WHOLE LOT, WHETHER IT'S MONEY, TIME, EFFORT, AND TO SORT OF WITHDRAW THE FRUITS OF THAT INVESTMENT, THAT WORK, THAT EFFORT, SEEMS TO BE UNFAIR TO THE PERSON WHO MADE THE COMMITMENT TO WORK ON THE LINES. WE COULD TALK ABOUT HOW IN THE LONG RUN IT WOULD REALLY HAVE A CHILLING EFFECT ON SCIENTISTS BEING WILLING TO CARRY OUT RESEARCH.

AND THEN ONE OF YOU IDENTIFIED A THIRD PRINCIPLE, WHICH IS RESPECT, WHICH IS PRIVACY.

DR. ROBERTS: THAT SOUNDED LIKE ROD'S POINT WHERE IDENTIFICATION WOULD MAKE A DIFFERENCE.

CHAIRMAN LO: AND IT DOES TO SOME EXTENT. IT STRIKES ME, AS I LOOK AT THIS LIST, NO. 3, IT SEEMS TO ME, REALLY SORT OF HINGES ON THE IDENTIFICATION AND PRIVACY THAT IF IT'S NOT IDENTIFIABLE, IF I'M DOING SOMETHING TO YOUR CELLS

OR YOUR MATERIALS AND THEY'RE NOT IDENTIFIABLE ANYMORE, THEN I CAN'T HARM YOU. AND I'M NOT SURE I TOTALLY AGREE WITH THAT. THE HAVASUPAI CERTAINLY DIDN'T THINK THAT.

I'M CONCERNED ABOUT THREE. AND I DON'T KNOW IF -- NICOLE, YOU ALLUDED TO THIS IN YOUR PRESENTATION. I DON'T QUITE REMEMBER -- IS THAT IF I GET A REQUEST FROM A DONOR SAYING I'VE CHANGED MY MIND, I'M REALLY SORRY, BUT I JUST DON'T WANT YOU TO KEEP MY FROZEN SKIN BIOPSY. I UNDERSTAND. I READ THE CONSENT FORM THAT ALL THE WORK YOU'VE DONE STANDS AND THE LINES CAN BE GIVEN OUT, BUT I'D LIKE YOU TO STOP THE USE OF THE IDENTIFIED NATIVE MATERIALS.

AND THEN I SAY, OKAY. I GOT THE LETTER, BUT I'M GOING TO RUN TO MY LAB AND STRIP THE IDENTIFIERS OFF THAT SKIN BIOPSY AND NOW SAY, WELL, IT'S DEIDENTIFIED. I CAN'T HARM THE PATIENT'S PRIVACY. ACCORDING TO THE COMMON RULE, THERE'S NO HARM THAT CAN BE DONE. SO I CAN JUST CONTINUE TO USE THE NATIVE MATERIALS PROVIDED I HAVE DEIDENTIFIED. THAT JUST DOESN'T -- I'M PERSUADED THAT'S THE TACK WE WANT TO FOLLOW. I THINK, THE LAWYERS CAN CORRECT ME, I THINK THAT IS -- I KNOW THAT'S DONE WITH SOME IRB'S. THEY SAY YOU WANT TO

WITHDRAW RESEARCH, FINE. WE'LL JUST DEIDENTIFY YOUR MATERIALS AND JUST CONTINUE.

SO WHAT I'M HEARING IS THAT NO ONE IS SAYING PEOPLE SHOULDN'T HAVE THE RIGHT TO ONE AND TWO. PEOPLE ARE SAYING THAT, FIVE, THE TRANSFORMED MATERIALS, THAT HAS TO GO FORWARD. IF YOU'VE GIVEN INFORMED CONSENT, YOU CAN LATER ON SAY I WANT TO WITHDRAW THE TRANSFORMED MATERIALS THAT PEOPLE HAVE ALREADY GOT. BUT I GUESS --

DR. ROBERT TAYLOR: I'M NOT SO SURE THAT I BUY THAT PART. I KIND OF AGREE WITH DOROTHY ON THIS LEVEL. SO I'M LOOKING FOR SOME LEGAL SPACE, I GUESS, WHERE WE CAN PROTECT SOME OF THOSE RELIANT SAMPLES THAT HAVE HAD A LOT INVESTED IN THEM AND TO TRY TO COME UP WITH SOME GUIDELINES THAT WE CAN SLEEP AT NIGHT WITH THAT WOULD ALLOW US TO CONTINUE TO USE THOSE AND NOT HAVE TO GO ALL THE WAY TO THE ENDS OF THE EARTH BOTH FIGURATIVELY AND LITERALLY TO FIND ANY SAMPLE THAT MIGHT HAVE ULTIMATELY BEEN DERIVED FROM AN ORIGINAL.

DR. KIESSLING: ISN'T THE CLEANEST ANSWER TO THAT TO MAKE IT TIME LIMITED? YOU'VE GOT TWO YEARS, NAME A TIME, A YEAR, TWO YEARS, THREE YEARS, SOME PERIOD OF TIME. AFTER THAT --

DR. ROBERT TAYLOR: THAT SOUNDS LIKE A

LEGAL KIND OF A QUESTION TO ME.

DR. PATRICK TAYLOR: WE SHOULD ALMOST DISTRIBUTE THIS *NATURE* PIECE. WHAT THEY WERE BASICALLY SAYING IS, LOOK, UNLESS YOU WRITE PAPERS BASED ON UNRESTRICTED SAMPLES, WE'RE NOT GOING TO PUBLISH YOUR PAPERS ANYMORE. I THINK BERNIE'S POINT ABOUT A CHILLING EFFECT IS RIGHT ON POINT. THAT'S WHAT THEY SEE AS NECESSARY TO REALIZE SCIENTIFIC NORMS.

DR. KIESSLING: BUT WOULD TIME LIMITATION SATISFY THAT?

DR. PATRICK TAYLOR: UNRESTRICTED IS WHAT -- I'M NOT SAYING THAT *NATURE* SHOULD DICTATE TO THE WORLD, BUT RESTRICTIONS THAT ACTUALLY END UP MAKING IT IMPOSSIBLE TO REPLICATE WORK ARE DIFFICULT.

I WONDER IF THERE'S SOME COMPROMISE HERE BASED ON THE BASES OF THE REVOCATION. I THINK THE EXAMPLE THAT YOU GAVE, ROB, WHICH IS A PRETTY IMPORTANT EXAMPLE, WAS SOMEBODY THINKS THAT THE WORK THAT'S BEING DONE HAS ACTUALLY BECOME UNETHICAL. AND WE'VE TALKED ABOUT GOVERNANCE AND OTHER MECHANISMS HERE, WHICH HAS BEEN REALLY DESIGNED TO MAKE SURE THAT THE WORK REMAINED ETHICAL. KEEPING DONORS INVOLVED MORE THOROUGHLY AND FOCUSING ON THE

THINGS THAT DONORS REALLY CARE ABOUT. IF WE'VE DONE THOSE THINGS RIGHT, THEN HAVEN'T WE ADDRESSED THE CONCERN, WHICH IS A LEGITIMATE CONCERN THAT YOU'RE TALKING ABOUT, AND ALSO EFFECTIVE RELIANCE.

SO MAYBE A WAY OF RESPONDING TO THIS IS TO REFLECT IN THE DESIGN OF A BANK PARTICIPANT INVOLVEMENT AND ENSURE OVERALL IT'S FUNCTIONING IN A GOOD WAY, SO WE COULD AVOID THAT SITUATION. OF COURSE, IF THERE'S SOME AUDIT BY THE STATE TREASURER THAT SAYS, YEAH, THERE'S ALL THIS UNETHICAL STUFF GOING ON, THERE OUGHT TO BE A LOT OF TERMINATION OF SAMPLE INVOLVEMENT, NOT JUST ONE OR TWO. THAT MIGHT BE A VERY LEGITIMATE WAY, I HOPE, OF RESPONDING TO THE VERY IMPORTANT CONCERN.

CHAIRMAN LO: LET ME SORT OF POSE THE QUESTION. NO. 5, WHICH IS I THINK THERE'S MORE THAN ONE ETHICAL PRINCIPLE AT STAKE HERE. I GUESS MY QUESTION IS DO WE DO SOME SORT OF BALANCING AND SAY THAT, YES, WE BELIEVE IN RESPECT FOR DONORS, RESPECT FOR THEIR AUTONOMY, BUT WE BALANCE THAT OFF AGAINST JUSTIFIABLE RELIANCE AND BENEFITS TO SOCIETY. THE RIGHT TO WITHDRAW IS NOT ABSOLUTE. AND THAT IN NO. 5 WE MIGHT DO A BALANCING AND SAY THAT AT THAT SITUATION YOU CAN'T WITHDRAW. WHEREAS, WE MAY SAY FURTHER UP THE LINE, MAYBE EVEN FOUR, WE'D SAY, YES,

YOU CAN WITHDRAW EVEN IF IT MEANS ROB'S GOT TO GO ROOTING AROUND IN HIS FREEZER AND SPEND A DAY GETTING FROSTBITE.

IT SEEMS TO ME THAT'S DIFFERENT THAN SAYING, WELL, ROB JUST LOST TWO YEARS OF RESEARCH DERIVING AN IPS LINE THAT TIM IS NOW DOING CARDIOLOGY RESEARCH ON. IT STRIKES ME THAT THERE'S SOME LEVEL OF RELIANCE ON USING THE MATERIALS FOR THE PUBLIC GOOD FOR GENERALIZABLE KNOWLEDGE THAT IN THAT SITUATION OUTWEIGHS THE RIGHT OF THE RESEARCH -- THE DONOR TO WITHDRAW.

DR. KAMP: IS THAT THE SORT OF THING THAT COULD BE CLARIFIED IN THE CONSENT FORM ITSELF? TO ME THAT SEEMS LIKE THE MOST LOGICAL WAY TO DEAL WITH THAT, TO MAKE IT QUITE CLEAR AT THE TIME OF CONSENT.

CHAIRMAN LO: ABSOLUTELY. I THINK WHATEVER WE SAY, IT'S GOT TO BE CLEAR. AND IT STRIKES ME TO THE EXTENT WE REALLY WANT TO BE SURE PEOPLE UNDERSTOOD WHAT THE TERMS OF THE AGREEMENT WERE, THAT'S SOMETHING WE REALLY WANT TO MAKE SURE THEY UNDERSTOOD, THAT YOU CAN ONLY WITHDRAW UP TO HERE. I THINK WE'RE STILL DEBATING THAT. YOU CAN CERTAINLY WITHDRAW NO FURTHER CONTACT, NO FURTHER CONTACT, NO FURTHER COLLECTION OF MEDICAL INFORMATION.

I GUESS THE QUESTION -- I THINK WE'RE SAYING THAT FIVE YOU CAN'T WITHDRAW. YOU CAN'T SAY I'M GOING TO STOP YOU FROM WITHDRAWING -- FROM USING TRANSFORMED MATERIAL. SO THE QUESTION IS NO. 3 AND NO. 4. IF YOU WITHDRAW, CAN I SAY, WELL, I'M GOING TO ANONYMIZE IT AND STILL USE IT? AND FOUR, IT SEEMS TO ME, IS DO I HAVE THE RIGHT TO ASK ROB TO ROOT AROUND IN HIS FREEZER TO GET THE PRIMARY SAMPLE THAT NO ONE'S DONE ANYTHING OTHER THAN JUST TO PUT IT IN LIQUID NITROGEN, I THINK, AND MAKE SURE IT'S STORED AT THE RIGHT TEMPERATURE, BUT THAT'S ALL. THEY HAVEN'T REALLY DONE MORE THAN THAT.

I GUESS WHAT I'M SUGGESTING IS THAT AS WE BALANCE THE RIGHT OF AUTONOMY VERSUS JUSTIFIABLE RELIANCE, IF I RELIED ON IT A LOT, I HAVE MORE OF A SAY IN THAT BALANCE. WHERE IF I'VE RELIED ON IT A LITTLE, THEN I SHOULD GIVE MORE DEFERENCE TO THE RIGHT OF THE PATIENT TO WITHDRAW.

STEVE, YOU HAD YOUR HAND UP BEFORE.

DR. PECKMAN: SO THIS IS AN AREA THAT I'VE ACTUALLY PUT A LOT OF THOUGHT IN. AND GEOFF AND I HAVE ACTUALLY WORKED TOGETHER QUITE A BIT ON THIS. AND I THINK THERE ARE SEVERAL ETHICAL PRINCIPLES INVOLVED THAT YOU'VE ARTICULATED. AND ONE IS THE CONCEPT OF AUTONOMY, WHICH IS REPRESENTED BY THE

ABILITY TO WITHDRAW FROM RESEARCH. ONE EXERCISES THEIR AUTONOMY THROUGH THAT PROCESS.

NOW, THE QUESTION IS WHAT DOES IT MEAN TO WITHDRAW? WHAT DOES IT MEAN TO PARTICIPATE? THE FEDERAL REGULATIONS SAY, AND CALIFORNIA LAW SAYS THAT THE SUBJECT HAS THE RIGHT TO WITHDRAW FROM THE RESEARCH. SO, THEREFORE, THE SUBJECT HAS THE RIGHT TO NO MORE INTERACTION OR INTERVENTION WITH THAT PERSON. SO THE QUESTION IS WHO OR WHAT IS THE SUBJECT THEN? AND ARE WE CONFUSING A SUBJECT WITH AN OBJECT?

THE MATERIAL REMOVED FROM THE DONOR, IF WE SAY THE DONOR HAS THE RIGHT TO REMOVE THAT MATERIAL FROM THE RESEARCH LATER, ARE WE SAYING, THEN, THAT THAT MATERIAL IS THE PROXY FOR THE DONOR'S PARTICIPATION AND REPRESENTS THAT PERSON? SO I THINK WE HAVE TO THINK ABOUT BOTH THE SUBJECT AND THE OBJECT IN THIS CASE.

THE SECOND ETHICAL PRINCIPLE IS ONE OF ACTUALLY BENEFICENCE OF BALANCING THE RISKS AND BENEFITS OF PARTICIPATING IN THE RESEARCH. AND I THINK WHEN WE TALK ABOUT ANONYMIZATION, WE'RE TALKING ABOUT BENEFICENCE, WHICH IS MINIMIZING THE RISK OF PARTICIPATING IN THE RESEARCH. AND THAT IS, ANONYMIZATION IS A METHODOLOGY FOR ACCOMPLISHING

THAT GOAL.

NOW, I THINK, THIRD, YOU HAVE A PRECEDENT YOU HAVE TO DEAL WITH WITHIN OUR OWN REGULATIONS AT CIRM, WHICH IS FOR EMBRYO DONATION, AND THIS IS CONSISTENT WITH NAS AND NIH, WHICH IS THE DONOR HAS THE ABILITY TO WITHDRAW THE EMBRYO FROM THE RESEARCH BEFORE THE DERIVATION PROCESS BEGINS. AT THE POINT OF INITIATION OF THE DERIVATION PROCESS, THE DONOR NO LONGER HAS THE ABILITY TO WITHDRAW THE MATERIAL. CERTAINLY AFTER THE DERIVATION PROCESS IS AN EXTENSION OF THAT PRINCIPLE. SO I THINK IT'S IMPORTANT TO KEEP THAT IN MIND.

AND THOUGH I APPRECIATE BERNIE'S IDEA OF KIND OF BALANCING THE ETHICAL PRINCIPLES, I THINK IN THIS CASE I WOULDN'T BALANCE THEM, BUT I WOULD DEFINE THEM AND MAKE THE APPROPRIATE DECISIONS BASED ON THOSE DEFINITIONS. ONE IS THE CONCEPT OF AUTONOMY, ADDRESSING THE CONFUSION BETWEEN SUBJECT AND OBJECT, ENSURING THAT BENEFICENCE IS UPHELD AND WE'RE ABLE TO MINIMIZE THE RISKS AND BENEFITS OF PARTICIPATING IN THE RESEARCH WITHOUT DAMAGING THE RESEARCH.

AND THIS IS A VERY IMPORTANT CONCEPT TO WHAT SHERRY WAS TALKING ABOUT, WHICH IS DAMAGING THE SCIENCE. AND IF WE THINK ABOUT BEING FORCED TO

ANONYMIZE CELLS, YOU MAY ACTUALLY DAMAGE DOWNSTREAM RESEARCH IN TERMS OF YOUR ABILITY TO TRANSLATE IT INTO ACTUAL THERAPIES. BECAUSE IF YOU CUT OFF THAT LINK BETWEEN THE IDENTIFICATION OF THE DONOR AND THE AFFILIATED MEDICAL INFORMATION THAT GOES WITH THAT BIOLOGICAL SAMPLE OR THE MATERIAL THAT'S CREATED FROM THAT BIOLOGICAL SAMPLE, THEN YOU'RE DIMINISHING THE ABILITY TO MEET FDA STANDARDS FOR TRANSLATION.

CHAIRMAN LO: LET ME JUST CLARIFY A COUPLE THINGS. WHEN WE TALK ABOUT ANONYMIZATION, WHAT'S GENERALLY MEANT IS THAT YOU ANONYMIZE -- YOU STILL LINK THE EXISTING MATERIALS WITH THE EXISTING CLINICAL ANNOTATIONS YOU HAVE. YOU JUST DEIDENTIFY IT IN A HIPAA SENSE, BUT IT'S STILL LINKED. YOU CAN PRESENT IT TO THE FDA AS SUBJECT 0001. HERE'S THE SAMPLE, HERE'S THE DATA ON THE SAMPLE, HERE'S THE CLINICAL INFORMATION. SO WE'RE NOT TALKING ABOUT SEVERING THE LINK BETWEEN CLINICAL INFORMATION AND THE SPECIMEN AND THE DATA.

DR. PECKMAN: IF THAT'S THE DEFINITION OF ANONYMIZATION, I AGREE COMPLETELY.

CHAIRMAN LO: THAT'S WHAT'S TYPICALLY DONE, MY UNDERSTANDING, WITH BIOBANKS. THEY GIVE A RESEARCHER THE COMBINATION PACKET OF MATERIALS, DATA, CLINICAL INFORMATION WITH A CODE, AND PROMISE

NEVER TO BREAK THE CODE.

DR. PECKMAN: AT THE END OF THE DAY, YOU DON'T WANT TO CREATE A SITUATION WHERE THE RESEARCHER HAS THE CODE AND IS THEN RESPONSIBLE FOR BREAKING HIS OR HER OWN CODE AND ANONYMIZING HIS OR HER OWN SAMPLE, WHICH THEN RESULTS IN THE FACT THAT EVERYONE IN THE WORLD GETS TO USE THE CELLS EXCEPT FOR THE RESEARCHER WHO ORIGINALLY OBTAINED THEM BECAUSE FOR HIS OR HER RESEARCH THEY NO LONGER HAVE THE ABILITY TO CREATE THOSE LINKS. AND SO I THINK YOU NEED TO BE CAREFUL IN THE PROCESS OF WHERE THESE DISTINCTIONS OCCUR AND WHAT THE DOWNSTREAM EFFECTS ARE TO EVERYONE IN THE PROCESS.

CHAIRMAN LO: AGAIN, I THINK THAT RESEARCHERS ARE ENCOURAGED OR ACTUALLY REQUIRED UNDER HIPAA TO USE THE LEAST IDENTIFIABLE FORM OF INFORMATION CONSISTENT WITH THE GOALS SO THAT IF THE RESEARCHER -- THAT'S ONE OF THE REASONS MANY PEOPLE ARE ADVOCATING BIOBANKS BECAUSE THE BIOBANK KEEPS IT IN IDENTIFIED FORMAT, AND THEN THE RESEARCHER GETS IT IN ANONYMIZED OR DEIDENTIFIED FORMAT. I THINK RATHER THAN -- I THINK WE MAY BE GETTING TOO DOWN IN THE DETAILS, BUT I THINK STEVE RAISED A REAL CHALLENGE, WHICH IS TO SAY, THERE ARE COUPLE OF ISSUES, DOES RESPECT FOR PERSONS MEANS THAT YOU HAVE

NO CONTROL OVER THE MATERIALS YOU DONATED ONCE YOU DONATED THEM?

LET ME JUST SAY THERE'S ARGUMENTS ON THE OTHER SIDE. SO IN CATALONA VS. WASH U ST. LOUIS, THE APPEALS COURT SAID NO. YOU HAVE THE RIGHT TO SAY GIVE IT BACK TO ME. I DONATED MY PROSTATE TISSUE. I DON'T WANT TO DO IT ANYMORE. I THINK WASH U ACTED UNETHICALLY IN SORT OF DEPRIVING MY DOCTOR OF THE SAMPLES I DONATED TO HIM.

THEY CLAIMED THAT AT THE UNIVERSITY. COURT SAID YOU CAN GET THEM REMOVED. WHAT YOU CAN'T DO IS SAY I WANT TO TAKE IT OUT OF YOUR REPOSITORY AND SORT OF WALK ACROSS TO CHICAGO WHEREVER MY PROFESSOR NOW IS AND GIVE IT TO HIM. I THINK THERE'S PRECEDENT ON BOTH SIDES TO SAY THAT MY RIGHT AS A DONOR DOESN'T STOP WHEN THE CELLS HAVE LEFT MY BODY. I STILL HAVE SOME CONTROL OVER THEM UP TO A CERTAIN POINT.

SECOND THING -- BUT I THINK WE NEED TO KEEP ANONYMIZATION IT IS CONSISTENT WITH THE COMMON RULE, BUT I'M NOT SURE MANY PEOPLE -- SO THERE ARE PHYSICAL HARMS AND THERE ARE PRIVACY HARMS, PHYSICAL HARMS IN TISSUE RESEARCH. THERE ARE NO -- THOUGHT TO BE NO PRIVACY HARMS IF IT'S REALLY DEIDENTIFIED. SO THEN THE QUESTION IS IS IT STILL DEIDENTIFIED IF

IT'S GOT A WHOLE GENOME SEQUENCE ATTACHED?

BUT THERE ARE WRONGS AS WELL AS HARMS IN THE PRIVACY SENSE. AND I THINK INCREASINGLY WHAT WE'RE SEEING IS PEOPLE SAYING, YOU KNOW, IF YOU DEIDENTIFIED THIS AND DO RESEARCH, THAT DOESN'T SOLVE MY OBJECTION. IT'S THE PEOPLE WHO HAVE LEFT-OVER EMBRYOS THAT SAY I DON'T WANT THEM USED FOR EMBRYO RESEARCH, AND RESEARCH SAYS, WELL, WE CAN DEIDENTIFY THEM, AND WE DON'T HAVE TO TELL YOU, AND WE'RE USING THEM. SO WE TEND TO SAY NO, AND THAT'S A SPECIAL EXAMPLE BECAUSE EMBRYOS ARE OF SPECIAL MORAL SIGNIFICANCE TO SOME. BUT I THINK YOU CAN THINK OF A LOT OF OTHER EXAMPLES WHERE PEOPLE OBJECT TO CERTAIN TYPES OF RESEARCH. ANONYMIZING DOESN'T RESOLVE MY OBJECTION. I THINK WE NEED TO -- I THINK WE HAVE TO GIVE A LOT OF DEFERENCE TO THE COMMON RULE BECAUSE IT'S WHAT CONTROLS FEDERALLY FUNDED RESEARCH.

COMMON RULE IS A FLOOR. IT DOESN'T MEAN THAT YOU CAN'T IN ANY INDIVIDUAL CASE OR INSTITUTION OR RESEARCHER OR FUNDER REQUIRE OTHER THINGS. SO I THINK WE HAVE A LOT OF THINGS. NICOLE, YOU'VE BEEN STRUGGLING WITH THIS AS WELL.

DR. LOCKHART: I WOULD AGREE. IN TERMS OF OPTION 3, PURPOSEFUL ANONYMIZATION IN RESPONSE TO A

REQUEST TO WITHDRAW I THINK IS LEGAL, BUT COMPLETELY ETHICALLY UNTENABLE. IF SOMEONE CARES ENOUGH TO TRACK YOU DOWN AND ASK YOU TO STOP USING THEIR TISSUE AND YOU RESPOND TO THAT BY ANONYMIZING SO THAT YOU CAN CONTINUE USE, I THINK THAT'S VERY DISRESPECTFUL. I DON'T REALLY THINK THAT'S A VIABLE OPTION.

I WOULD SAY THAT IDENTIFIABLE SPECIMENS STILL CONSTITUTE HUMAN SUBJECT RESEARCH UNDER THE COMMON RULE IF THEY'RE TRULY IDENTIFIABLE. EVEN IF THEY'RE CODED, IF YOU HAVE THE LINK, SOMEONE HAS THE LINK, AND YOU CAN WITHDRAW THE SPECIMEN, THEN I THINK YOU PROBABLY SHOULD. THAT LINE DOES MAKE SENSE TO ME. AT LEAST IN MY MIND, I AM WILLING TO VIEW TRANSFORMED MATERIALS AS DISTINCT. I THINK FROM THE INTELLECTUAL PROPERTY PERSPECTIVE, THEY WOULD PROBABLY BE CONSIDERED DISTINCT. AND I THINK ANOTHER ETHICAL PRINCIPLE WE CAN THINK ABOUT, AND I DON'T REALLY KNOW PRECISELY WHAT TO CALL THIS, IS HARM TO RESEARCH IN GENERAL.

SO IF YOU CHOOSE FIVE PATIENTS WITH HEART DISEASE TO DEVELOP AN IPSC LINE, AND ONE OF THEM WITHDRAWS, DO YOU HAVE TO DESTROY ALL DOWNSTREAM MATERIALS OR STOP USING ALL DOWNSTREAM LINES? THAT'S NOW 20 PERCENT. THAT HARMS THE OTHER PEOPLE

WHO CONTRIBUTED TO RESEARCH IN SOME WAY TOO, AND YOU COULD HAVE CHOSEN SOMEONE ELSE. YOU COULD HAVE ALLOWED SOMEONE ELSE TO HAVE THAT OPPORTUNITY. IT DOES MAKE SENSE TO ME TO DRAW THE LINE AT BEING ABLE TO WITHDRAW PRIMARY TISSUE, BUT NOT TRANSFORMED MATERIALS.

MS. FEIT: MAYBE THIS IS NAIVE ON MY PART, COULD BE, BUT IT SEEMS LIKE WE MAY BE MAKING A BIG MISTAKE WITH EVEN DISCUSSING WITHDRAWAL AS AN OPTION. BECAUSE IN ORGAN TRANSPLANT, IF I GIVE UP A KIDNEY AND SOMEBODY TURNS INTO AN ALCOHOLIC AND I WANT MY KIDNEY BACK, IT DOESN'T WORK THAT WAY.

DR. LOCKHART: THAT'S ENTIRELY DIFFERENT.

MS. FEIT: IT IS AND IT ISN'T. I THINK WE'RE MAKING IT DIFFERENT WITH THE RULES WE SET UP BECAUSE IT'S STILL TISSUE, IT'S PART OF A PERSON'S BODY, AND THEY GAVE IT UP FOR A BENEFICIAL PURPOSE TO SOMEBODY ELSE. AND NOWHERE IN ANY OF THOSE CONSENTS DOES IT SAY AT ANY TIME YOU CAN WITHDRAW THE ORGAN. AND I THINK -- SO SHOULDN'T WE START TALKING ABOUT WHY DO WE HAVE -- IF SOMEBODY WANTS TO TALK ABOUT, WELL, I WANT THE OPTION TO TAKE THAT BACK, I THINK RIGHT AWAY WE HAVE THE RISK OF HAVING THAT HAPPEN BECAUSE WE CAN'T DREAM UP ALL THE POSSIBLE CIRCUMSTANCES THAT CAN COME UP THAT THAT

PERSON WILL NOT LIKE OR NOT WANT. AND THAT WILL CHANGE IN TIME. SO I'M JUST SAYING THAT AS A RELATIVE BECAUSE TO ME IT FEELS THE SAME.

CHAIRMAN LO: SO, MARCY, ONE OTHER WAY OF FRAMING YOUR ANALOGY IS TO SAY THAT ONCE YOU'VE DONATED AN ORGAN FOR TRANSPLANT AND IT'S BEEN TRANSPLANTED, THAT RECIPIENT HAS REALLY RELIED ON YOU. SO CERTAINLY IF IT'S SOMETHING LIKE A LIVER, TO BE ABLE TO WITHDRAW IT WOULD BE FATAL. SO I THINK THAT'S THE EXTREME EXAMPLE OF THE JUSTIFIABLE RELIANCE. HOWEVER, I WOULD IMAGINE, I WOULD FIND IT HARD TO BELIEVE A TRANSPLANT TEAM WOULD SAY IF I GIVE CONSENT OR, I GUESS, IF I GIVE CONSENT FOR SOME OF MY FAMILY AND I CHANGE MY MIND BEFORE THEY HARVEST THE ORGAN, THEY SAY, WELL, TOO BAD.

CERTAINLY IF I WERE A LIVING DONOR AND DECIDED I ACTUALLY DIDN'T WANT TO GIVE MY RIGHT LOBE OF MY LIVER TO --

MS. FEIT: I JUST BRING IT UP BECAUSE I THINK WE'VE INSERTED WITHDRAWAL. MAYBE THESE PEOPLE SELF-SELECT OUT. MAYBE THEY AREN'T DONORS BECAUSE THEY HAVE ALL THE PREBIASED SITUATIONS THEY MAY THINK OF IN THE BEGINNING. I DON'T KNOW HOW MANY PEOPLE THAT WOULD REPRESENT. THOSE OF YOU WHO WORK WITH TISSUE HARVESTING AND CELL HARVESTING WOULD

KNOW MORE HOW MANY DONORS WOULD YOU LOSE IF YOU SAID YOU'RE IN THE PROGRAM AND YOU GIVE -- AND THERE IS NO WITHDRAWAL BECAUSE WHAT'S USED UNDER THESE GUIDELINES. I DON'T KNOW --

CHAIRMAN LO: LET ME JUST BE CLEAR. WE HAVEN'T INSERTED THIS. THIS IS FEDERAL REGULATION, THAT YOU HAVE THE RIGHT TO WITHDRAW FROM RESEARCH. RESEARCH IS REALLY DIFFERENT.

MS. LANSING: BUT YOU'RE BRINGING UP A VERY INTERESTING POINT. I TEND TO -- I KNOW THEY'RE DIFFERENT, BUT I TEND TO REALLY UNDERSTAND WHAT YOU'RE SAYING. AGAIN, AND AGAIN, I GO BACK TO FIRST WHEN WE WERE PROTECTING THE PATIENT AND NOW I'M REALLY TRYING TO PROTECT THE SCIENTIST. THERE IS EXISTING LAWS THAT SAY THAT. WE'RE NOT GOING TO CHANGE THAT. BUT TO GO BEYOND WHAT'S EXISTING, IT SEEMS TO ME TO BE DOING SOMETHING THAT CAN REALLY HARM SCIENCE. AND WE AT CIRM, AND THIS IS SOMETHING THAT, BERNIE, YOU HAVE BROUGHT UP, SO I DON'T WANT TO TAKE CREDIT FOR THIS, WE AT CIRM COULD DECIDE NOT TO TAKE ANYONE THAT -- WE COULD SAY YOU CAN'T OPT OUT ONCE YOU'RE DOING IT. WE COULD DO THAT AT CIRM TO PRESERVE WHATEVER SCIENCE WE WANT.

WE COULD, GOING BACK TO THE FIRST ISSUE, SAY WE'RE NOT TAKING -- WE'RE DOING A LIMITED AMOUNT

OF RESEARCH. BERNIE, YOU BROUGHT THIS UP. WE COULD SAY WE'RE NOT TAKING ANYONE WHO WON'T LET US USE THE LINES FOR ALL DISEASES. WE HAVE THE RIGHT TO DO THAT. THE PATIENT DOESN'T HAVE TO DO IT, AND I UNDERSTAND THAT POSITION.

MS. FEIT: THAT IS THE ANALOGY I WAS TRYING TO MAKE. CAN WE MAKE THAT DECISION?

MS. LANSING: WE HAVE LIMITED AMOUNT OF WORK THAT WE CAN DO, AND WE CAN DECIDE THAT WE WANT TO MAXIMIZE IT TO THE MOST.

MS. FEIT: I HONESTLY, AFTER LISTENING FOR THIS A COUPLE HOURS TODAY, DON'T KNOW HOW YOU'RE EVER GOING TO TRACK THAT DOWNSTREAM FIVE, TEN YEARS FROM NOW. HOW ARE YOU GOING TO TRACK THAT? YOU ARE GOING TO FAIL. SOMEWHERE ALONG THE LINE, YOU'RE GOING TO SET YOURSELF UP TO FAIL. AND WE'RE ALL GOING TO GO TO DR. TAYLOR AND SAY WHY DID YOU LET IT GO? GEE, THAT WAS FIVE YEARS AGO. I DON'T REMEMBER. THIS DOESN'T SEEM LIKE IT'S GOING TO WORK.

GOING BACK TO WHAT NICOLE SAID, DON'T SAY YOU ARE GOING TO DO SOMETHING AND NOT DO IT.

DR. FEIGAL: THE ONLY ANALOGY, IT'S A LITTLE BIT DIFFERENT, BUT I WANT TO BRING IT UP. A CLINICAL TRIAL YOU COLLECT BIOLOGICAL SPECIMENS.

OKAY. IT MAY BE DONE UNDER A REGULATORY FRAMEWORK. YOU'RE COLLECTING THEM TO HELP ANSWER A QUESTION AND THE PATIENT ENROLLED, AND THEN MAYBE AT X POINT PATIENT DOESN'T WANT TO CONTINUE THAT TRIAL. THAT'S THEIR RIGHT TO STOP OUT OF ANY FURTHER INTERACTIONS OR TREATMENT. I THINK WHAT WOULD BE A MISTAKE, WHICH IS NOT DONE, IF SOMEBODY ENTERED THE TRIAL AND THEY HAVE SPECIMENS THAT NEED TO HAVE CERTAIN THINGS LOOKED AT BEFORE THEY SAID I DON'T WANT TO BE IN THE TRIAL ANYMORE, BUT YOU HAVEN'T ACTUALLY DONE THE LABORATORY ASSESSMENT, YOU DON'T NOT DO IT. IN A CLINICAL TRIAL YOU ACTUALLY DO PERFORM THE INFORMATION THAT'S NEEDED FROM THOSE SPECIMENS.

SO THE FACT THAT YOU DIDN'T DO THAT LAB TEST AT THE TIME, THE SPECIFIC TIME THE SAMPLE WAS OBTAINED, YOU COULD ARGUE THE TECHNICALITIES OF IT. BUT IF YOU LOOK AT THE BIGGER PICTURE, MISSING DATA IS ONE OF THE BIGGEST ISSUES IN RESEARCH THAT CAUSE QUESTIONS NOT TO BE ANSWERED IN A VALID WAY. AND YOU'RE NOT JUST IMPACTING THAT ONE INDIVIDUAL. YOU'RE IMPACTING THE WHOLE PROGRAM.

SO I DO THINK IT'S A SPECIAL CASE, BUT JUST LIKE TO HAVE THAT COME UNDER THE RADAR, UNDER THE ILLUMINATION TOO OF WHAT WE'RE DOING.

MS. LANSING: I THINK THERE IS A

DIFFERENCE UNLESS I'M UNDERSTANDING CLINICAL TRIALS INCORRECTLY. A PATIENT IS PARTICIPATING IN CLINICAL TRIALS. WHATEVER IS BEING DONE WITH THEIR TISSUE WHILE THEY'RE PARTICIPATING I THINK CAN CONTINUE, BUT THE PATIENT, THAT'S WHERE YOU DISAPPEAR, THE PATIENT DISAPPEARS, I MAY BE IN CLINICAL TRIALS AND SAY THIS IS JUST TOO TOXIC. I CAN'T TAKE THIS ANYMORE. I DON'T WANT THE DRUG ANYMORE. OF COURSE, THAT'S LIKE SAYING I'VE DECIDED NOT TO DONATE. BUT WHATEVER HAS BEEN -- WHATEVER RESEARCH IS BEING DONE ON THE CELL OR THE TISSUE, WHATEVER, I THINK THAT SHOULD BE ALLOWED TO CONTINUE.

DR. FEIGAL: IT IS. IT IS, BUT WHAT I'M SAYING IS THE ANALOGY IS THE SPECIMEN WAS COLLECTED, BUT THE TEST WAS NOT DONE YET. WE DO THE TEST.

MS. LANSING: THAT'S WHAT I'M SAYING. I AGREE.

DR. FEIGAL: I'M SAYING THERE'S SOMEWHAT OF AN ANALOGY THERE.

DR. ROBERT TAYLOR: IT'S KIND OF LIKE STEVE'S OBJECT AND SUBJECT. THAT WOULD BE A REALLY CLEAN WAY TO DO IT IF WE COULD. I REALLY LIKE THAT ANALOGY. I DON'T KNOW THAT WE CAN GET AWAY WITH THAT LEGALLY.

DR. ROBERTS: IF IN THE CLINICAL TRIAL,

THOUGH, THAT PATIENT WHO WITHDREW SAID I ALSO WANT MY TISSUE BACK, WHAT HAPPENS THEN?

MS. LANSING: YOU CAN'T GET IT BACK.

DR. ROBERTS: YOU CAN'T GET IT BACK.

MS. LANSING: THAT'S WHY I'M SAYING WHY WOULD WE DO A STRONGER THING? WHY WOULD YOU DO SOMETHING STRONGER THAN WHAT'S ALREADY BY THE LAW? YOU ARE GOING TO REALLY HARM YOUR SCIENTISTS.

DR. KIESSLING: I WANT TO COME BACK TO THE WHOLE TIME THING. I THINK THAT THERE SHOULD BE A PERIOD OF TIME AFTER YOU'VE DONATED TISSUE IN WHICH YOU HAVE A TIME TO REFLECT, AND THEN AFTER THAT IT'S DONE.

MS. LANSING: THAT WOULD HAVE TO BE A SHORT PERIOD OF TIME.

DR. KIESSLING: RIGHT. A MONTH, TWO WEEKS.

MS. LANSING: THEN THAT WOULD MEAN THAT YOU COULDN'T START ON ANYTHING FOR A MONTH OR TWO WEEKS. I DON'T KNOW WHAT HAPPENS TO THE MATERIAL.

CHAIRMAN LO: I THINK THE LAWYERS ARE GOING TO HAVE HELP ME OUT HERE, BUT I THINK WE HAVE AN EXISTING LEGAL FRAMEWORK WHERE WE CAN'T MAKE PEOPLE SIGN AWAY THEIR RIGHTS TO BE IN THE RESEARCH PROJECT. WE HAVE TO GIVE PEOPLE THE RIGHT TO

WITHDRAW.

DR. FEIGAL: NOBODY IS SAYING THE PERSON CAN'T WITHDRAW. NOBODY IS SAYING THAT.

CHAIRMAN LO: I ACTUALLY THINK I WOULD LIKE TO ACTUALLY GET A LEGAL ANALYSIS OF THAT AS TO WHETHER -- THERE MUST BE CASE LAW ON THIS.

DR. FEIGAL: WHAT'S YOUR SPECIFIC QUESTION, BERNIE?

CHAIRMAN LO: WHETHER A PATIENT --

DR. FEIGAL: ON A CLINICAL TRIAL.

CHAIRMAN LO: -- LOSES THE RIGHT TO WITHDRAW SPECIMENS BECAUSE CATALONA CLEARLY IN THE APPELLATE DECISION SAID, NO, YOU'VE GOT THAT RIGHT. SO I THINK THERE'S GOT TO BE AT LEAST SOME PRECEDENT ON THE SIDE OF, NO, YOU MAY WITHDRAW TISSUE. AND THAT WAS A BIOBANK. PROSTATE TISSUE COLLECTED FOR RESEARCH.

MS. FEIT: AND WE SET UP A BANK THAT DOESN'T ACKNOWLEDGE THAT. THAT'S THE QUESTION.

DR. PARTICK TAYLOR: BERNIE, TO SOME DEGREE STATE'S INTERPRETATIONS VARY. BUT THE RECOVERY OF THE SPECIMEN VERSUS STOPPING RESEARCH ON THE SPECIMEN AND USE OF DATA ON IT PROSPECTIVELY COME TO BE SOMEWHAT BLURRED. SO IF SOMEBODY DOESN'T WANT WORK DONE, THEN IT'S LESS AN ISSUE OF CAN YOU

FIND THE LITTLE THING AND GIVE IT BACK TO THEM INTACT BY REGISTERED MAIL. IT'S CAN YOU ACTUALLY MAKE SURE THEY DON'T HAVE ACCESS TO THIS DATA.

THERE'S REALLY TWO WAYS THAT CAN HAPPEN. ONE WAY IS ACTUALLY WHEN THROUGH INABILITY TO TRACE IT, THEY ACTUALLY REALLY DON'T HAVE ACCESS TO IT. THEN THE STRUCTURE OF THE THING AND ENSURING IN THE SENSE THAT TO A LARGE EXTENT THE PERSON'S WISHES ARE OBSERVED.

THE OTHER WAY IS ACTUALLY IF THEY ACTUALLY CAN. THROUGH GOOD FAITH EFFORTS, THEY KNOW WHAT IT IS AND THEY SEE IT AND YOU CAN REALLY STOP RESEARCH ON IT. BUT THE RECONCILIATION OF RESEARCH ON THE THING AND THE DATA THAT RESULTS, THERE'S ALWAYS BEEN SOME BLURRING AND IT'S GETTING BLURRIER WITH DNA STUFF.

CHAIRMAN LO: AGAIN, JUST TO SORT OF MAKE SURE I UNDERSTAND. SO IS IT -- WOULD YOU SAY THAT THERE IS NO CLEAR LEGAL CONSENSUS THAT IN A RESEARCH PROJECT, ONCE YOU'VE AGREED TO THE RESEARCH, YOU MAY NOT STOP TESTS OR THINGS BEING DONE TO THE SAMPLE BEFORE IT'S BEEN TRANSFORMED, ASSUMING THEY CAN FIND IT?

DR. PATRICK TAYLOR: I THINK THAT IF THINGS ARE ORGANIZED SO THAT SAMPLES REMAIN

IDENTIFIABLE AND SOMEONE WANTS TO WITHDRAW FROM ONGOING WORK, THEN THE EFFECT OF A REVOCATION IS TO STOP RESEARCHERS IN THAT CIRCUMSTANCE WITH THAT FEASIBILITY PATHWAY FROM CONTINUING TO USE DATA IN THEIR STUDIES DERIVED FROM THAT SAMPLE. THAT'S LITERALLY WHAT IT MEANS. AND THAT WOULD BE THE IRB'S REMEDY, OF COURSE. IT'S NOT AS IF SOMEONE CAN SEND TO THE SHERIFF TO MAKE SURE THAT THE SAMPLE IS THERE. THAT'S WHAT IT MEANS.

ON THE OTHER HAND, IF THE DATA HAS ALREADY BEEN SET UP IN A WAY THAT'S FULLY AGGREGATED, SO IT'S IMPOSSIBLE, THEN THE REMEDY IS REALLY LIMITED TO NOT BEING ABLE TO DO ANYTHING. NO ONE IS GOING TO SAY, OKAY, GO BACK AND DO ALL THIS WORK. AND THE EXTENT TO WHICH SOMEONE CAN ACTUALLY BREAK CODE IS PROBABLY A PRODUCT OF THE IRB'S TOLERANCES.

BUT I HAVE NEVER SEEN A SITUATION WHERE THE RIGHT TO REVOKE WAS FARTHER THAN THAT IN THE CONTEXT OF A BASIC SCIENCE ORIENTED BANK. INTERVENTIONAL STUDIES ARE SO DIFFERENT. OF COURSE, THIS STRUCTURE WAS SET UP WITH INTERVENTIONAL STUDIES IN MIND WHERE THE REAL MEANING OF IT WAS STOP INTERVENING ON MY BODY. IT WAS SORT OF DERIVED FROM THE CLINICAL RIGHT TO REVOKE CONSENT.

CHAIRMAN LO: YOU IN YOUR ROLE AS HOSPITAL

ATTORNEY IN A RESEARCH INSTITUTION WHO ARE PRESENTED THE CASE OF SOMEONE WHO WAS A RESEARCHER WHO WAS FACED WITH A CLEAR WITHDRAWAL OF PARTICIPATION AND RESEARCH FROM A SUBJECT AND SPECIFICALLY SAID I UNDERSTAND THE LINES HAVE BEEN DERIVED, THE DATA FROM THAT, THAT'S GOING TO CONTINUE, BUT I JUST DON'T WANT YOU TO CONTINUE TO USE MY ORIGINAL SPECIMEN IN ANY OTHER WAYS, BUT YOU CAN CONTINUE TO USE THE IPS LINE WITH THOSE FOUR OTHER DONORS.

DR. PATRICK TAYLOR: THEY WOULD ACTUALLY THINK THAT DONOR WAS MAKING A REQUEST REMARKABLY CONSONANT WITH WHAT THE LAW ACTUALLY PROVIDES TO THE EXTENT THAT THEIR INDIVIDUAL SAMPLE REMAINS IDENTIFIABLE TO THE EXTENT IT HAS. THERE'S A VARIETY OF STRUCTURES HERE.

CHAIRMAN LO: YOU WOULD ADVISE THEM TO, IF THEY CAN FIND THE SAMPLE, TO WITHDRAW IT FROM FURTHER RESEARCH?

DR. PATRICK TAYLOR: TO MAKE SURE IT'S NOT INCLUSION FOR THE RESEARCH STUDIES, YEAH. I WOULDN'T SAY THEY HAD TO NECESSARILY GO -- IF ALL THE OTHER REFRIGERATOR FROZEN SAMPLES ARE OFF SOMEWHERE ELSE AND NO ONE IS EVEN USING THEM, YOU WANT TO MAKE SURE THE RIGHT IS RESPECTED, BUT THERE ARE A LOT OF WAYS OF DOING THAT.

DR. LOCKHART: IF I CAN JUST ADD ONE OTHER MINOR THING WHICH MAY OR MAY NOT BE A CONSEQUENCE TO YOU. IF YOU ARE GOING TO BE OR THIS BANK WOULD BE STORING TISSUE SAMPLES, IT MAY BE POSSIBLE THAT IN THE FUTURE PATIENTS MAY WANT THEIR SAMPLES BACK FOR THEIR OWN CLINICAL PURPOSES. THAT'S BECOMING MORE COMMON NOW, ESPECIALLY WITH THE MOVE TOWARDS PERSONALIZED MEDICINE, THAT MAYBE A PATIENT HAD A TUMOR SAMPLE OR SOME SAMPLE REMOVED AT SOME POINT. THEY NOW NEED IT TO ENTER A NEW CLINICAL TRIAL OR SOMETHING. IT HAS TO BE A FROZEN SPECIMEN. THE ONLY FROZEN SPECIMEN IS IN THE BIOBANK.

SO YOU MAY ALSO WANT TO CONSIDER WHAT YOU WOULD DO IN THAT INSTANCE WHERE A PATIENT IS WANTING A SPECIMEN, NOT TO WITHDRAW BECAUSE THEY DON'T WANT TO PARTICIPATE IN RESEARCH, BUT BECAUSE THEY NEED THAT SPECIMEN FOR THEIR OWN CARE. THAT'S ALSO SOMEWHAT UNCOMMON, BUT I WOULD THINK IT MIGHT BECOME MORE AND MORE COMMON.

DR. ROBERTS: IT SOUNDS TO ME LIKE IT MAY BE POSSIBLE TO DRAW A LINE BETWEEN THE FURTHER USE OF THE SPECIMEN ITSELF, EITHER THE USE OF IT OR THE ACTUAL PHYSICAL CUSTODY OF IT. SO THE DONOR RETAINS THE RIGHT TO TAKE BACK THE SPECIMEN AND THE RIGHT TO STOP ANY FURTHER USE OF THE SPECIMEN. BUT IF IT'S

ALREADY BEEN TRANSFORMED, ALREADY THE LINES HAVE BEEN DERIVED, THAT THEN THE RELIANCE ON IT, THE HARM THAT WOULD COME TO THE RESEARCHERS AS A RESULT OF STOPPING THAT RESEARCH OVERRIDES, THEN, THE RIGHTS, THE INTERESTS THAT THE DONOR HAS IN RETAINING CONTROL OVER THE USE OF WHAT'S BEEN DERIVED -- AND THE PROVIDED FOR ALL OF THIS IS THAT ALL OF THIS WAS IN THE INFORMED CONSENT PROCESS, AND THE DONOR WAS TOLD THAT THIS IS WHAT DISTINCTION WOULD BE MADE AND WHAT WOULD HAPPEN AND WHAT THE ANSWER WOULD BE TO A FUTURE REQUEST TO WITHDRAW.

DR. ROBERT TAYLOR: I ARGUED AGAINST THAT A LITTLE BIT EARLIER, BUT IT WAS REALLY NICOLE'S COMMENT ABOUT PATENT LAW SUPPORTING THE IDEA OF ONCE YOU'VE ACTUALLY TRANSFORMED THESE CELLS, YOU CREATED SORT OF AT LEAST A LEGALLY NEW ENTITY. THAT SORT OF RESONATES WITH ME A LITTLE BIT AS ANOTHER WAY OF KIND OF FORMING SOME LINE OF DEMARCATION. SO I ACTUALLY LIKE WHERE YOU GUYS ARE GOING WITH THIS.

DR. ROBERTS: I'M NOT SURE IF I AGREE. I'M JUST STATING I THINK THERE IS A PRINCIPLED WAY. ALTHOUGH I WOULD ALSO SAY, THOUGH, THAT THE WHOLE ISSUE AT LEAST OF GENE PATENTING IS STILL UP IN THE AIR. IT'S BEFORE COURTS NOW. IT'S BEING LITIGATED, AND THERE'S QUITE A CONTROVERSY AROUND THAT.

DR. ROBERT TAYLOR: THAT AT LEAST IS NOT BECAUSE IT'S NOT REALLY -- THE TRANSFORMATIONAL PROCESS, I GUESS, SEEMS TO BE AN ARGUABLE STEP.

DR. ROBERTS: IT IS. IT IS. I'M JUST SAYING I DON'T THINK THAT THE CURRENT STATE OF PATENT LAW DEFINITIVELY SAYS THAT THE -- THAT DEFINITIVELY PROVIDES THE ANSWER FOR GENE SEQUENCING.

CHAIRMAN LO: WHERE DO WE STAND?

DR. PATRICK TAYLOR: EVEN APART FROM THE PANEL ON STUFF, IT'S REMARKABLE HOW DISCIPLINES DEVELOP THEIR OWN LANGUAGE, THEIR OWN CULTURE. SO WITHIN TECHNOLOGY TRANSFER, THESE TERMS OF DERIVATIVES AND MODIFICATIONS ACTUALLY HAVE PRETTY WELL-ESTABLISHED MEANINGS UNDER WHICH PEOPLE AGREE, WHICH IS, I THINK, IMPORTANT. IF THEY HAVE DISPUTES, THEY CAN AVOID THEM OR RESOLVE THEM RAPIDLY BASED ON SORT OF THEIR LOOK, WHETHER THE CELLS HAVE BEEN MODIFIED OR OTHERWISE. IT SEEMS TO ME THERE'S A TREMENDOUS ADVANTAGE FOR EVERYBODY IN RELYING ON THOSE KINDS OF DEFINITIONS WHICH DO EXIST STARTING ACTUALLY FROM THE ORIGINAL VARMIS ERA UNIFORM BIOLOGICAL MATERIAL TRANSFER AGREEMENT. AND SEEING EVERYTHING ALIGNED THERE SO WE DON'T CREATE SOME CATASTROPHE FOR RESEARCHERS WHERE PEOPLE ARE

REVOKING ACROSS OTHER STRUCTURAL LINES THAT ARE IMPORTANT TO THE TRANSLATION OF RESEARCH INTO PRACTICE.

CHAIRMAN LO: I'M HEARING A NUMBER OF PEOPLE SAYING THAT FOR A COMBINATION OF REASONS, WHICH MAY BE PRECEDENT, THAT THIS IS CONSISTENT WITH IP AND TECH TRANSFER AGREEMENTS, OR THAT THERE'S SOME SORT OF ATTEMPT TO HAVE SOME SORT OF PRINCIPLED EXPLANATION, THAT DRAWING THE LINE BETWEEN, I GUESS, WHAT YOU CALLED, GEOFF, THE PRIMARY SAMPLE THAT WAS DONATED VERSUS A MODIFIED SAMPLE OR DERIVATIVE, THAT WE WILL ALLOW WORK WITH THE DERIVATIVES AND MODIFICATIONS TO CONTINUE EVEN DESPITE AN EXPLICIT REQUEST FROM THE PATIENT TO WITHDRAW FROM RESEARCH.

BUT AM I HEARING THAT WE WOULD ALLOW THE PATIENT TO SAY IF YOU STILL HAVE THAT PRIMARY SAMPLE AND IT'S JUST FROZEN, YOU CAN'T THEN CONTINUE TO PROCEED WITH NEW RESEARCH ON THAT SPECIMEN?

DR. ROBERTS: AND I CAN GET IT BACK.

CHAIRMAN LO: YOU MAY EVEN GET IT BACK.

DR. FEIGAL: CAN I ASK YOU A QUESTION? SORRY TO INTERRUPT. BUT I'M TRYING TO LOOK -- I AM LOOKING AT THE PRECEDENTS WITH CLINICAL TRIALS. I KNOW WE'RE FOCUSED ON BIOBANKS. PRESUMABLY THE PRINCIPLE IS WHAT YOU'RE LOOKING AT OF WHY YOU'RE

DOING IT. SO I DO KEEP ON COMING BACK TO A CLINICAL TRIAL WHERE MORE AND MORE WE'RE COLLECTING BIOSPECIMENS AS PART OF IT. AND I DON'T THINK WE WANT AT THE END OF IT THAT SOMEBODY CAN RECLAIM SPECIMENS THAT WERE DONATED AS PART OF THE NECESSARY PART OF THE CLINICAL TRIAL, AND THEN BASICALLY YOU LOSE ALL THAT INFORMATION IF YOU'RE DOING THE SAME PRINCIPLE, THAT SOMEBODY HAS THE RIGHT TO REMOVE THEIR PRIMARY SPECIMEN. MAYBE IT'S GETTING TOO TANGENTIAL AND MAYBE JUST FOCUS ON BIOBANKS IS FINE, BUT I DO HAVE TO THINK ABOUT WE'RE COLLECTING BIOSPECIMENS IN THE CONTEXT OF CLINICAL TRIALS ALL THE TIME.

DR. ROBERT TAYLOR: IF I COULD ASK IN A CLINICAL TRIAL, IF I'M IN A CLINICAL TRIAL AND WE'RE SEVEN-EIGHTHS OF THE WAY THROUGH THE TRIAL AND I WITHDRAW, I'M SORT OF A DROPOUT FROM YOUR TRIAL, YOU ARE GOING TO USE MY BIOCHEMICAL DATA, THOUGH, IN YOUR ANALYSIS OF THAT TRIAL? I'M DROPPING OUT OF THE CLINICAL END POINTS OF YOUR TRIAL. ARE YOU ACTUALLY -- IS IT SCIENTIFICALLY, FRANKLY, RIGOROUS TO USE MY BIOCHEMICAL DATA THAT WERE COLLECTED?

DR. FEIGAL: IT DEPENDS ON WHAT THE TRIAL IS. I MEAN WHAT IF IT WAS PK? CLINICAL TRIALS ARE ALL DIFFERENT. BUT IT DEPENDS. MAYBE I DON'T NEED

THAT FINAL OUTCOME INFORMATION LONG TERM. MAYBE IT'S RELATIVELY SHORT AND YOU DROPPED OUT FOR A VARIETY -- YOU COULDN'T GET A CAR TO GET YOU TO THE CLINIC, WHATEVER. THERE WERE REASONS. SO I'M JUST POINTING IT OUT IS WE'RE MAKING THIS SPECIFIC FOR BIOBANKS, WHICH IS FINE, BUT I'M ALSO THINKING OF THESE OTHER SCENARIOS WHERE WE'RE COLLECTING BIOSPECIMENS.

CHAIRMAN LO: ELLEN, COULD YOU -- MAYBE THIS ISN'T THE TIME, BUT IT WOULD BE INTERESTING TO US, I THINK, TO LOOK SPECIFICALLY AT HOW THAT IS PRESENTED AND ENFORCED IN THE CLINICAL TRIAL SETTING. IS THERE LANGUAGE IN THE CONSENT FORM? DO IRB'S EXPLICITLY APPROVE THAT? OR IS IT JUST SOMETHING THAT IS DONE WITHOUT SORT OF -- IS THERE AN EXPLICIT RATIONALE -- IS THERE EXPLICIT RECOGNITION THAT WHEN I SAY I'M WITHDRAWING FROM A CLINICAL TRIAL, MY SPECIMENS MAY CONTINUE TO BE USED FOR WHATEVER THE PURPOSE OF THE TRIAL, AND IS THERE A PLACE WHERE THE RATIONALE FOR THAT IS ACTUALLY WRITTEN OUT? BECAUSE THAT WOULD BE HELPFUL FOR US TO LOOK AT.

DR. LOMAX: IT'S PART OF THE FDA REQUIREMENT OF BEING IN A CLINICAL TRIAL. IT'S WITHIN THE POLICY OF RETAINING DATA AND TRIAL

INTEGRITY. THAT'S THE SORT OF GENESIS. SO IT'S NOT ABOUT WITHDRAWAL SO MUCH. IT'S ABOUT DATA RETENTION IN THE CONTEXT OF THE TRIAL.

CHAIRMAN LO: I THINK IT WOULD BE HELPFUL TO ACTUALLY LOOK AT THE LANGUAGE AND ASK PAT AND DOROTHY.

DR. FEIGAL: PATIENTS, THE PERSON ALWAYS HAS THE RIGHT TO WITHDRAW CONSENT, AND IT'S EITHER PARTIAL OR COMPLETE. AND WHERE YOU ALWAYS GO THROUGH SOME CONUNDRUMS, DOES THAT MEAN I CAN'T LOOK AT A DEATH REGISTRY, OR DOES IT MEAN I JUST CAN'T GO BACK TO THE MEDICAL RECORD?

CHAIRMAN LO: THEY'RE NOT A SUBJECT ANYMORE. SO I'D LIKE TO ACTUALLY LOOK AT HOW THE FDA AND SEE IF THERE'S A CROSS MATCH BETWEEN THAT. THE PROBLEM IS EVERYONE TALKS ABOUT THE RIGHT TO WITHDRAW AND DOESN'T SPECIFY WHAT THAT MEANS. SO UNLESS IT'S ACTUALLY SPECIFIED, WE GET INTO THESE SITUATIONS. I THINK IT WOULD BE VERY IMPORTANT TO LOOK AT THAT FDA LANGUAGE.

DR. ROBERTS: JUST ONE OTHER REFINEMENT OF IT. A PATIENT CAN WITHDRAW FROM THE CLINICAL TRIAL, AS YOU SAID. THEY JUST CAN'T GET TO IT, SO THEY JUST BACK OUT. THAT DOESN'T NECESSARILY MEAN THAT THEY THEN REQUEST THAT YOU STOP DOING RESEARCH ON

THE SPECIMENS THAT THEY DONATE. SO THIS WOULD BE NOT JUST A CASE OF WITHDRAWAL. DOES THAT MEAN THAT THE RESEARCHERS HAVE TO STOP DOING RESEARCH ON THE SPECIMENS THAT ARE LEFT BEHIND? BUT SPECIFICALLY IF THE SUBJECT REQUESTS THAT YOU STOP DOING RESEARCH ON THE SPECIMENS, DOES THE RESEARCHER HAVE TO STOP?

DR. FEIGAL: I DIDN'T MEAN TO TAKE US DOWN THIS PATHWAY, BUT THERE'S A LOT OF THINGS WE COULD TALK ABOUT OFFLINE, BUT THERE'S DIFFERENT NUANCES.

CHAIRMAN LO: LET'S DO THIS OFFLINE AND TRY AND SEE TO WHAT -- WE'RE COME UP WITH ANALOGIES. AS ANY LAW PROFESSOR KNOWS, THE WHOLE QUESTION IS CAN WE DISTINGUISH THE CASE WE'RE TALKING ABOUT FROM THE OTHER CASES THAT WE'RE TALKING ABOUT, AND DOES THE REASONING CARRY OVER EVEN IF THE CASE IS DISTINCT?

SO I'M TRYING TO -- SO I THINK I'M NOT HEARING ANYONE OBJECT TO A PATIENT WITHDRAWING IN THE SENSE OF ONE AND TWO. I THINK I'M HEARING AGREEMENT THAT EVEN IF YOU WITHDRAW, FIVE CONTINUES. AND I GUESS THREE, YOU'RE ALLOWED TO WITHDRAW FROM ONE, TWO, AND -- ONE AND TWO. YOU'RE NOT ALLOWED TO SORT OF WITHDRAW IN THE SENSE OF FIVE. AND I TAKE IT WE'RE STILL NOT DECIDED ON FOUR. AND I THINK, I'M NOT SURE THAT WE HAVE AGREEMENT ON WHETHER IN

THE FACE OF AN EXPLICIT REQUEST TO WITHDRAW, IT'S OKAY TO ANONYMIZE AND THEN CONTINUE.

BUT CERTAINLY AT THOSE EXTREMES, WHICH I THINK ARE THE ONES THAT ARE MOST LIKELY TO HAPPEN, IT STRIKES ME THAT WE HAVE SOME AGREEMENT. I THINK THIS IS -- THREE AND FOUR TO ME ARE WHERE WE NEED MORE INFORMATION AND SOME MORE DISCUSSION BASED ON THAT.

MS. ISASI: CAN I ASK A QUESTION? A QUESTION WAS POSED FOR US FOR SOME STEM CELL BANKS WHERE THE ISSUE OF, OKAY, YOU WITHDRAW THE PRIMARY SAMPLE AND YOU ANONYMIZE THE SAMPLE, NOT FOR THE CONTACT WITH THE DONOR, THAT DATA IS GONE, WHAT HAPPENS WITH DATA ASSOCIATED IN THE CASE OF STEM CELL LINE, IPSC LINE, FOR EXAMPLE, THAT IS PUBLISHED IN A PUBLICLY AVAILABLE DATABASE?

CHAIRMAN LO: I THINK WE'RE SAYING YOU CAN'T WITHDRAW TRANSFORMED MATERIALS.

MS. ISASI: INCLUDING THE DATA BECAUSE SOME DONORS WILL UNDERSTAND THAT IT'S JUST THE LINE THAT KEEPS GOING IMMORTALIZED TO DIFFERENT INSTITUTIONS, BUT THEY DISCONNECT WITH THE DATA ASSOCIATED WITH THE LINE.

CHAIRMAN LO: SO I THINK WHAT WE'RE REALLY -- WE'RE CLEARLY ALLOWING PEOPLE TO WITHDRAW

IT IF YOU HAVEN'T DONE ANYTHING TO MY SPECIMEN OTHER THAN FREEZE IT, I HAVE THE RIGHT TO SAY STOP THERE, DON'T DO ANYTHING FURTHER. ONCE IT'S BEEN TRANSFORMED, BOTH THE SPECIMEN AND THE DATA THAT GO WITH IT CAN'T BE REVOKED.

DR. ROBERT TAYLOR: SO WE'RE GOING TO SAY THAT ABOUT THE DATA TOO BECAUSE THAT SEEMS TO ME TO BE ANOTHER -- THE CLINICAL DATA ARE THAT PATIENT'S, THAT SUBJECT'S PERSONAL, PRIVATE, UNTRANSFORMED INFORMATION. SO --

CHAIRMAN LO: I WAS REFERRING IN THE SENSE IF IT'S BEEN USED IN A PUBLICATION SO THERE'S A CORRELATION BETWEEN MY BAD CLINICAL OUTCOME AND A CERTAIN CHARACTERISTIC ON MY LINE, I CAN'T SAY I WANT YOU TO ERASE THAT PART OF THE DATA. WHAT'S DONE IS DONE.

DR. ROBERT TAYLOR: YOU CAN DELETE -- I DON'T KNOW THAT WE WANT TO, BUT I'M JUST SORT OF ARGUING THAT DELETING A DATABASE, A PATIENT'S PERSONAL HEALTH DATABASE FROM THE COMPUTER AT THE TIME THAT THEY WITHDRAW FROM THE STUDY, THAT COULD BE DONE AT ANY TIME, WHETHER THEY'RE 1, 2, 3, 4, OR 5. I'M NOT SURE THAT THE 5, IF WE BUY THAT 5 IS SOMEHOW -- WE CAN'T REEL THAT BACK, BUT WE CAN SAY THAT THE DATA HAS TO FOLLOW THAT?

CHAIRMAN LO: WITH 5, FOR EXAMPLE, I THINK THAT WE'RE SAYING ONCE YOU'VE TRANSFORMED IT AND YOU HAVE A STEM CELL LINE, IT STRIKES ME TO SAY YOU CAN USE THE MATERIALS, BUT YOU CAN'T TAKE ANY OF THE CLINICAL ANNOTATION WITH IT REALLY UNDERMINES THE --

DR. ROBERT TAYLOR: I AGREE THAT IT UNDERMINES THE SCIENTIFIC VALIDITY. THAT'S NOT THE ARGUMENT THAT I'M TRYING TO MAKE.

CHAIRMAN LO: I THINK IF WE FOLLOW THE IDEA THAT JUSTIFIABLE RELIANCE MEANS THAT YOU CAN'T THEN WITHDRAW. IF SOMEONE HAS RELIED ON THE COMBINATION OF YOUR MATERIALS PLUS YOUR DATA, THAT'S GOT TO STAND.

DR. ROBERT TAYLOR: I GUESS I'M RELYING LESS ON RELIANCE THAN I AM ON TRANSFORMATION. I COULD BE TALKED INTO IT.

DR. PECKMAN: IF I CAN JUST MAKE A -- THE COMMON RULE IS ENFORCED BY THE OFFICE FOR HUMAN RESEARCH PROTECTION, OHRP. AND IT WAS ALLUDED TO EARLIER IN THE MAJOR TALK THAT THEY HAVE ISSUED GUIDANCE ABOUT DATA AND WITHDRAWAL. AND IT'S VERY EXPLICIT, THAT THE RESEARCHER DOES HAVE NOT TO REMOVE THE DATA UPON THE SUBJECT'S REQUEST TO WITHDRAW FROM THE RESEARCH. AND THE RESEARCHER IS CAPABLE AND AUTHORIZED TO CONTINUE TO WORK ON THE

DATA.

SO I THINK THAT -- AND THEN BERNIE'S POINT IS VERY IMPORTANT, IS TO DETACH THE DATA FROM THE SAMPLES TO DO REAL DAMAGE TO THE RESEARCH AS WELL.

CHAIRMAN LO: SO WHY DON'T WE SORT OF MOVE ON TO SOMETHING I THINK WAS A VERY INTERESTING AND IMPORTANT TOPIC THIS MORNING, WHICH IS -- I'M GOING TO SKIP, GEOFF, AND GO TO D RATHER THAN C, WHICH IS RETURN OF INDIVIDUAL DATA TO DONORS AND MATERIALS USED TO DERIVE IPSC'S. AND SO, FIRST, I WANT TO SORT OF TRY AND MAKE SOME DISTINCTIONS WHICH WE MADE THIS MORNING, AND I WANT TO MAKE SURE WE'RE CLEAR.

SO, ONE, I WANT TO DISTINGUISH BETWEEN RETURNING TO THE DONORS MATERIALS THE GENERAL RESULTS OF WHAT'S BEING DONE IN THE FIELD. SO THE KINDS OF STUDIES BEING DONE, LAYPERSON'S SUMMARIES, ABSTRACTS OF PUBLICATIONS, SO IT'S NOT INDIVIDUAL RESULTS. IT'S SORT OF THE OVERALL RESEARCH FINDINGS AS PUBLISHED. AND IT STRIKES ME THAT THERE AREN'T A WHOLE LOT OF OBJECTIONS, IT SEEMS TO ME, TO OFFERING TO DO THAT IF PEOPLE WANT TO RECEIVE THOSE RESULTS AND JUST MAKING IT EASIER SO THEY DON'T HAVE TO GO TO THE INTERNET TO TRACK THIS DOWN.

I THINK THE QUESTION THAT WE NEED TO DISCUSS IS WHAT ABOUT THE DONOR'S PERSONAL FINDINGS

ON THE RESULTS OF THE RESEARCH, WHICH COULD BE ANYTHING FROM A CELL MARKER TO SOMETHING ABOUT THE GENOMIC SEQUENCE? AND SOME OF THE THINGS THAT CAME UP THIS MORNING WHEN WE STARTED TO TALK ABOUT IT WERE IS IT ANY FINDING? IS IT ONLY A CERTAIN SUBCLASS OF FINDINGS, ONES THAT ARE EITHER VALID IN AN ANALYTIC RESEARCH SENSE, THAT IF SOMEONE ELSE WERE TO REPLICATE THE STUDY, THEY'D GET THE SAME RESULT AS OPPOSED TO I DID IT ONCE AND I'M NOT SURE THE ASSAY STILL WORKS. SO ANALYTIC VALIDITY.

THE OTHER IS SOME SORT OF CLINICAL VALIDITY WHERE I AT LEAST HAVE SOME SENSE OF WHAT THIS MEANS CLINICALLY AS OPPOSED TO JUST GIVING YOU THE NAKED GENOME SEQUENCE.

AND THIRD IS CLINICAL SIGNIFICANCE, OR I THINK THE TERM GEOFF USED WAS ACTIONABLE, WHICH IS ANOTHER, WHICH IS IT'S NOT JUST ANY DATA THAT IS CLINICALLY VALID, BUT IT ACTUALLY WOULD LEAD TO AT LEAST A CONSIDERATION, IF NOT A RECOMMENDATION, OF CHANGES IN MANAGEMENT.

AND SHERRY AND I TALKED AT THE BREAK ABOUT SOME OF THE THINGS THAT WERE DEEMED ACTIONABLE WITH REGARD TO EARLY BRCA1 RESEARCH, WHICH TURNED OUT NOT TO STAND UP UNDER ADDITIONAL STUDY.

I ALSO WANT TO SAY THAT WHAT WE'RE REALLY

TALKING ABOUT HERE IS OFFERING THE SUBJECT THE OPTION TO GET INDIVIDUAL RESULTS BACK. I DON'T THINK ANYBODY IS TALKING ABOUT SORT OF FORCING A SUBJECT TO RECEIVE RESULTS THAT THEY DON'T WANT TO KNOW ABOUT. AND THERE ARE VARIOUS OTHER OPTIONS -- THERE ARE OTHER THINGS WHICH I THINK ARE SECONDARY, WHETHER IT GOES TO BOTH THE DOCTOR AND THE PATIENT, OR PATIENT HAS THE OPTION OF GETTING IT WITHOUT THE DOCTOR, WHERE THERE'S AN OFFER OF COUNSELING, EDUCATION, AND SO FORTH. BUT I THINK WHAT WE'RE TALKING ABOUT IS INDIVIDUAL RESEARCH FINDINGS. AND WE SEPARATE EVEN IF THEY DON'T -- EVEN IF THE CLINICAL SIGNIFICANCE IS NOT KNOWN, SHOULD WE ROUTINELY BE OFFERING THAT TO THE PATIENT? SHOULD IT BE UP TO THE INDIVIDUAL INVESTIGATOR HOW SHE/HE WANTS TO HANDLE THAT?

WE STARTED TO TALK ABOUT IT THIS MORNING, BUT I THINK IT'S A REALLY CUTTING EDGE AND IMPORTANT TOPIC. I'D BE INTERESTED IN SORT OF WHAT ALL OF YOU THINK.

MS. LANSING: I CAN START YOU OFF BECAUSE THIS TO ME IS REALLY -- THIS TO ME IS WHERE YOU OPEN UP A WHOLE BUNCH OF STUFF. SO NOW I SUBMIT MY DATA -- I SUBMIT MY TISSUE, CELLS, WHATEVER, AND LET'S USE THE BRCA GENE. IT'S AN INTERESTING THING.

SO LOTS OF WOMEN ARE DOING THAT. NOW THEY STUDY WHATEVER MORE, AND THEY FIND THROUGH THIS THAT, MAYBE THEY DO A WHOLE GENOME SEQUENCE OR SOMETHING, AND THEY DISCOVER THAT I HAVE A CURABLE DISEASE THAT I DON'T EVEN KNOW I HAVE. NOW, IT WOULD SEEM TO ME THAT THERE IS A MORAL OBLIGATION TO TELL SOMEBODY YOU HAVE THIS DISEASE. IF YOU TAKE THIS PILL, YOU ARE GOING TO BE FINE. WE DON'T WANT YOU TO DIE FROM IT.

ON THE OTHER HAND, THEY DISCOVER I HAVE A DISEASE OR A PROPENSITY TO A DISEASE OF WHICH THERE IS NO HELP WHATSOEVER, AND I CAN LIVE IN FEAR FOR THE REST OF MY LIFE, WAIT FOR THE BOMB TO TICK, WHICH, I GUESS, IS A CHOICE THAT THE PATIENT HAS THE RIGHT TO MAKE, THE DONOR HAS THE RIGHT TO MAKE. BUT, BOY, THAT'S WHEN YOU REALLY GET INTO YOU BETTER UNDERSTAND WHAT THAT BOX MEANS WHEN YOU SAY YOU WANT BACK ALL THE DATA. YOU REALLY BETTER MAKE IT CRYSTAL CLEAR. DO YOU WANT BACK THE DATA ONLY INVOLVING THIS DISEASE AND THIS RESEARCH? DO YOU WANT THE DATA ONLY INVOLVING DISEASES THAT WE CAN HELP YOU WITH, AND YOU DON'T WANT TO KNOW -- OR DO YOU REALLY WANT TO KNOW EVERY POSSIBLE THING THAT CAME OUT OF THIS?

I THINK WE CAN DESIGN SOMETHING THAT GIVES

YOU THAT OPTION. I WOULD JUST HATE TO THINK THAT SOMEBODY WHO CHECKED THE DISEASE ONLY BOX AND THEN YOU FOUND OUT THAT THEY HAD SOMETHING THAT COULD BE CURED BY TAKING A PILL, BUT THEY WOULD NOT FIND OUT ABOUT IT TILL TOO LATE. THAT WOULD BE A TERRIBLE THING SHOULD THERE BE SUCH A THING.

DR. PATRICK TAYLOR: SINCE I'VE WRITTEN SOMETHING ABOUT THIS, I THINK I'LL JUST GET SOME LOW HANGING FRUIT OFF THE TABLE JUST SO THE DISCUSSION CAN BE MORE PRODUCTIVE.

FIRST, THERE'S BEEN SO MUCH DISCUSSION AROUND THIS OVER THE LAST FIVE YEARS THAT I THINK HAS BEEN HELPFUL IN SOME WAYS. FIRST IS NO ONE WHO IS RESPONSIBLE IS SUGGESTING AT THIS POINT THAT UNVALIDATED, SPECULATIVE THINGS OUGHT TO BE DISCLOSED TO PATIENTS AND PARTICIPANTS AS IF THEY'RE REAL. THAT'S A STRAWMAN ISSUE. OR THAT NON-CLIA CERTIFIED LABS OUGHT TO BE ABLE TO PRODUCE RESULTS. THAT'S ONE IMPORTANT POINT.

SECOND POINT IS I THINK YOU HAVE TO TAKE AS A GIVEN THAT, ALTHOUGH IT'S NOT EASY WHEN ONE TALKS ABOUT RETURNING RESULTS, THE POINT IS TO RETURN NONMISLEADING RESULTS. THAT TAKES SOME WORK TO DO THAT PROBABLY BECAUSE IT MEANS INVOLVING YOURSELF IN WHAT PARTICIPANTS REALLY MEAN BY RESULTS

AND PARTLY BECAUSE IT TAKES SOME MODESTY WITH RESPECT TO WHAT GENETIC ASSOCIATIONS ACTUALLY MEAN AS OPPOSED TO SAYING THIS GENE IS ASSOCIATED WITH THIS, WHAT WE REALLY KNOW IS THIS GENE IS POTENTIALLY ASSOCIATED WITH THIS IN CONNECTION WITH ENVIRONMENTAL FACTORS WE HAVEN'T IDENTIFIED AND SO ON.

SO THE BASIC THING I THINK THAT DRIVES SOME OF US IS THE BELIEF THAT IN CLINICAL AND EXPERIENCE, IN CLINICAL AND OTHER CONTEXTS, PATIENTS ARE PERFECTLY CAPABLE OF UNDERSTANDING HIGHLY PROBABILISTIC AND UNCERTAIN INFORMATION. IF YOU'VE EVER BEEN IN A HOSPITAL WITH, SAY, TAKING CARE OF YOUR KIDS, AND YOU SEE EXACTLY HOW MANY DIFFERENT STORIES YOU GET ABOUT WHAT'S GOING TO HAPPEN NEXT, YOU KNOW ABOUT, WELL, IT'S NOT THAT EASY NECESSARILY TO DEAL WITH PROBABILISTIC AND DIFFERENT INFORMATION. WE ALL HAVE TO DEAL WITH IT.

SO WHAT'S SO SPECIAL ABOUT GENETICS? YOU CAN GO INTO A SERIES OF CLINICAL ENCOUNTERS WHERE SOMEONE SAYS BASED ON THE FOLLOWING CONSTELLATION OF CLINICAL THINGS, WHICH ARE DIFFERENT THAN THE LAST DOCTOR I SAW, I THINK YOU HAVE THIS. AND THEN YOU GET A DIFFERENT SET OF RESPONSES. WHAT IS IT ABOUT GENES THAT SAYS IF I TELL YOU THAT YOU MIGHT HAVE

THIS, YOU ARE GOING TO GO OUT AND SHOOT YOURSELF? WELL, THERE IS NO EVIDENCE FOR THE BELIEF THAT GENETIC INFORMATION IS SOMEHOW SO OVERPOWERINGLY POWERFUL. IF YOU ACTUALLY TELL SOMEONE THE TRUTH ABOUT THEMSELVES IN ACCORDANCE WITH THEIR PREFERENCES, THEY JUST CAN'T HANDLE IT. IN FACT, THERE'S A LOT OF EVIDENCE TO THE CONTRARY.

SO THE WHOLE POINT IS RESULTS OUGHT TO BE ANALYTICALLY VALID. THEY OUGHT TO BE TESTED. THEY OUGHT TO BE PEER REVIEWED, OF COURSE, ALL THAT STUFF. AND YOU REALLY HAVE TO SET UP SYSTEMS TO FIND OUT HOW TO DO IT. AND THERE ARE GOING TO BE SITUATIONS WHERE IT SHOULDN'T BE DONE, SITUATIONS WHERE IT SHOULD BE, BUT MORE EMPIRICAL RESEARCH IS CALLED FOR.

THE ONLY REASON I MENTION THIS, AND I WON'T GET INTO MORE OF THE KIND OF THINKING THAT MY GROUP HAS DONE, IS JUST SO THAT WE DON'T SPEND A LOT OF TIME DISCUSSING THINGS THAT AREN'T REAL ISSUES, LIKE GIVING VALID RESULTS OR SO ON.

CHAIRMAN LO: LET ME -- I THOUGHT CHRIS HEMPEL THIS MORNING SAID SHE WANTED EVERYTHING BACK, GOOD AND BAD, EVEN IF THE RESEARCHERS DIDN'T QUITE KNOW WHAT IT ALL MEANT.

MS. HEMPEL: NO. THAT'S CORRECT. I WAS

JUST GOING TO TRY TO GIVE AN EXAMPLE OF GETTING DATA BACK THAT LED TO SOMETHING THAT WAS POSITIVE. WE TOOK SOME SPINAL FLUID FROM MY TWINS, AND WE HAD IT ANALYZED IN A RESEARCH LAB THAT'S NOT CLIA CERTIFIED AND ALL THESE OTHER TYPES OF THINGS, BUT THEY FOUND IN THESE SAMPLES THAT THEY COULDN'T FIND ANY COPPER IN MY TWINS' SPINAL FLUID FOR WHATEVER REASON. WE STILL DON'T KNOW. THAT INFORMATION WAS SENT BACK TO ME, AND PARTIALLY BECAUSE I WAS FUNDING THAT RESEARCH, SO I GOT THE DATA BACK. BUT IT LED ME TO ANOTHER RESEARCHER WHO HAPPENS TO BE ONE OF THE TOP METALS AND COPPER EXPERTS IN THE WORLD. SO I CONTACTED HIM AND SAID, HEY, THIS IS WHAT WAS FOUND IN THE TWINS, AND YOU'RE A LEADING ALZHEIMER'S RESEARCHER. WHAT DO YOU THINK?

OUT OF THAT DATA WE SET UP A GIANT EXPERIMENT TO TAKE WHAT WE -- THESE INITIAL FINDINGS, PILOT FINDINGS, A LOT FURTHER TO LOOK AT MANY MORE NIEMANN PICK KIDS, ANIMAL DATA, AND NOW WE'RE AT A POINT WHERE HE'S GETTING READY TO PUBLISH A BIG PAPER ON HIS FINDINGS IN ANIMALS AND CHILDREN AROUND METAL DISRUPTIONS IN OUR DISEASE.

SO THAT WOULD BE ONE EXAMPLE OF DATA THAT CAME BACK, AND I HAVEN'T ACTED UPON IT. I'M NOT GIVING MY KIDS COPPER SUPPLEMENTS OR ANYTHING LIKE

THAT. IT'S JUST DATA THAT LED TO FURTHER RESEARCH TO MOVE THINGS FORWARD. SO I THINK GETTING DATA BACK IS IMPORTANT TO PATIENT ADVOCATES WHO CAN MAYBE TRY TO MOVE THE RESEARCH FORWARD OR WHO ARE INVOLVED. AND I DON'T THINK EVERYBODY IS JUST GOING TO RUSH OUT AND DO DRASTIC THINGS BY GETTING DATA. THAT'S JUST ONE EXAMPLE. I COULD GIVE YOU MULTIPLE EXAMPLES OF HOW IMPORTANT IT IS TO GET DATA BACK TO MOVE RESEARCH FORWARD.

DR. PATRICK TAYLOR: IF I CAN JUST ADD ONE COMMENT. SO THERE'S PLENTY OF EVIDENCE THAT NOWADAYS WITH HEALTHCARE SO FRAGMENTED, WHO'S ACTUALLY HOLDING A PATIENT'S CARE AND TREATMENT TOGETHER OVER TIME. AND WE WISH THAT PRIMARY CARE DOCTORS AND INTERNAL MEDICINE PEOPLE WERE NOT SO OVERWORKED THEY COULD ACTUALLY DO IT, BUT A LOT OF TIMES THEY CAN'T. SO WHO IS? USUALLY IT'S ACTUALLY THE PATIENTS OR THE PATIENTS' FAMILIES. SO TO ME THAT IS A GREAT EXAMPLE OF THINGS I'VE SEEN ALL THE TIME, WHICH IS SOMEBODY IS HOLDING TOGETHER DATA AND TRYING TO FIGURE OUT. AND WHO IS THE PERSON? IT'S THE PERSON WHO CARES MOST ABOUT THAT KID.

SO OF YOU KNOW PARENTS OF AUTISTIC CHILDREN, THEY DON'T GO OUT AND SAY, GEE, SOMEBODY TOLD ME THAT THERE MIGHT BE SOME LINK WITH ZINC.

I'M GOING TO OVERDOSE MY KID WITH ZINC BECAUSE THEY'RE PARENTS AND THEY'RE SMART PEOPLE AND THEY CARE ABOUT THEIR KIDS, SO THEY DO RESPONSIBLE THINGS. SO WHEN PEOPLE ARE FACED WITH UNSOLVABLE MEDICAL PROBLEMS, GIVING THEM MORE INFORMATION TO WORK WITH IN A WORLD WHICH IS FILLED WITH UNCERTAINTY, AND THEY KNOW THAT WELL, IT IS SOMETHING THEY CAN DEAL WITH, AND WE DON'T HAVE TO ASSUME THAT THEY'RE STUPID.

CHAIRMAN LO: PAT, NOW I'M HAVING A LITTLE TROUBLE UNDERSTANDING. I THINK EARLIER I HEARD YOU SAY THAT WE SHOULDN'T BE TALKING ABOUT GIVING RESULTS BACK IF THEY'RE NOT VALIDATED AND NOT FROM CLIA LABS. YET, AS I UNDERSTOOD CHRIS' EXAMPLE, AT LEAST FOR THE SAKE OF ARGUMENT, THIS WASN'T A CLIA LAB AND THE RESEARCHER REALLY JUST SAID THIS IS A FINDING. I REALLY DON'T KNOW WHAT IT MEANS, AND I HAVEN'T DONE OTHER KIDS WITH CSF FOR THIS DISEASE. SO MAYBE IT'S JUST SOME INTERFERENCE WITH THE ASSAY.

MS. HEMPEL: OR WE NEED TO DO IT AGAIN. WE TALKED ABOUT MAYBE DOING IT AGAIN TO REPLICATE IT. THE OTHER THING THAT I FIND INTERESTING IS THAT WE'RE INVOLVED IN A TRIAL WITH MY TWINS WITH THE FDA, AND IT SEEMS LIKE A LOT OF THE RESEARCHERS KEEP SAYING, WELL, THESE RESULTS AREN'T, LIKE, CLIA

CERTIFIED. AND THEN WE WENT AND WE TALKED TO THE FDA. THEY SAID THESE RESULTS, THAT'S OKAY. WE WANT THIS INFORMATION. GO AHEAD AND SUBMIT IT. IT DOESN'T NEED TO BE A CLIA CERTIFIED LAB. BECAUSE ACTUALLY ONE OF THE LABS WE'RE WORKING WITH IS THE ONLY LAB IN THE WORLD THAT EVEN HAS THE CAPABILITY OF DOING THIS TESTING, AND IT'S NOT CLIA CERTIFIED, BUT THEY WANT THE DATA. SO PEOPLE GET CAUGHT UP IN THE CLIA CERTIFICATION.

CHAIRMAN LO: WE HAVE TO DISTINGUISH BETWEEN CLIA CERTIFICATION TO GIVE RESULTS BACK TO A PATIENT AS OPPOSED TO CLIA CERTIFICATION FOR EITHER PUBLICATION OR FDA.

DR. PATRICK TAYLOR: SO IN REALITY IN MY OWN EXPERIENCE, RESEARCH LABS CERTAINLY DO A MUCH BETTER JOB THAN ANY CLIA CERTIFICATION IMPLIES. BUT CERTAINLY THE LAW ADDS TO THE EXTENT THAT RESULTS ARE TO BE MADE AVAILABLE BY A LAB FOR PURPOSES OF CLINICAL CARE, THEN YOU ACTUALLY MUST MAKE THE RESULTS AVAILABLE IN THAT WAY. SO IF YOU HAVE PATIENTS WHO IN THE COURSE OF EXPRESSING A PREFERENCE FOR SOMETHING SAY, YES, I WANT THINGS THAT ARE CLINICALLY ACTIONABLE, AS WAS DISCUSSED THIS MORNING, IT'S HARD TO ACTUALLY SAY YOU'RE PROVIDING RESULTS NOT FOR CLINICAL PURPOSES.

I THINK THE EXAMPLE OF GETTING SORT OF ANALYTIC RESULTS ABOUT THE PRESENCE OF SOMETHING IN THE BLOOD STREAM IS A LITTLE BIT DIFFERENT THAN WHAT SOMEBODY ACTUALLY MAY THINK OF A DNA SEQUENCE AND SORT OF THE GENETIC KIND OF INFORMATION. WHEN ONE IS SETTING UP A SYSTEM, IT'S DESIGNED TO ACTUALLY RETURN RESULTS WHICH GIVES PEOPLE A SET OF CHOICES. I THINK YOU HAVE TO HAVE STEPS IN PLACE THAT ARE NONRANDOM OR NONGNARLY. MY SON, WHO USES THAT GNARLY IS A GOOD WORD. OF COURSE, THAT'S 14. EVERYTHING BAD IS GOOD. BUT IN ANY EVENT, YOU HAVE TO HAVE SOMETHING THAT'S SYSTEMATIC, OF COURSE. AND THAT'S WHAT IT REQUIRES.

IN TERMS OF SAYING WE DON'T KNOW WHAT IT MEANS, THOUGH, THAT'S WHAT I MEANT BY MODESTY. THERE ARE ALL KINDS OF GENETIC RESULTS WHERE THE TRUTH IS WE DON'T REALLY KNOW WHAT IT MEANS. AND IF PARTICIPANTS WANT TO KNOW, AS OVERWHELMING SURVEY RESULTS SUGGEST THEY DO, WE WANT TO KNOW THINGS THAT YOU DON'T KNOW WHAT THEY MEAN EITHER, BUT NONE OF US KNOW THE MEANING OF MUCH OF THE UNIVERSE. THAT'S FINE AS LONG AS WE'RE HONEST ABOUT IT. BUT TO SAY TO SOMEBODY YOU HAVE FOUR TIMES THE CHANCE OF THE POPULATION OF GETTING X, WHEN WE DON'T EVEN KNOW WHAT N IS AND WE DON'T EVEN KNOW WHETHER THAT KIND

OF CONSTRUCT IS LEGITIMATE IS TO ME INHERENTLY MISLEADING. GIVING RESULTS THAT SAY THERE'S BEEN A GENE THAT'S BEEN ASSOCIATED WITH THIS IN THIS WAY WITH THIS, BUT WE DON'T KNOW WHY AND WE DON'T KNOW WHAT TRIGGERS AND WE DON'T KNOW A LOT OF THINGS IS A WAY OF ADMITTING OUR IGNORANCE AS PART OF TELLING THE TRUTH.

CHAIRMAN LO: OTHER COMMENTS, THOUGHTS? ANYONE HAVE CONCERNS ABOUT GIVING PEOPLE RESULTS BACK THAT MAY NOT BE VALIDATED?

MS. ISASI: I JUST WANTED TO MAKE A COMMENT THAT THIS IS AN AREA WHERE MUCH POLICY GUIDANCE IS NEEDED. WE HAVE BEEN APPROACHED BY SEVERAL STEM CELL BANKS THAT ARE STRUGGLING WITH THIS ISSUE, AND THEY HAVE ALREADY COME TO THE ATTENTION OF RESEARCHERS APPROACHING THE BANK, THE BIOREPOSITORY ITSELF, AND SAYING WE HAVE THIS INCIDENTAL FINDINGS, IT'S NOT CLINICALLY SIGNIFICANT INFORMATION, BUT IT'S INCIDENTAL FINDING THAT TELL US SOMETHING ABOUT THE GENETIC DISORDERS AND THE CONDITION OF THE DONORS. HOW DO WE HANDLE THAT?

AND THE PRELIMINARY RESULTS OF OUR SURVEY WAS THAT MOST OF THE BANKS DO NOT HAVE A SPECIFIC POLICY IN PLACE. IF THEY DO, IT'S NOT CLEAR HOW THEY WILL PUT INTO PLACE THE RESPONSIBILITIES FOR

RESEARCHERS BECAUSE YOU HAVE -- YOU IMPOSE A RIGHT OR YOU CONSIDER A DONOR'S RIGHT TO GET BACK INFORMATION, THEN THE COUNTERPART IS RESPONSIBILITY TO RESEARCHERS TO DELIVER FOR SECONDARY USES, WHICH IS GOING TO HAPPEN IN THIS BANK, THIS IS GOING TO BECOME A KEY ISSUE. AND I JUST WANTED TO SAY THAT FROM AN INTERNATIONAL PERSPECTIVE, THAT THIS IS AN AREA WHERE CIRM COULD DO A GREAT JOB IN GUIDING POLICY.

DR. KIESSLING: THIS MIGHT HAVE TO BE A CONSENT FORM ISSUE BECAUSE AN EXAMPLE THAT ROB TAYLOR GAVE THIS MORNING, I THINK, IS A REALLY GOOD EXAMPLE OF HOW CONFUSED THIS IS. THERE ARE PATIENTS WHO GO THROUGH INFERTILITY TREATMENT AND IVF SO THAT THEY CAN HAVE THEIR EMBRYOS DIAGNOSED WITH SERIOUS DISEASES LIKE HUNTINGTON'S CHOREA BECAUSE THEY KNOW THAT THEY HAVE THAT GENE IN THEIR FAMILY. THEY THEMSELVES, HOWEVER, DON'T WANT TO KNOW IF THEY HAVE IT. THEY WANT SOME ASSURANCE THAT THE EMBRYO THAT'S GOING TO BE TRANSFERRED DOESN'T HAVE IT. BUT THEY DON'T WANT THE INFORMATION ABOUT THEMSELVES BECAUSE IT'S JUST NOT SOMETHING THEY WANT TO LIVE WITH. AND I THINK THE BRCA GENE IS ANOTHER EXAMPLE OF THAT.

SO IT'S POSSIBLE THAT YOU'RE GOING TO HAVE PEOPLE WHO DONATE TISSUES WHO SAY I WANT TO KNOW

EVERYTHING YOU FIND BECAUSE I CAN HANDLE IT JUST AS WELL AS YOUR FAMILY. AND THERE ARE GOING TO BE PEOPLE WHO SAY, YOU KNOW, I DON'T WANT TO KNOW ANYTHING UNLESS YOU'RE REALLY SURE ABOUT IT. SO IT'S POSSIBLE THAT THE POLICY NEEDS TO BE IT'S GOT TO BE PART OF THE CONSENTING PROCESS TO FIND OUT EXACTLY HOW MUCH THESE PEOPLE WANT IN RETURN.

MS. LANSING: NOT ONLY JUST IF YOU'RE SURE ABOUT IT, BUT I WOULD ADD -- THERE'S LIKE THREE THINGS. I WANT TO KNOW EVERYTHING NO MATTER WHETHER YOU'RE SURE OR NOT SURE. I WANT TO KNOW ONLY IF YOU'RE SURE. I WANT TO KNOW ONLY IF YOU'RE SURE AND I CAN DO SOMETHING ABOUT IT. AND I DON'T WANT ANYTHING BECAUSE --

DR. ROBERT TAYLOR: MAYBE I CAN DO SOMETHING ABOUT IT.

MS. LANSING: THAT'S A BIG THING WHEN YOU CAN DO SOMETHING. THE HUNTINGTON'S THING, I TOTALLY UNDERSTAND IT, IS THERE'S NOTHING YOU CAN DO ABOUT IT BASICALLY, SO PEOPLE ARE SITTING THERE EVERY TIME SOMETHING HAPPENS WORRYING FOR THE REST OF THEIR LIVES AND RUINING THE QUALITY OF THEIR LIVES. A YOUNG WOMAN DOESN'T NECESSARILY WANT TO KNOW ABOUT THE BRCA GENE UNTIL AFTER SHE'S HAD HER CHILDREN OR WHATEVER THE CHOICES ARE.

SO THIS IS WHERE -- I REMEMBER, ANN, WHEN YOU SAID THIS IS WHERE INFORMED CONSENT IS REALLY NOT A PIECE OF PAPER, YOU KNOW. BECAUSE YOUR NATURAL THING IS, OH, SURE I WANT TO KNOW EVERYTHING, BUT YOU HAVE NO IDEA WHAT THAT MEANS. IT'S REALLY SITTING DOWN AND REALLY SPENDING A GREAT DEAL OF TIME EXPLAINING TO THE PEOPLE WHAT THEY CAN FIND OUT. WE'RE NOT SAYING YOU WILL, BUT WHAT YOU COULD FIND OUT.

DR. KIESSLING: IN OUR EXPERIENCE IT TAKES AT LEAST FOUR OR FIVE ENCOUNTERS TO GET A REALLY GOOD INFORMED CONSENT. AND ONE OF THOSE ENCOUNTERS HAS TO BE WITH SOMEBODY WHO'S NOT PART OF THE TEAM.

DR. ROBERT TAYLOR: THAT'S THE INFORMED CONSENT. ROSIE IS BRINGING UP THE POINT SO YOU GET BACK A BAD RESULT, AND YOU'RE THREE STEPS DOWN THE PROCESS. YOU DO THE DNA SEQUENCING ON THE NEW STEM CELL LINE THAT YOU GENERATED, AND THERE'S A BUNCH OF TRIPLET REPEATS IN THE HUNTINGTON'S GENE OR SOMETHING. SO THEN THEY CALL UP CIRM, THE BIOBANK, AND THEY SAY WE'VE GOT A PROBLEM WITH YOUR PATIENT THAT DONATED THIS DONOR. WHO'S GOING TO TELL THEM BECAUSE THAT'S GOING TO BE A LONGER CONVERSATION THAN YOUR FOUR-HOUR CONSENT PROCESS. SO THIS RESPONSIBILITY ISSUE REALLY CAN'T BE TAKEN TOO

LIGHTLY.

MS. ISASI: THERE'S A REAL CASE THE UK STEM CELL BANK IS FACING ON AN ALMOST DAY-TO-DAY BASIS. WHAT DO WE DO? WHAT HAPPENED WITH THE RESEARCHER WHO HAS NO ACCESS TO THE CODE OR THE SAMPLE?

MS. LANSING: OR THE GOOD NEWS IS YOU DISCOVERED A CANCER OR SOMETHING AND IT CAN BE CURED; BUT IF WE WAIT SIX MONTHS, IT'S GOING TO METASTASIZE. INADVERTENTLY YOU CAN SAVE SOMEONE'S LIFE TOO. IT'S GOT A LOT OF POSITIVE THINGS TO IT.

DR. PATRICK TAYLOR: IT IS VERY IMPORTANT. THE DISCUSSION AROUND THE POVERTY OF THE INFRASTRUCTURE PROVIDING SUPPORTS FOR PEOPLE ON THE RESEARCH SIDE IS VERY REAL. IT'S QUITE A DISPARITY. SO YOU CAN'T CHANGE JUST ONE THING. IF ONE IS GOING TO GIVE RESEARCH RESULTS, THEN ONE HAS TO RECOGNIZE THAT PEOPLE'S PREFERENCES MAY NOT BE DURABLE. AND SO YOU NEED TO HAVE SOME WAY OF MAKING THE RESEARCH SYSTEM RESPONSIVE TO THAT, A LITTLE BIT OF A SAFETY NET, AND SO ON.

SO I THINK THE ANSWER IS IF ONE IS GOING TO GIVE RESEARCH RESULTS, YOU'VE GOT TO DO IT RIGHT. AND THAT MAY REQUIRE SOME OTHER KINDS OF INVESTMENTS AND CHANGE WHICH PEOPLE HAVE TO THINK ABOUT.

CHAIRMAN LO: LET ME ASK A COUPLE QUESTIONS HERE. THE DISTINCTION IS OFTEN MADE IN THE LITERATURE, AND GEOFF CITES AN ARTICLE THAT SUSAN WOLF AND HER COLLEAGUES WROTE, AND SHE'S CONTINUING TO WORK ON THIS, INCIDENTAL FINDINGS VERSUS FINDINGS RELATED TO THE TOPIC OF THE RESEARCH. SO IT'S ONE THING TO SAY, WELL, I WAS RECRUITED TO THE CIRM STEM CELL LINE BANK TO DO RESEARCH ON WHATEVER, DIABETES, NIEMANN PICK. I WANT TO KNOW EVERYTHING ABOUT THAT CONDITION BECAUSE THAT'S WHAT MOTIVATED ME. YOU MAY FIND SOMETHING THAT HAS NOTHING TO DO WITH THOSE CONDITIONS, NOT EVEN REMOTELY. SO IT'S NOT EVEN THAT IT HAS SOMETHING TO DO WITH CENTRAL NERVOUS SYSTEM FUNCTIONING. IT'S GOT SOMETHING TO DO WITH SOMETHING THAT APPARENTLY IS TOTALLY UNRELATED.

THERE ARE SOME CONCERNS THAT THOSE INCIDENTAL FINDINGS MAY NEED TO BE LOOKED AT DIFFERENTLY THAN FINDINGS ABOUT THE CONDITION BECAUSE THOSE INCIDENTAL FINDINGS COULD BE (INAUDIBLE). AND THE OTHER THING IS THAT EXCEPT FOR A FEW CIRCUMSTANCES IN WHICH WE REALLY KNOW WHAT THOSE FINDINGS MEAN, AND I THINK THE TRINUCLEOTIDE REPEATS IN HUNTINGTON'S IS A GOOD EXAMPLE, BRCA1 IS A CLEAR EXAMPLE NOW, OR THE LYNCH SYNDROME GENES,

THOSE ARE ACTIONABLE. BUT THERE ARE LOTS OF OTHER THINGS THAT COME UP, INCLUDING MISATTRIBUTED PATERNITY, SMALL INCREASES IN RISK FOR COMMON CONDITIONS LIKE CORONARY ARTERY DISEASE OR HYPERTENSION.

AND, IN FACT, THERE WAS A MAJOR STUDY PUBLISHED IN *LANCET* OVER THE SUMMER WITH A WHOLE GENOME SEQUENCE DONE ON A STANFORD RESEARCHER WHO'S WELL-KNOWN THAT LOOKED AT THE CLINICAL SIGNIFICANCE OF FINDINGS FROM A WHOLE GENOME SEQUENCE DONE. AND PEOPLE CAN READ THAT ARTICLE IN A COUPLE OF WAYS. ONE IS THAT, YEAH, HE HAS A SMALL INCREASED RISK FOR HEART DISEASE, HYPERTENSION; BUT WHEN YOU REALLY GET DOWN TO IT, IT WAS, WELL, YOU OUGHT TO EXERCISE MORE, BE PRUDENT ABOUT YOUR DIET, AND KEEP YOUR WEIGHT DOWN. NOW, SOME PEOPLE SAY, BUT IT'S REALLY DIFFERENT IF I GET THAT JUST FROM MY PRIMARY CARE DOCTOR WHO SAYS THAT TO EVERYBODY VERSUS GETTING IT WITH SOME DATA ATTACHED. I MAY TAKE THAT MORE SERIOUSLY.

I THINK THE EVIDENCE IS REALLY MIXED THAT GETTING GENOMIC RESULTS BACK OR HIGH TECH RESULTS BACK ACTUALLY CHANGES PEOPLE'S HEALTH BEHAVIOR. ON THE OTHER HAND, IT MAY JUST BE SOME PEOPLE WANT TO KNOW. AND THEY MAY SAY THAT PART OF THE QUID PRO

QUO IS I GIVE YOU MY SPECIMENS, YOU GET TO DO THIS MARVELOUS RESEARCH, AND I'M CURIOUS. I JUST WANT TO KNOW. MAYBE IT IS EVERYTHING GOOD OR BAD NO MATTER WHAT. I THINK WE'VE TALKED ABOUT MAKING THIS PART OF THE CONSENT PROCESS. THIS IS A REALLY COMPLICATED PART OF THE CONSENT PROCESS. YOU GOT TO TALK ABOUT FALSE POSITIVES, FALSE NEGATIVES.

LET ME ALSO JUST PICK ON SOMETHING THAT ROSIE SAID, WHICH IS HOW DO WE FRAME THIS? IS IT THAT THE RESEARCHER MAY CHOOSE TO OFFER RESULTS BACK? CIRM ENCOURAGES RESEARCHERS TO BE MORE FORTHCOMING THAN TRADITIONALLY? WE REQUIRE RESEARCHERS, AND THEN WHAT RESEARCHERS?

DR. KIESSLING: WHY WOULD IT NOT BE A HUMAN SUBJECT?

CHAIRMAN LO: LET ME JUST FINISH. SO IF I GET A STEM CELL LINE THAT WAS DERIVED BY A CIRM RESEARCHER, PUT IN THE BANK, AND I'M THE FIRST ONE TO DO WHOLE GENOME SEQUENCING AND IT'S BLINDED TO ME. DO I HAVE AN OBLIGATION NOW, AND I'M REALLY LOOKING AT IT TO LOOK FOR GENES FOR LONG QT SYNDROME, FOR EXAMPLE. DO I NOW HAVE TO GO LOOK FOR BRCA GENES, LYNCH SYNDROME GENES, TRINUCLEOTIDE REPEATS WHEN THAT WASN'T THE POINT OF MY DOING THE RESEARCH AND I'M NOT REALLY TRAINED TO DO THAT? IF

I DON'T, THEN AM I MISLEADING SUBJECTS TO OFFER THEM I WANT ALL THE INFORMATION BACK GOOD OR BAD NO MATTER WHAT? IF I'M OFFERING SOMETHING, IS IT AN OFFER THAT REALLY HAS MEANING? IS IT A RIGHT TO THE INFORMATION? IF SO, WHO HAS THE CORRELATIVE OBLIGATION TO ACTUALLY LOOK FOR IT AND GET IT BACK TO THE PERSON?

SO THESE ARE -- I THINK WE'RE ALL SORT OF SAYING, I HEAR A LOT OF SENTIMENT THAT WE HAVE TO BE MORE FLEXIBLE AND RESPECT DONORS WHO WANT TO HAVE A LOT OF INFORMATION BACK EVEN IF IT'S NOT ACTIONABLE, EVEN IF IT'S NOT CLIA CERTIFIED, EVEN IF WE DON'T KNOW THE VALIDITY ANALYTICALLY OR CLINICALLY. BUT WHAT DO WE DO OTHER THAN SAY IT'S NOT A BAD THING IF YOU DO IT WELL?

DR. ROBERT TAYLOR: BERNIE, I WOULD JUST ADD THAT WE'RE SETTING GENOMEWIDE, WHOLE GENOME SEQUENCING AS KIND OF THE ULTIMATE, BUT THE TRUTH IS THERE'S GOING TO BE AN EPIGENOME, AND THEN WE'RE GOING TO WANT TO KNOW ABOUT THE ACETYLOME OF CHROMATIN. EVERY COUPLE OF YEARS WE'RE GOING TO HAVE SOMETHING MORE THAT WILL BE OF INTEREST. AND HOW DEEP THAT ANALYSIS HAS TO GO TO BE ABLE TO PROVIDE THE INFORMATION BACK TO CIRM, IF IT'S A CIRM REQUIREMENT TO GET THAT INFORMATION, IS GOING TO BE

A MOVING TARGET.

DR. PATRICK TAYLOR: I GUESS MY OWN REACTION, BERNIE, IS THAT WE DON'T ACTUALLY KNOW HOW TO DO THIS RIGHT YET. THERE ARE A LOT OF THINGS THAT NEED TO HAPPEN. IN THE PAPERS WE FOCUSED ON THE NEED TO FIGURE OUT WAYS TO DO IT IN THE CONTEXT OF A SAFETY-NETTED SYSTEM AND ALSO IN THE CONTEXT OF CAREFUL EVALUATION OF WHAT STUDIES IT'S APPROPRIATE FOR IN TERMS OF THEIR RIGOR AND A LOT OF OTHER THINGS.

I GUESS MY OWN RECOMMENDATION WOULD BE THAT CIRM SHOULD BECOME A VERY ACTIVE PARTICIPANT IN DISCUSSING HOW TO DO THAT. AND THAT WOULD BE BOTH OF GREAT BENEFIT TO A NATIONAL DISCUSSION AROUND IT, WHICH DOESN'T INVOLVE ACTUALLY THAT MANY PEOPLE, AND ALSO A BENEFIT TO THINKING ABOUT HOW YOU MIGHT FRAME REQUIREMENTS. THERE CERTAINLY ARE GUIDELINES OUT THERE, THE RECENT PUBLICATION THAT WAS REFERRED TO, WHICH GIVES SOME SENSE OF WHEN PEOPLE MAY DO IT. AND THIS MAY SOUND A BIT SURPRISING. THOSE ARE ACTUALLY DECONTEXTUALIZED FROM AN INFRASTRUCTURE THAT WOULD DO IT AS WELL. CREATE ABSTRACT STANDARDS. DO WE WANT TO SAY ACTIONABILITY IS REQUIRED OR NOT AND SO ON? I THINK THE CONTEXT OF HOW IT'S DONE IS ACTUALLY QUITE IMPORTANT.

DR. KIESSLING: IT SEEMS TO ME LIKE THIS IS A HUMAN SUBJECTS REVIEW COMMITTEE JOB. HUMAN SUBJECTS COMMITTEES HAVE KIND OF STRUGGLED WITH THIS KIND OF NOT TO THE IN DEPTH THAT WE CAN DO IT NOW, BUT THIS IS NOT A NEW THOUGHT TO A HUMAN SUBJECTS REVIEW COMMITTEE THAT'S REALLY THOUGHT ABOUT THESE ISSUES, THE INCIDENTAL FINDINGS ISSUE. THIS IS NOT A NEW IDEA. SO I DON'T KNOW WHY HUMAN SUBJECTS COMMITTEES OR HUMAN GUIDELINES FROM HUMAN SUBJECTS COMMITTEES ISN'T BEING PUT IN PLAY HERE. MAYBE THE CIRM PANEL SHOULD HAVE AN IRB REVIEW COMMITTEE THAT REVIEWS INCIDENTAL FINDINGS, BUT THIS IS NOT A NEW THOUGHT TO HUMAN SUBJECTS REVIEW.

MS. ISASI: NO. ACTUALLY WE ARE PART OF THE SUSAN WOLF TEAM, AND BUT THERE'S NO CONSENSUS. AND --

DR. KIESSLING: I REALIZE THERE'S --

MS. ISASI: THERE'S GUIDANCE ABSOLUTELY. WE JUST MAP, FOR EXAMPLE, THE POLICIES AS PERTAINING TO STEM CELL RESEARCH AND STEM CELL BANKS. AND THERE'S LITTLE. THERE'S JUST GENERIC -- ACROSS THE GLOBE, THERE'S JUST GENERIC PROVISIONS THAT SAYS IT SHALL BE PART OF THE INFORMED CONSENT PROCESS. BANKS SHOULD HAVE POLICIES IN PLACE TO HELP TO MANAGE, BUT THEY DON'T DEFINE. AND A KEY ISSUE IS

WHAT BERNIE SAID, TERMINOLOGY. SO DONORS, RESEARCHERS, AND EVERYBODY INVOLVED UNDERSTAND WHAT IS INDIVIDUAL RETURN OF RESULTS, WHAT IS AN INCIDENTAL FINDING, AND WHEN THEY ARE NOT. BUT THERE'S GUIDANCE, BUT THERE'S NOT ENOUGH.

AND ANOTHER EXERCISE IS WHAT IPSC BY NATURE CHANGED THINGS AND REQUIRE SPECIFIC ANALYSIS OR APPROACH.

MS. HEMPEL: I WAS ALSO GOING TO ADD JUST THAT THERE'S A LOT OF COMMERCIAL COMPANIES TOO, COMPANIES LIKE NOME OR 23 AND ME WHERE PEOPLE ARE SUBMITTING THEIR GENETIC INFORMATION, AND THEY ARE PROVIDING RESULTS BACK TO PEOPLE. AND SO THERE MUST BE SOME PROCESSES IN PLACE WITH THESE COMMERCIAL COMPANIES AS WELL AS HOW DO THEY DO THAT AND WHAT KIND OF STUMBLING BLOCKS DO THEY SEE IN PROVIDING INFORMATION TO PEOPLE ON JUST THEIR GENERAL GENETIC DATA.

DR. ROBERTS: ALSO THE CONGRESS IS INVESTIGATING THEM. THEY'RE UNDER INVESTIGATION BY MANY DIFFERENT GOVERNMENT. AT ONE POINT THEY HAD A CEASE AND DESIST ORDER FROM THE STATE OF CALIFORNIA, STATE OF NEW YORK. SO I THINK THERE'S A LOT OF CONCERN ABOUT WHAT KIND OF INFORMATION THEY'RE GIVING BACK AND WHAT THEY'RE PROMISING ABOUT WHAT

THIS INFORMATION CAN TELL YOU. SO, AGAIN, EVEN THAT'S CONTROVERSIAL AS WELL.

DR. PECKMAN: I THINK THIS IS A GREAT DISCUSSION. I THINK IT'S CLEAR FROM THE LITERATURE THERE'S NO CONSENSUS ON WHAT TO DO WITH WHOLE GENOMEWIDE ANALYSIS. I THINK THAT WHAT THIS COMMITTEE HAS ARTICULATED IS NOT ALL DATA ARE THE SAME, AND YOU NEED TO THINK ABOUT THE TYPES OF DATA AND THE INFORMATION THAT WILL BE PROVIDED TO DONORS.

I THINK MORE FUNDAMENTAL TO THIS DISCUSSION IS WHAT WAS JUST BROUGHT UP. IF WE'RE TALKING ABOUT DOING GENOMEWIDE SEQUENCING OF PRIMARY CELLS, THAT'S ONE THING WHEN YOU'RE TALKING ABOUT RETURNING DATA TO DONORS. IF YOU'RE TALKING ABOUT DOING GENOMEWIDE DATA SEQUENCING ON AN IPS LINE, SO ITS PRIMARY CELL HAS BEEN REPROGRAMMED, HOW ARE YOU GOING TO BE ABLE TO PARSE OUT WHAT IS FROM THE DONOR AND WHAT IS FROM THE REPROGRAMMING PROCESS? AND WHAT IS THE SIGNIFICANCE AND MEANING OF THOSE FINDINGS TO THE DONOR FOR WHO THE ORIGINAL MATERIAL HAS BEEN TOTALLY TRANSFORMED?

AND SO, AGAIN, I THINK THE DEVIL IS IN THE DETAILS WHEN YOU THINK ABOUT THIS WHEN YOU'RE APPLYING IT TO AN IPS BANK.

DR. ROBERT TAYLOR: I THINK EXPRESSION IS

ONE THING, BUT THE GENOMIC SEQUENCE PROBABLY ISN'T GOING TO BE DRAMATICALLY ALTERED UNTIL THE CELLS --

DR. PECKMAN: WELL, WHAT WE HAVE SEEN WITH HUMAN EMBRYONIC STEM CELL LINES IS EVEN WITH AGE OF THE LINES, THEY CHANGE IN THEIR GENETIC SEQUENCE. SO IF YOU WORK ON LINE FROM 23 FROM LINE 1, YOU'RE GOING TO SEE A CHANGE IN THE GENOME. AND SO WE'RE TALKING ABOUT SOMETHING FUNDAMENTALLY DIFFERENT THAN DOING A SEQUENCING ON A PRIMARY CELL.

CHAIRMAN LO: THERE'S A SET OF ARTICLES IN *NATURE* OVER THE SUMMER DOCUMENTING GENOMIC PROBLEMS, EPIGENOMIC PROBLEMS, AND NUCLEOTIDE REPEAT PROBLEMS. THE COMEBACK TO THAT IS I CAN IMAGINE A DONOR SAYING TELL ME, AND I CAN ALWAYS SCRAPE UP THE MONEY TO GO TO NAVIGEN IS 2020 IF THEY'RE STILL IN BUSINESS, AND THEY'RE GOING TO DO A WHOLE GENOME SEQUENCING, AND I'LL BE ABLE TO COMPARE. AGAIN, I THINK IT'S ABSOLUTELY RIGHT. WE REALLY DON'T KNOW WHAT THOSE ABNORMALITIES MIGHT MEAN, WHETHER THEY'RE IN THE LINE OR IN THE REPROGRAMMING, BUT I CAN IMAGINE SOMEONE SAYING, WELL, LET ME KNOW. I KNOW IT'S UNCERTAIN AND LET ME TAKE THE NEXT STEP.

DR. FEIGAL: I GUESS GOING BACK TO THE PRINCIPLES OF WHAT DO WE WANT TO DO, I THINK WE ALL WANT TO DO A BETTER JOB COMMUNICATING TO PATIENTS

ABOUT OUR RESEARCH AND THE TYPES OF ADVANCES IT MAKES. I THINK WHAT WE DON'T WANT TO DO ON AN INDIVIDUAL BASIS IS HYPE, PARTICULARLY WITH INFORMATION WHERE WE REALLY DON'T KNOW THE QUALITY OF THE DATA, THE ASSAY CHARACTERISTICS. AND WE DON'T WANT TO EVEN GIVE A PERCEPTION THAT WE'RE SAYING THIS IS USEFUL INFORMATION TO YOU.

SO I THINK I JUST WOULD BE CONCERNED IF WE TAKE THE APPROACH THAT WE'RE GOING TO TELL EVERYTHING. I THINK THAT WE NEED TO PROVIDE INFORMATION IN A GOOD WAY BACK TO PATIENTS ABOUT WHAT WE'RE DOING WITH THEIR RESEARCH AND HOW THAT HAS APPLICABILITY TO THEM. BUT I THINK ON AN INDIVIDUAL BASIS, WE SHOULD EXERCISE A VERY DELIBERATIVE THOUGHT PROCESS ABOUT WHAT WE WANT TO PROVIDE BACK BECAUSE THERE'S A LOT OF NOISE IN THE SYSTEM AND EXPLORATORY RESEARCH, AND THERE'S A TREMENDOUS AMOUNT OF FALSE POSITIVES.

CHAIRMAN LO: I THINK THIS IS THE BREADTH OF OPINION HERE. ELLEN SUMMARIZED THE CONCERNS ABOUT GIVING INFORMATION THAT'S OF UNKNOWN MEANING AND MAY BE MISLEADING AT LEAST TO SOME. CHRIS SORT OF GAVE THE OTHER APPROACH OF FOR AT LEAST ONE COMMITTED AND WELL-INFORMED DONOR, THIS IS ALL VERY IMPORTANT AND, IN FACT, HELPS THE RESEARCH.

SO ONE QUESTION THAT COMES TO MIND, AND WE'VE TALKED A LOT ABOUT THE CONSENT PROCESS REALLY NEEDS TO KIND OF BE PRETTY ROBUST HERE, DO WE WANT TO DO SOME SORT OF EVALUATION? IF THIS, AND THIS IS A BIG IF, IF WE'RE GOING TO ALLOW INDIVIDUAL NONEVALUATED RESULTS TO BE OFFERED, DO WE THEN ASK THE PEOPLE WHO SAY, YES, I'D LIKE THAT TO UNDERGO SOME SORT OF EDUCATION, COUNSELING PROCESS SO THAT WE'RE PERSUADED, WHOEVER IS DOING IT, WHETHER IT'S THE CIRM BANK OR THE CIRM-FUNDED RESEARCHER OR IT'S THE SECONDARY RESEARCHER, IS CONVINCED THAT THAT PERSON ISN'T GOING TO MISINTERPRET.

DR. FEIGAL: I DON'T KNOW HOW DO YOU THAT RESEARCH.

CHAIRMAN LO: THAT'S A BIG BURDEN. THAT'S HUGE. SO IT SEEMS TO ME THAT'S HARD. I WANT TO COME BACK TO THE FACT THAT WHO HAS THE RESPONSIBILITY HERE OF GIVING RESULTS BACK. WE MAY PUT SOMETHING IN THE UP-FRONT CONSENT FORM FOR THE CIRM-FUNDED RESEARCHER WHO'S JUST GOING TO DERIVE THE IPS LINES, BUT THAT RESEARCHER MAY NOT DO MORE THAN JUST DERIVE THE LINE AND GIVE IT OVER TO SOMEONE LIKE TIM AND SAY, HERE. THIS SHOULD BE A NEAT LINE. WORK WITH IT. AND HOW FAR DOWN THAT SECONDARY USE OF THE LINES DOES THIS ANY OBLIGATION

OR AGREEMENT TO OFFER RESULTS BACK GO BECAUSE THE FURTHER DOWN YOU GET, THE FURTHER AWAY FROM THE PATIENT, IT'S GOING TO BE VERY HARD TO DO.

CHRIS HAS, AS I UNDERSTAND IT, PERSONAL CONNECTIONS TO A LOT OF THESE RESEARCHERS. SHE TAKES THE TROUBLE UP FRONT TO SAY LET ME TELL YOU THIS ISN'T JUST 90071. THIS IS MY TWO DAUGHTERS AND I'LL TELL YOU ABOUT THEM. I WANT TO KNOW.

MS. HEMPEL: RIGHT. I CONTACT THEM, BUT I THINK A LOT OF PEOPLE SAY, WELL, HOW ARE YOU GETTING STUFF DONE? HOW DO YOU HAVE AN FDA APPROVAL TO DO THIS TREATMENT ON YOUR TWINS? HOW DID YOU GET THE IPS CELLS DONE? THE ONLY WAY THAT YOU CAN DO THAT IS THROUGH GETTING THE DATA TO PEOPLE TO LIKE MOVE FORWARD AND LIKE TAKE THE NEXT STEP TO GO TO THE NEXT PLACE. AND THE DATA LEADS YOU IN THESE DIFFERENT DIRECTIONS. THAT'S REALLY THE ONLY WAY THAT I'VE BEEN ABLE TO DO IT. SO I THINK IT'S A REALLY CHALLENGING SUBJECT, BUT FOR ME IT'S IMPORTANT TO GET THE DATA. IF I DON'T HAVE THE DATA, I ACTUALLY FEEL A LOT MORE STRESSED OUT BY NOT KNOWING WHAT'S HAPPENING THAN I DO BY KNOWING WHAT IS HAPPENING.

DR. ROBERT TAYLOR: I THINK IT MIGHT BE FAIR TO SAY THAT YOU'RE EXTREMELY EXCEPTIONAL. I

DON'T KNOW THAT THE SYSTEM NEEDS TO RELY ON HAVING EVERYBODY BEHAVE THE WAY YOU'VE DONE, WHICH IS REMARKABLE. SO IT WOULD SEEM TO ME THAT THIS WOULD BE SOMETHING WHERE CIRM WOULD ACTUALLY HAVE A SET-ASIDE FUND TO PROVIDE BECAUSE, AGAIN, I SEE THIS THE FURTHER AWAY THAT IT GETS FROM THE REPOSITORY, THE MORE CHALLENGING IT'S GOING TO BE TO HAVE THAT KIND OF COUNSELING. I WOULD ALMOST -- I DON'T KNOW IF THAT'S COME OUT OF YOUR DISCUSSIONS WITH OTHER STEM CELL CENTERS, BUT IT WOULD SEEM THAT SHOULD BE MAYBE AN INTEGRAL PART OF THE PROGRAM.

MS. ISASI: ABSOLUTELY. IT WAS A KEY ISSUE. IF YOU DECIDE TO PROVIDE SOME INFORMATION, I'LL PUT IN QUOTATIONS, WHETHER IT'S IN THE CLINICAL SIGNIFICANT FINDINGS, ETC. BACK TO THAT, YOU HAVE TO HAVE A SYSTEM IN PLACE, AN INFRASTRUCTURE FOR THEM. AND ONE OF THEM IS HAVING GENETIC COUNSELORS AS PART. OTHERWISE IT WILL BREACH INTO THE RESPONSIBILITIES OF WHOEVER IS IN CHARGE OF DELIVERING THE INFORMATION IN A MANNER THAT WILL EVENTUALLY HARM THE DONORS THEMSELVES. AND LIKE ACTING UP ON FALSE INFORMATION, MISREPRESENTING, ETC. SO PREIMPOSED COUNSELING WAS RECOMMENDED.

AND THIS COULD BE VERY FARFETCHED, BUT I HEARD ONE OF THE BANKERS AND RESEARCHERS USING,

WELL, WE DON'T GO BACK TO THE GENETIC TESTING MODEL IN WHICH WE HAVE PRE AND POSTCOUNSELING BEFORE CONVEYING INFORMATION TO DONORS. AGAIN, DEPENDS ON THE TYPE OF INFORMATION YOU ARE FEEDING BACK.

DR. ROBERT TAYLOR: THAT WOULD BE WONDERFUL VALUE ADDED FOR THE COMMUNITY AND FOR THE INVESTIGATORS AND REALLY FOR EVERYBODY. GREAT IDEA.

DR. LOCKHART: I'M NOT SURE IF THIS WOULD BE HELPFUL, BUT I WONDER AS YOU TALK THROUGH THESE DISCUSSIONS IF IT MIGHT BE USEFUL TO DRAW SOME CONFINES AROUND THE RESPONSIBILITY AS YOU KIND OF DID WITH THE ISSUE OF WITHDRAWAL. SO ONE THING I'VE HEARD IS HOW FAR DOES THE RESPONSIBILITY TO RETURN CONTINUE? IS IT JUST PRIMARY RESEARCHERS THAT RECEIVE CELLS FROM THE CIRM BANK DIRECTLY? IS IT ANYONE THEY THEN GIVE THEIR FURTHER TRANSFORMED CELLS TO? IS THERE SOME BOUNDARY YOU'D BE WILLING TO DRAW?

AND BERNIE MENTIONED EARLIER IS THERE A DUTY TO HUNT? SO IF YOU'RE DOING CARDIOVASCULAR RESEARCH, THAT'S YOUR AREA OF INTEREST, BUT YOU'RE DOING A LARGE-SCALE SEQUENCING, DO YOU HAVE TO LOOK FOR OTHER THINGS? COULD YOU CONSIDER THAT OUTSIDE OF THE BOUNDS OF RESPONSIBILITY THAT THERE IS NO DUTY TO HUNT? THERE'S ONLY A DUTY TO REPORT THINGS

THAT YOU HAPPEN TO FIND. THAT MIGHT BE A WAY TO CONFINE THIS.

AND THEN IS THERE SOME KIND OF LENGTH OF TIME OR OTHER WAY, HOW LONG DOES THIS DUTY TO REPORT EXIST? SO YOU INITIALLY FIND A NUMBER OF VARIANTS, NONE OF THEM ARE CLINICALLY SIGNIFICANT AT THE TIME. WOULD RESEARCHERS HAVE SOME RESPONSIBILITY TO GO BACK AND KEEP REVISITING ARE THEY SIGNIFICANT NOW? SOMETHING LIKE THAT WOULD BE VERY BURDENSOME. SO IS THERE A WAY YOU CAN LIMIT RESPONSIBILITY OR DELINEATE THIS AND MAKE IT A LITTLE CLEARER?

CHAIRMAN LO: LET ME TRY AND -- GEOFF REMINDED ME THAT I HAVE THIS VERY BAD HABIT OF NOT ALLOWING FOR BATHROOM BREAKS. I NOTICE I NEED TO GET A BATHROOM BREAK.

ON YOUR WAY TO EITHER COFFEE OR THE BATHROOM OR BOTH, WHY DON'T WE THINK ABOUT THE FOLLOWING ISSUES. IT STRIKES ME THAT THIS IS A VERY COMPLICATED AND VERY HOT ISSUE. WE'RE NOT GOING TO SETTLE IT TODAY. IT SEEMS TO ME THERE ARE A COUPLE THINGS I'VE HEARD.

ONE IS THAT IF WE'RE GOING TO DO THIS -- IF A RESEARCHER IS GOING TO DO THIS, IT'S GOT TO BE DONE REALLY WELL AND REALLY CAREFULLY. WE'VE GOT TO PAY ATTENTION TO NOT CREATING AN EXPECTATION THAT IS

SO OUTSIZED THAT WE WON'T BE ABLE TO FOLLOW THROUGH. WE NEED TO BE VERY AWARE OF HOW PEOPLE, DONORS MAY VARY IN BOTH THEIR DESIRE TO HAVE RESULTS BACK AND IN THEIR ABILITY TO USE THEM IN A WAY THAT'S HELPFUL TO THEM.

AND I THINK WE'VE HEARD FROM CHRIS ON ONE HAND AND OTHERS THAT YOU CAN IMAGINE SCENARIOS WHERE IT'S WONDERFUL FOR THE DONOR, THE DONOR'S FAMILY, AND THE RESEARCH ENTERPRISE. YOU CAN ALSO THINK OF INSTANCES WHERE THIS MISUNDERSTANDING, ELLEN USED THE TERM "HYPE" IN SORT OF THINKING THAT SOMETHING'S MORE SERIOUS OR MORE ESTABLISHED THAN IT IS. SO HOW DO WE KIND OF ALLOW -- DO WE WANT TO TRY AND ALLOW PEOPLE LIKE CHRIS TO GET WHAT SHE NEEDS; WHEREAS, WE ALSO WANT TO BE CAREFUL NOT TO OFFER OR ENCOURAGE PEOPLE TO RECEIVE RESULTS THAT THEY'RE NOT GOING TO UNDERSTAND, DON'T HAVE THE EDUCATIONAL SUPPORT IN PLACE, OR HAVE A MISCONCEPTION OF WHAT IT IS?

SO STRIKES ME IN TERMS OF POLICY, DO WE JUST SAY IT'S PERMISSIBLE TO BE WORKED OUT BY THE RESEARCHER AND THE DONOR ON A ONE-TO-ONE BASIS, AND HERE ARE SOME GUIDELINES ON HOW TO DO IT WELL? DO WE WANT TO ENCOURAGE IT? DO WE WANT TO CALL ATTENTION TO THE RISKS OF DOING IT? IF YOU ARE GOING TO DO IT, YOU NEED TO PLAN HOW TO ADDRESS ALL

THESE RISKS. OR DO WE JUST WANT TO DO A POINTS TO CONSIDER, THAT THIS IS A HOT TOPIC, A LOT OF PEOPLE ARE DISCUSSING IT. ON THE ONE HAND, YOU HAVE DONOR FAMILIES LIKE CHRIS WHO REALLY THRIVE ON THIS AND IT ACCELERATES THE RESEARCH PROCESS. AND THEN ON THE OTHER HAND, WE HAVE TO BE AWARE OF OTHER SITUATIONS.

SO THIS IS SOMETHING JUST TO THINK ABOUT. I WANT TO TRY AND COME BACK AFTERWARDS AND SEE IF THERE'S SOMETHING TO -- AGAIN, WE'RE THINKING ABOUT NEXT STEPS, NOT NECESSARILY SOLVING THEM. AND THEN THERE ARE A COUPLE OTHER THINGS GEOFF PUT ON OUR AGENDA TO WANT TO DEAL WITH.

WE ARE LIMITED IN OUR TIME. BEFORE FOUR, WE WANT TO MAKE SURE THAT WE'VE SORT OF GIVEN THE BIG PICTURE. SO THAT DOESN'T GIVE US A WHOLE LOT OF TIME. TEN MINUTES.

(A RECESS WAS TAKEN.)

CHAIRMAN LO: WE'RE PROBABLY GOING TO END THE FORMAL MEETING CLOSER TO FOUR THAN TO FIVE. AND THEN WE CAN HAVE SOME INFORMAL DISCUSSIONS.

LET ME TRY AND WRAP UP HERE. THIS HAS BEEN A VERY RICH AND THOUGHTFUL AND COMPLICATED DISCUSSION. THESE ARE REALLY TOUGH ISSUES. AGAIN, I WANT TO REMIND US THAT WHAT WE'RE REALLY DOING IS THINKING ABOUT THE NEXT STEPS. WE'RE NOT HAVING TO

SOLVE ALL THESE PROBLEM TODAY. WE'RE JUST THINKING ABOUT WHAT WE DO NEXT.

AND FIRST OF ALL, THE POINTS THAT REALLY STRUCK ME ARE THAT THERE IS A TREMENDOUS VARIATION IN WHAT DONORS NEED TO KNOW TO MAKE AN INFORMED DECISION AND HOW MUCH THEY WANT TO BE INVOLVED, AND FOR THAT MATTER, WHAT THEY WANT WITH REGARD TO RESEARCH RESULTS. I THINK ONE THAT THING THAT I HEARD AS A THEME IS THAT, WHERE POSSIBLE, WE WANT TO OFFER DONORS OPTIONS, HELP THEM UNDERSTAND WHAT THOSE OPTIONS MEAN, AND ALLOW THEM TO MAKE INFORMED CHOICES, AND THEN STICK TO WHAT WE PROMISED WE WOULD DO.

I THINK THAT WITH REGARD TO CONSENT, WE ALL, I THINK, AGREED THAT CONSENT IS TERRIBLY IMPORTANT. IT'S MORE THAN JUST A CONSENT FORM. IT'S A PROCESS. WE NEED TO MAKE SURE PEOPLE UNDERSTAND WHAT WE TALK TO THEM ABOUT. AND WE WANT THAT PROCESS TO BE BASED ON WHAT DONORS NEED TO KNOW, WHAT THEY HAVE TROUBLE UNDERSTANDING, AND SHOULD TURN TO THE EMPIRICAL LITERATURE. AND I'VE TALKED TO GEOFF, AND HE'S GOING TO WORK ON SORT OF DRAWING TOGETHER WHAT WE KNOW IN OTHER CONTEXTS AND MAYBE SEE IF THERE ARE PROPOSALS FOR CIRM TO DO SOME RESEARCH, ADDITIONAL RESEARCH, ON STEM CELL-SPECIFIC

ISSUES, BUT SHERRY BROUGHT UP THE POINT THAT THERE ARE RESOURCE CONSTRAINT ISSUES.

SO IN TERMS OF CONSENT, I THINK WE HAVE A PLAN GOING FORWARD. WITHDRAWAL OF SUBJECTS FROM RESEARCH, I HEARD A LOT OF AGREEMENT AT THE TWO EXTREMES, THAT ON THE ONE HAND, IF YOU JUST DONATE YOUR TISSUE AND THE SCIENTIST HADN'T DONE ANYTHING WITH IT EXCEPT PUT IT IN THE FREEZER, YOU COULD CERTAINLY WITHDRAW FROM FURTHER CONTACT, PROVIDING ADDITIONAL MEDICAL INFORMATION. AT THE OTHER EXTREME, THAT ONCE THE SCIENTIST HAD TRANSFORMED YOUR CELLS, DERIVED THE STEM CELL LINE, CARRIED OUT ADDITIONAL RESEARCH, YOU NO LONGER COULD JUST WITHDRAW YOUR MATERIALS, THAT YOU COULD DECLINE TO BE INVOLVED IN FURTHER STUDIES, BUT YOU LET GO FORWARD THE RESEARCH WITH THE TRANSFORMED MATERIALS.

DR. ROBERTS: BERNIE, I DON'T MEAN TO INTERRUPT, BUT IT'S THAT YOU CAN NO LONGER WITHDRAW THE TRANSFORMED MATERIALS, BUT THERE'S STILL A QUESTION ABOUT TISSUE.

CHAIRMAN LO: RIGHT. THE ORIGINAL TISSUE, TO THE EXTENT THAT THAT'S THERE AND LOCATABLE AND TRACTABLE, I THINK THAT'S SOMETHING WE NEED TO THINK MORE ABOUT BECAUSE I HEARD DIFFERENT POINTS OF VIEW. AND I THINK WHAT I'M GOING TO ASK GEOFF TO DO IS

FOCUS ON THAT ISSUE AND SORT OF LAY OUT THE POLICY OPTIONS AND THE ARGUMENTS TO REALLY HELP THE ICOC AND THE PEOPLE WHO DRAW UP THE GRANTS POLICY AND THE RFA'S TO SORT OF CONSIDER THAT.

WITH REGARD TO RETURN OF DATA, CLINICALLY INCIDENTAL AND SIGNIFICANT, AGAIN, I THINK WE SAW A LOT OF DIFFERENT VIEWS. AND, AGAIN, I THINK IT'S JUST BEEN, I THINK FOR ALL OF US, CHRIS, A REAL HONOR TO HEAR FROM YOU ABOUT HOW YOU ARE THE SORT OF PARADIGM OF GIVING PEOPLE RESULTS BACK IN WAYS THAT NOT ONLY WILL THEY NOT MAKE UNWISE CLINICAL DECISIONS BY GIVING KIDS COPPER WHEN THEY MAYBE DON'T NEED IT, BUT ALSO USE THAT VERY UNCERTAINTY AS TO WHAT'S IT MEAN TO PUSH THE RESEARCH TO A NEW DIMENSION. TO THE EXTENT THAT WE CAN CAPITALIZE ON THAT KIND OF VISION AND DETERMINATION ON THE PART OF OUR DONORS, WE WANT TO DO THAT.

SO I THINK, AGAIN, THERE'S A LOT OF WORK BEING DONE. I THINK WHAT WE'RE GOING TO ASK GEOFF TO DO IS SORT OF HELP -- GO BACK ON THE TRANSCRIPT AND SUMMARIZE WHERE WE NOW STAND. AND I THINK THAT JUST TO MAKE PEOPLE AWARE OF WHAT THE CURRENT PRACTICES ARE, AND OUR OWN SENSE THERE'S A BIG DIFFERENCE BETWEEN RESEARCH THAT'S OF UNCERTAIN VALIDITY AND UNCERTAIN SIGNIFICANCE FROM INCIDENTAL

FINDINGS THAT REALLY WILL CAUSE A MAJOR CHANGE IN WHAT YOU RECOMMEND FOR THAT PATIENT. WE SHOULD BE MINDFUL OF THOSE AND, AGAIN, LEAVE IT AS AN OPTION FOR DONORS, THAT THEY'RE THE ONES WHO WILL MAKE THAT CHOICE. WE CAN OFFER THEM THE RESULTS, BUT WE KNOW THAT SOME PEOPLE WILL DECLINE INFORMATION THAT WE THINK WOULD REALLY BENEFIT THEIR HEALTHCARE.

THERE ARE A NUMBER OF OTHER ISSUES WHICH WE'RE NOT GOING TO GET TO. I THINK THE MATERIALS RELEASE, TRANSFER AGREEMENTS, I THINK, IS MORE TECHNICAL. AND I THINK, GEOFF, MY OWN SENSE IS YOU DON'T NEED INPUT FROM US.

DR. LOMAX: I THINK THE POINT THERE WAS THAT WE DO ALREADY HAVE A SYSTEM, A SET OF REGULATIONS AND POLICIES, AND THAT REALLY THOSE ARE THE MECHANISMS THROUGH WHICH WE CAN SORT OF TIE OUR EXPECTATIONS TO ANY RELEASE AND USE OF MATERIALS. AND THAT'S A TRIED AND TRUE MECHANISM. AND SO I THINK IT'S A LITTLE --

CHAIRMAN LO: I WOULD LIKE TO PROPOSE THAT WE TURN TO SHERRY FOR A WRAP-UP MINUTE OR SO BECAUSE SHE ALWAYS CAN PUT EVERYTHING IN THE BIG-PICTURE CONTEXT, AND THEN WE ADJOURN THE MEETING. AND I'M GOING TO HANG AROUND A BIT AND LOVE TO TALK ABOUT THINGS LIKE WHAT ABOUT KIDS WHOSE PARENTS DONATED

AND NOW ARE TURNING 18.

MS. LANSING: NO. I THINK YOU WRAPPED IT UP BEAUTIFULLY. YOU SUMMARIZED VERY MUCH THAT WE WERE IN AGREEMENT ON A MENU FOR INFORMED CONSENT, AND WE WERE ALSO IN AGREEMENT THAT INFORMED CONSENT REALLY MEANS MAKING SURE THAT PEOPLE UNDERSTAND WHAT THE VARIOUS OPTIONS ARE, AND THAT WE HAVE ACTUALLY DONE THAT BEFORE IN OUR WORK. THAT THERE WAS A POINT AT WHICH YOU COULD WITHDRAW MATERIAL, AND THAT THERE WAS A POINT AT WHICH IT WAS HARMING SCIENCE. IN THE FIRST CASE WE WERE EMPOWERING THE PATIENT. IN THE SECOND CASE WE DIDN'T WANT TO STOP SCIENTIFIC WORK.

I REALLY JUST WANT TO THANK THE MEMBERS OF THE GROUP. I WANT TO WELCOME OUR NEW MEMBER AND TELL YOU HOW MUCH WE APPRECIATE YOU JOINING OUR TEAM AND HOW VALUABLE IT'S BEEN. I WANT TO THANK ALL THE MEMBERS. WE'VE BEEN DOING THIS NOW, SOME OF US, FOR SIX YEARS. WHEN I SAID THAT WE WOULD BE MEETING AND THAT THIS WAS A WORK IN PROGRESS, I MEANT IT, BUT I DON'T THINK I REALLY, REALLY GRASPED HOW MUCH I MEANT IT. I THINK IT'S THRILLING BECAUSE I THINK I SPEAK FOR ALL OF US IN SAYING THAT WHAT WE THOUGHT SIX YEARS AGO, SOME OF IT STILL HOLDS, BUT A LOT OF IT HAS EVOLVED AND DEVELOPED IN A MORE HELPFUL WAY

FOR BOTH THE SCIENTISTS AS WELL AS THE PATIENT.

AND THAT BRINGS ME TO YOU, CHRIS. I CANNOT THANK YOU ENOUGH FOR BEING HERE. IT'S ALWAYS SO HELPFUL FOR US TO MEET A PATIENT ADVOCATE AND SOMEBODY WHO TELLS US WHAT ALL OF OUR PHILOSOPHICAL DISCUSSION REALLY IS ABOUT AND WHAT IS IMPORTANT ABOUT IT.

I WANT TO THANK THE STAFF FOR EVERYTHING THAT YOU DID TO MAKE THIS MEETING SO TERRIFIC. AND I DIDN'T MEAN FOR IT TO END AT FOUR, BUT I THINK THE STAFF IS LEAVING US. THEY'RE GONE. I GUESS THEY WERE ALL LEAVING. BUT I ACTUALLY THINK IT HAD NOTHING TO DO WITH ME BECAUSE THEY WERE OUT OF HERE LONG BEFORE. I ESPECIALLY WANT TO THANK BERNIE WHO'S JUST EXTRAORDINARY AND ALWAYS HAS THE MOST INCREDIBLE WAY OF LEADING A MEETING. OF COURSE, YOU AS WELL, GEOFF, FOR PREPARING ALL OF US. BUT I HAVE TO SAY IN CIRM THE WORD IS OUT, THAT WE'RE THE COMMITTEE THAT HAS THE MOST FUN AND IS THE MOST CONGENIAL AND REALLY THINKS OUT. AND EVERYBODY IS ALWAYS SAYING I'D LIKE TO BE ON THAT COMMITTEE, AND I HAVE THE PLEASURE OF SAYING IT'S FILLED BECAUSE NOBODY LEAVES US.

SO, BERNIE, YOU'RE JUST AN EXTRAORDINARY LEADER, AND YOU HAVE A WAY ABOUT YOU THAT HAS GREAT

CLARITY AND KINDNESS AND ENCOURAGES COLLABORATION. SO THANK YOU TO EVERYBODY.

CHAIRMAN LO: THANK YOU. YOU WILL HEAR FROM US AGAIN.

(THE MEETING WAS THEN CONCLUDED AT 03:58 P.M.)

REPORTER'S CERTIFICATE

I, BETH C. DRAIN, A CERTIFIED SHORTHAND REPORTER IN AND FOR THE STATE OF CALIFORNIA, HEREBY CERTIFY THAT THE FOREGOING TRANSCRIPT OF THE PROCEEDINGS BEFORE THE SCIENTIFIC AND MEDICAL ACCOUNTABILITY STANDARDS WORKING GROUP OF THE INDEPENDENT CITIZEN'S OVERSIGHT COMMITTEE OF THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE IN THE MATTER OF ITS ANNUAL MEETING HELD AT THE LOCATION INDICATED BELOW

HOTEL PALOMAR LOS ANGELES - WESTWOOD
10740 WILSHIRE BOULEVARD
LOS ANGELES, CALIFORNIA
ON
APRIL 29, 2011

WAS HELD AS HEREIN APPEARS AND THAT THIS IS THE ORIGINAL TRANSCRIPT THEREOF AND THAT THE STATEMENTS THAT APPEAR IN THIS TRANSCRIPT WERE REPORTED STENOGRAPHICALLY BY ME AND TRANSCRIBED BY ME. I ALSO CERTIFY THAT THIS TRANSCRIPT IS A TRUE AND ACCURATE RECORD OF THE PROCEEDING.

BETH C. DRAIN, CSR 7152
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