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

REGULAR MEETING

LOCATION: AS INDICATED ON THE AGENDA

DATE: JANUARY 25, 2017
10 A.M.

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

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JANUARY 25, 2017

10 A.M.

CHAIRMAN SHEEHY: GOOD MORNING, EVERYONE. THIS IS JEFF SHEEHY. I'M CALLING THE SCIENCE SUBCOMMITTEE MEETING TO ORDER. MARIA, COULD YOU CALL THE ROLL PLEASE.

MS. BONNEVILLE: DEBORAH DEAS. ANNE-MARIE DULIEGE. DAVID HIGGINS.

DR. HIGGINS: HERE.

MS. BONNEVILLE: STEVE JUELSGAARD.

MR. JUELSGAARD: HERE.

MS. BONNEVILLE: BERT LUBIN. SHLOMO MELMED.

DR. MELMED: HERE.

MS. BONNEVILLE: JEFF SHEEHY.

CHAIRMAN SHEEHY: HERE.

MS. BONNEVILLE: OS STEWARD.

DR. STEWARD: HERE.

MS. BONNEVILLE: JONATHAN THOMAS.

CHAIRMAN THOMAS: HERE.

MS. BONNEVILLE: ART TORRES.

MR. TORRES: HERE.

MS. BONNEVILLE: KRISTINA VUORI.

DR. VUORI: HERE.

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CHAIRMAN SHEEHY: THANK YOU. SO THE FIRST ITEM ON THE AGENDA IS CONSIDERATION OF THE ALPHA CLINICS CONCEPT PLAN. AND I THINK NEIL LITTMAN IS GOING TO TAKE US THROUGH A PRESENTATION ON THAT.

MR. LITTMAN: THANK YOU, JEFF. SO AS JEFF MENTIONED, THIS IS NEIL LITTMAN. I'M THE DIRECTOR OF BUSINESS DEVELOPMENT AND STRATEGIC INFRASTRUCTURE HERE AT CIRM. AND I WILL BE WALKING THROUGH THE CONCEPT PROPOSAL FOR THE ALPHA STEM CELL CLINICS NETWORK EXPANSION AWARD. THE PRESENTATION IS UP FOR THOSE OF YOU FOLLOWING ALONG ON WEBEX.

SO JUST VERY BRIEFLY, I'M GOING TO START WITH A BRIEF OVERVIEW OF THE EXISTING NETWORK AND PROGRESS TO DATE. I'M GOING TO TALK ABOUT THE CONCEPT PROPOSAL FOR THIS EXPANSION AWARD, THE TIMELINE, BUDGET, AND EXPECTED OUTCOMES.

AS YOU ALL ARE AWARE, THE MISSION OF CIRM IS TO ACCELERATE STEM CELL TREATMENTS TO PATIENTS WITH UNMET MEDICAL NEEDS. TO SUPPORT THIS MISSION, CIRM CREATED THE ALPHA STEM CELL CLINIC NETWORK TO CONDUCT HIGH QUALITY STEM CELL CLINICAL TRIALS. THE ORIGINAL AWARD WAS LAUNCHED IN DECEMBER OF 2015, AND THE NETWORK CURRENTLY INCLUDES SITES AT LEADING ACADEMIC MEDICAL CENTERS, INCLUDING CITY OF HOPE, UC SAN DIEGO, UCLA IN PARTNERSHIP WITH UCI.

THE ALPHA CLINIC NETWORK HAS ONE UNIFYING GOAL, WHICH IS TO ACCELERATE THE DEVELOPMENT AND DELIVERY OF HIGH QUALITY STEM CELL CLINICAL TRIALS TO PATIENTS. THE NETWORK IS CURRENTLY SUPPORTING 29 CLINICAL TRIALS, HAVING ENROLLED OVER 150 PATIENTS TO DATE. THESE TRIALS INCLUDE BOTH CIRM-FUNDED PROGRAMS AS WELL AS NON-CIRM-FUNDED BOTH ACADEMIC AND INDUSTRY SPONSORED TRIALS. SEVEN OUT OF THE 29 TRIALS CURRENTLY ARE SUPPORTED BY CIRM FUNDING, 65 PERCENT OF THE TRIALS ARE INDUSTRY SPONSORED, AND 35 PERCENT OF THE TRIALS ARE INVESTIGATOR SPONSORED. YOU CAN SEE THE PATIENT ENROLLMENT NUMBERS AT EACH ALPHA CLINIC SITE UNDER THE BAR GRAPH ON THE CHART.

THE OBJECTIVE OF THIS EXPANSION AWARD IS TO SUPPORT ADDITIONAL ALPHA CLINIC SITES THAT WILL DELIVER CORE SERVICES NECESSARY TO CONDUCT HIGH QUALITY STEM CELL CLINICAL TRIALS, SUPPORT THE TRAINING AND CAREER DEVELOPMENT OF PHYSICIANS SEEKING TO PERFORM CLINICAL TRIALS, AND ENHANCE THE OVERALL VALUE OF THE NETWORK. THE PROPOSED SITES COULD ENHANCE THE VALUE OF THE NETWORK BY, FOR EXAMPLE, BROADENING THE NETWORK'S GEOGRAPHIC REACH, PROVIDING NEW OR UNIQUE TECHNICAL CAPABILITIES, OR OTHER ELEMENTS THAT ACCELERATE OR SUPPORT STEM CELL CLINICAL TRIALS.

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IF APPROVED, THIS AWARD WILL PROVIDE A TOTAL OF $16 MILLION FOR TWO NEW ALPHA CLINIC SITES OR A TOTAL OF 8 MILLION PER AWARD OVER A FOUR-YEAR PERIOD. FUNDING WILL GO TOWARD PROVIDING CLINICAL INFRASTRUCTURE TO CALIFORNIA-BASED MEDICAL CENTERS TO OPERATE AN ALPHA CLINIC STEM CELL CENTER. THE CLINICS WILL PROVIDE A PLATFORM, I.E., PERSONNEL, FACILITIES, AND OPERATIONS, SPECIFICALLY DEDICATED TO SUPPORT THE UNIQUE NEEDS OF CLINICAL TRIALS AND INVESTIGATIONAL CELL THERAPIES.

IN TERMS OF THE TIMELINE, WE INTEND TO TAKE THIS PROPOSAL TO THE ICOC IN FEBRUARY, RELEASE THE RFA THE BEGINNING OF MARCH, APPLICATION DEADLINE IS MAY 15TH. ASSUMING A POSITIVE GWG REVIEW IN JUNE OR JULY, WE INTEND TO TAKE THIS BEFORE THE ICOC FOR FINAL APPROVAL IN AUGUST, WITH AN ESTIMATED LAUNCH DATE FOR THE NEW EXPANSION SITES IN OCTOBER.

EXPECTED OUTCOMES OF THE AWARD MUST DEMONSTRATE CONTINUOUS IMPROVEMENTS IN TRIAL START-UP TIME; PROTOCOL OPTIMIZATION; AND PIPELINE EXPANSION; TO INTEGRATE WITH OTHER CIRM INFRASTRUCTURE PROGRAMS, INCLUDING EXISTING NETWORK AS WELL AS OUR NEW STEM CELL CENTER; AND TO CREATE A SUSTAINABLE PLATFORM FOR ONGOING DELIVERY OF STEM CELL TREATMENTS TO PATIENTS.

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ORGANIZATIONS FUNDED UNDER THIS AWARD MUST PARTICIPATE IN A COORDINATED EFFORT TO DEVELOP SYSTEMS AND CAPACITIES TO ACCELERATE THE EFFICIENT DELIVERY OF TREATMENTS TO PATIENTS. THE ALPHA CLINIC STEM CELL NETWORK IS ONE OF MULTIPLE COORDINATED INFRASTRUCTURE PROGRAMS DESIGNED TO OVERCOME OBSTACLES AND ACCELERATE THE PROGRESSION OF TREATMENTS THROUGH TRANSLATIONAL, THROUGH CLINICAL, AND CLINICAL TRIALS IN SUPPORT OF CIRM'S MISSION OF DELIVERING STEM CELL TREATMENTS TO PATIENTS WITH UNMET MEDICAL NEEDS.

WITH THAT, I WILL PAUSE AND ANY QUESTIONS.

CHAIRMAN SHEEHY: ARE THERE ANY QUESTIONS FROM ANY OF THE SITES FROM ANY MEMBERS OF THE BOARD?

DR. JUELSGAARD: JEFF, THIS IS STEVE JUELSGAARD. I HAVE A COUPLE QUESTIONS.

CHAIRMAN SHEEHY: SURE.

DR. JUELSGAARD: SO, NEIL, THE FIRST QUESTION IS I JUST WANT TO CONFIRM THAT THE NON-CIRM TRIALS THAT ARE GOING ON AT THE FOUR DIFFERENT CENTERS, THEY'RE ALL STEM CELL OR REGENERATIVE MEDICINE TRIALS; IS THAT RIGHT?

MR. LITTMAN: THAT'S CORRECT. YES, THAT'S CORRECT.

DR. JUELSGAARD: AND THEN THE SECOND

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THING, I FOUND IT INTERESTING THAT THE CITY OF HOPE HAS SO MANY MORE TRIALS GOING ON THAN THE OTHER THREE CENTERS. WHAT IS IT THAT THE CITY OF HOPE IS DOING THAT CAUSES IT TO BE SUCH A GREAT CENTER FOR DOING CLINICAL TRIALS? DO YOU HAVE ANY INSIGHT INTO THAT?

MR. LITTMAN: VERY GOOD QUESTION. THE CITY OF HOPE IS A LEADING ACADEMIC CENTER FOR TRANSPLANTS, HEMATOPOIETIC STEM CELL TRANSPLANTS. I THINK THEY DO THE SECOND MOST TRANSPLANTS IN THE COUNTRY. AND SO THEY ARE HIGHLY FOCUSED ON CANCER. OBVIOUSLY CANCER IS A LARGE COMPONENT OF NOT ONLY CIRM'S PORTFOLIO, BUT WHAT THE INDUSTRY IS TARGETING IN TERMS OF REGENERATIVE MEDICINE AND CELL THERAPIES. AND BECAUSE OF CITY OF HOPE'S EXPERTISE, PARTICULARLY IN CANCER, THEY HAVE A VERY ACTIVE AND ROBUST PROGRAM.

DR. JUELSGAARD: SO I TAKE IT FROM THAT WHAT YOU ARE SAYING IS IS THAT MOST OF THE CLINICAL TRIALS THAT ARE ON THAT BAR CHART ARE REALLY RELATED TO THE CANCER AREA IN TERMS OF STEM CELLS AND REGENERATIVE MEDICINE?

MR. LITTMAN: THAT IS CORRECT. FOR THE CITY OF HOPE, THAT IS CORRECT.

DR. JUELSGAARD: OKAY. THANK YOU.

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CHAIRMAN SHEEHY: ARE THERE OTHER --

MR. TORRES: I JUST MIGHT ADD THAT THE CITY OF HOPE, HAVING BEEN IN MY DISTRICT FOR YEARS, HAS BEEN AT THE FOREFRONT OF CANCER RESEARCH, AND THEY HAVE A GREAT AND LONG HISTORY.

CHAIRMAN SHEEHY: IT'S POSSIBLE THAT IT'S ALSO IMPACTED BY THEIR MANUFACTURING CAPACITY, WHICH I THINK IS PROBABLY WITH UC DAVIS THE BEST IN THE STATE, AT LEAST FOR EARLY STAGE CLINICAL TRIALS.

ARE THERE OTHER QUESTIONS FROM OTHER MEMBERS?

DR. VUORI: VERY NICE PRESENTATION, AND CONGRATULATIONS ON REALLY HAVING ESTABLISHED ALREADY THIS VERY ROBUST NETWORK. I WAS CURIOUS HOW MUCH COLLABORATION THERE IS BETWEEN THE VARIOUS ALPHA CLINICS. ARE THERE TRIALS THAT ENROLL PATIENTS WITH MULTIPLE SITES? OR GIVEN THE CLOSE GEOGRAPHIC PROXIMITY OF THE EXISTING SITES, THAT MAY NOT BE NECESSARY.

MR. LITTMAN: SO VERY GOOD QUESTION. THERE'S A LOT OF COLLABORATION BETWEEN THE SITES. IN FACT, WE'VE PUT IN PLACE WHAT WE CALL AVARS, OR ACCELERATING VALUE ADDED RESOURCES, ACROSS THE NETWORK. AND SO THERE'S VERY CLOSE COLLABORATION. WE HAVE MONTHLY CALLS BETWEEN ALL OF THE NETWORK

SITES. WE HAVE AN ANNUAL SYMPOSIUM THAT'S COMING UP IN MARCH. AND SO THE IDEA IS THAT THE NETWORK AS A WHOLE WILL CREATE AND ADD ADDITIONAL VALUE, THEN EACH SITE COULD OPERATE INDEPENDENTLY. SO THAT'S THE PART OF THE AVAR. SO, FOR INSTANCE, ONE PARTICULAR AVAR IS A PATIENT RECRUITMENT TOOL TO HELP ALL THE SITES RECRUIT PATIENTS FASTER FOR TRIALS WITHIN THE NETWORK.

DR. VUORI: THANK YOU.

CHAIRMAN SHEEHY: ANY OTHER QUESTIONS? SO COULD I GET A MOTION TO APPROVE THE CONCEPT PLAN?

MR. TORRES: SO MOVED.

CHAIRMAN SHEEHY: BY SENATOR TORRES. CAN I GET A SECOND?

CHAIRMAN THOMAS: SECOND.

CHAIRMAN SHEEHY: SECONDED BY CHAIRMAN THOMAS.

IS THERE ANY PUBLIC COMMENT AT ANY OF THE SITES? MARIA, COULD YOU CALL THE ROLL.

MS. BONNEVILLE: SURE. DEBORAH DEAS. ANNE-MARIE DULIEGE. DAVID HIGGINS.

DR. HIGGINS: YES.

MS. BONNEVILLE: STEVE JUELSGAARD.

MR. JUELSGAARD: YES.

MS. BONNEVILLE: BERT LUBIN. SHLOMO

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MELMED. DR. MELMED? JEFF SHEEHY.

CHAIRMAN SHEEHY: YES.

MS. BONNEVILLE: OS STEWARD.

DR. STEWARD: YES.

MS. BONNEVILLE: JONATHAN THOMAS.

CHAIRMAN THOMAS: YES.

MS. BONNEVILLE: ART TORRES.

MR. TORRES: AYE.

MS. BONNEVILLE: KRISTINA VUORI.

DR. VUORI: YES.

MS. BONNEVILLE: DR. MELMED.

DR. MELMED: YES.

MS. BONNEVILLE: THANK YOU.

CHAIRMAN SHEEHY: MOTION CARRIES. THANK YOU.

NOW FOR ITEM 4, DR. SAMBRANO WILL TAKE US THROUGH THAT.

DR. SAMBRANO: THANK YOU, MR. SHEEHY. I ALSO HAVE SLIDES THAT ARE ON WEBEX, AND THEY'VE BEEN DISTRIBUTED IF YOU'D LIKE TO FOLLOW ALONG. WHAT I'M GOING TO PRESENT TO YOU ARE SOME PROPOSED AMENDMENTS TO OUR CLINICAL, TRANSLATIONAL, AND DISCOVERY CONCEPTS THAT WILL IMPACT THE PROGRAM ANNOUNCEMENT THAT WE HAVE FOR ALL OF THESE RECURRING FUNDING OPPORTUNITIES. SOME OF WHAT I'M GOING TO GO OVER IS

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GOING TO BE APPLICABLE GLOBALLY, AND SOME OF THEM ONLY TO SPECIFIC CONCEPTS. AND I'LL LET YOU KNOW WHICH ONES THOSE ARE.

THERE IS A MEMO THAT WAS PROVIDED BY JAMES HARRISON THAT ALSO SUMMARIZES THE SPECIFIC CHANGES THAT WE INTEND TO MAKE AS WELL AS HOW THEY IMPACT THE SPECIFIC CONCEPT DOCUMENTS. SO THAT IS SHOWN WITH TRACK CHANGES IN THOSE DOCUMENTS.

WITH THE SLIDES, I'M JUST GOING TO GO OVER THE BIG PICTURE CONCEPT OF THESE. THE FIRST ONE THAT'S SHOWN ON THE FIRST SLIDE IS A GOOD STANDING REQUIREMENT. SO FOR SOME TIME NOW WE HAVE BEEN, THROUGH OUR APPLICATION PROCESS, COLLECTING INFORMATION FROM APPLICANTS WHERE WE ASK THEM TO VERIFY THAT THEY HAVE SYSTEMS IN PLACE TO TRACK CIRM FUNDS, THAT THE PI OR OTHER OFFICIALS FROM THE ORGANIZATION ARE NOT CURRENTLY UNDER INVESTIGATION FOR CRIMES INVOLVING FRAUD OR MISAPPROPRIATION. AND WE HAVEN'T REALLY HAD A SITUATION WHERE SOMEBODY HAS CHECKED AFFIRMATIVELY ON ANY OF THESE, BUT WE ALSO REALIZE THAT IF ANYBODY DOES, WE DON'T HAVE WITHIN THE CONCEPT OR THE PROGRAM ANNOUNCEMENT THE ABILITY TO DO SOMETHING ABOUT IT.

SO WHAT WE WANTED TO DO HERE IS MAKE IT AN ELIGIBILITY REQUIREMENT. SO THE ELIGIBILITY

REQUIREMENT WOULD BE THAT THE APPLICANT MUST DEMONSTRATE THAT THEY ARE IN GOOD STANDING AND WOULD VERIFY THAT THEY HAVE A SYSTEM IN PLACE TO TRACK FUNDS, THAT THEY HAVEN'T BEEN CONVICTED OF, UNDER INVESTIGATION FOR CRIMES AND MISAPPROPRIATION. AND, IN ADDITION, THAT THE PI IS NOT UNDER INVESTIGATION FOR RESEARCH MISCONDUCT AND IS NOT FAR EXCEEDING RESEARCH FUNDS BY THE OFFICE OF RESEARCH INTEGRITY. SO WE WANT TO INCLUDE THAT.

ON THE NEXT SLIDE THERE ARE A COUPLE OF ITEMS THAT RELATE TO PERSONNEL ELIGIBILITY. THE FIRST RELATES TO PROJECT MANAGER. WE WOULD LIKE, NOW THAT WE HAVE IN PLACE OUR STEM CELL OR TRANSLATING CENTER AND ACCELERATING CENTER, WHICH NOW JUST COMBINES THE STEM CELL CENTER, ALL APPLICANTS TO FULFILL THE REQUIREMENT OF HAVING A PROJECT MANAGER THROUGH THE CENTER SIMPLY BECAUSE IT ITSELF PROVIDES PROJECT MANAGEMENT SERVICES. SO WE WOULD LIKE TO ALLOW THAT TO BE A WAY OF DOING IT. AND THAT WOULD APPLY TO THE CLIN AND TRAN PROGRAMS.

NOW, FOR PERCENT EFFORT OF THE PI, AND THIS NOW APPLIES ONLY TO THE CLINICAL PROGRAMS, WE WOULD LIKE TO ALLOW A PI TO PROPOSE AND JUSTIFY THE PERCENT EFFORT THAT WOULD BE CONSISTENT WITH ACHIEVING THE PROJECT'S AIMS RATHER THAN

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SPECIFICALLY REQUIRING 30 PERCENT. WE'VE COME ACROSS SITUATIONS WHERE THE PERCENT EFFORT COULD BE LESS, AND WE DON'T WANT TO PREVENT OR RESTRICT WHAT WOULD BE THE MOST APPROPRIATE PI FROM PARTICIPATING IN THESE PROJECTS. AT THE SAME TIME, WE WANT TO MAKE SURE THAT THEY ARE DEDICATING SUFFICIENT TIME. SO RATHER THAN HAVING THIS ELEMENT BE PART OF THE ELIGIBILITY CRITERIA, WE WANT IT TO BE SOMETHING THAT'S THE SUBJECT OF THE PEER REVIEW SUCH THAT REVIEWERS WOULD DETERMINE WHETHER OR NOT THE PI IS DEDICATING SUFFICIENT EFFORT TO ACCOMPLISH THE ACTIVITIES THAT ARE PROPOSED.

ON THE NEXT SLIDE BEGINS SOME PROJECT ELIGIBILITY CHANGES THAT WE'D LIKE TO PROPOSE. THE FIRST IS A READINESS CRITERION FOR CLIN1 APPLICATIONS. THOSE ARE THE IND-ENABLING STUDIES UNDER THE CLINICAL PROGRAM. AND HERE WE WANT TO REDUCE THE TIME TO IND FILING FROM 24 MONTHS TO 18 MONTHS. SO THE REQUIREMENT HERE WOULD BE THAT SOMEBODY COMING IN WOULD HAVE, AS PART OF THEIR TIMELINE AND PROPOSAL, A PLAN TO ACHIEVE THE IND FILING NO LATER THAN 18 MONTHS INTO THE PROJECT. THE PROJECT ITSELF COULD EXTEND TO 24 MONTHS BECAUSE WE DO ALLOW CLINICAL START-UP ACTIVITIES, BUT THE GOAL HERE IS TO MAKE SURE THAT WE ARE ACHIEVING OUR

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GOAL OF REDUCING THE TIME TO GET A STEM CELL TREATMENT FROM DISCOVERY TO THE CLINIC AND REDUCING THAT BY 50 PERCENT. THAT IS ONE OF OUR BIG SIX GOALS, AND THIS IS ONE MECHANISM BY WHICH WE CAN DO THAT.

MR. TORRES: ON THAT POINT, DR. SAMBRANO, HAVE YOU HAD PUSHBACK FROM POTENTIAL GRANTEES IN RESPECT TO SHORTENING THAT TIME FRAME?

DR. SAMBRANO: NO. WELL, WE HAVEN'T IMPLEMENTED THIS YET. BUT HERE WE HAVE PROJECTS THAT WOULD EITHER COME IN AND BE READY FOR CLIN1, MEANING THEY'RE 18 MONTHS AWAY FROM FILING AN IND. IF THEY'RE NOT, THEY WOULD THEN GO INTO THE TRAN PROGRAM WHICH ALLOWS THEM TO CONDUCT STUDIES THAT GET THEM TO THE RIGHT READINESS POINT TO COME INTO THE CLIN1.

CHAIRMAN SHEEHY: SO I GUESS I'M CONFUSED BECAUSE THE DIFFERENCE OF SIX MONTHS THEN PUSHES SOMEBODY INTO A DIFFERENT POTENTIAL CATEGORY OF FUNDING?

DR. SAMBRANO: IF THEY'RE NOT WITHIN ABOUT 18 MONTHS AS OPPOSED TO WHAT WE PREVIOUSLY HAD OF 24 MONTHS, YES.

CHAIRMAN SHEEHY: I GUESS I'M NOT UNDERSTANDING THAT BECAUSE I DON'T KNOW WHAT WORK IN

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TRANSLATION WOULD BE DONE THAT WOULD MAKE SIX MONTHS' DIFFERENCE. WHAT'S THE LENGTH OF THE TRANSLATION GRANT TYPICALLY?

DR. SAMBRANO: TRANSLATION GRANT IS 24 TO --

DR. OLSON: SO I THINK WHAT WE'RE TRYING TO DO AND WHAT WE'VE NOTICED IN SOME OF THE CLIN1 PROGRAMS IS THAT THE MANUFACTURING AND THE PROCESS SCALE-UP IS NOT REALLY WHERE IT SHOULD BE. A LOT OF TIMES -- FROM A PRE-IND MEETING, SO THEY'RE DOING ADDITIONAL WORK. WHAT WE'D LIKE THEM TO DO AT THAT TIME IS WHEN YOU HAVE A PRE-IND MEETING, WE'D LIKE THEM TO HAVE DONE THE WORK IN TRANS. USUALLY YOU'RE SUPPOSED TO HAVE YOUR PROCESS LOCKED DOWN, YOU'RE SUPPOSED TO BASICALLY GET THE FDA'S INPUT ON YOUR PROPOSED CLINICAL TRIAL AND ON YOUR PIVOTAL SAFETY STUDIES.

SO IF YOU HAVE YOUR PROCESS LOCKED DOWN, IF YOU'VE GOT YOUR DOSE FIGURED OUT, IF YOU'VE ALREADY DECIDED ON YOUR INDICATION, ALL OF WHICH ARE KEY TRAN STAGE ACTIVITIES, THEN YOU SHOULD BE ABLE TO MOVE READILY AND MEET THESE 18-MONTH TIMELINES TO FILE AN IND.

CHAIRMAN SHEEHY: SO ARE WE REALLY KIND OF MOVING OUT OF THE VALLEY OF DEATH, THEN, BECAUSE

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WHAT YOU ARE DOING IS -- WHAT HAS BEEN OUR EXPERIENCE WITH CLIN1 FOLKS BECAUSE TRANS IS NOT VERY PERMISSIVE; WHEREAS, CLIN1 IS VERY PERMISSIVE.

DR. OLSON: I DON'T KNOW WHAT YOU MEAN BY PERMISSIVE.

CHAIRMAN SHEEHY: I MEAN THAT WE GET MORE APPLICATIONS THAN WE CAN FUND IN TRANS, AND WE END UP NOT FUNDING APPLICATIONS THAT GET GOOD SCORES. THE TIMELINE TO COME BACK IS ABOUT SIX MONTHS. FOR CLIN1, YOU CAN COME IN, YOU CAN GET A TWO, COME BACK THE NEXT MONTH OR TWO MONTHS LATER, AND THE COMPETITION IS LESS FIERCE. SO WE'RE DROPPING THESE FOLKS INTO A WHOLE RANGE AND A WHOLE GROUP OF APPLICATIONS IN WHICH THEIR SUCCESS RATE IS GOING TO BE MUCH LESS LIKELY THAN THEIR SUCCESS RATE IF THEY HAVE RIVAL APPLICATIONS IN CLIN1.

DR. OLSON: THE TRAN ROUND IS THREE TIMES A YEAR NOW, SO THERE'S A FOUR-MONTH DELAY. THERE'S FOUR MONTHS BETWEEN APPLICATIONS. I WANT TO STATE THAT FIRST.

AND I THINK THE ISSUE REALLY IS WHEN YOU ACCEPT CLIN1 PROJECTS THAT ARE ACTUALLY NOT AT A READINESS STATE THAT YOU'D LIKE, AND WE DON'T REALLY HAVE ENOUGH EXPERIENCE WITH OUR CLIN1 PROGRAMS YET TO SAY THIS, BUT WE DO KNOW THAT WHAT WE ARE FINDING

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TO BE THE SINGLE BIGGEST ISSUE IN THESE PROGRAMS IS THE MANUFACTURING. AND THAT THAT COULD END UP EXTENDING -- AND IT'S BAD FOR THEM BECAUSE WE HAVE THESE OPERATIONAL MILESTONES, AND WE ONLY FUND UP TO A CERTAIN POINT. SO THEY END UP HAVING TO CALL ON THEIR BACKUP FUNDS. THEY END UP -- THEY MISS MILESTONES, AND THE PROGRAM ENDS UP BEING LONGER THAN IT SHOULD BE.

CHAIRMAN SHEEHY: I GUESS I'M TRYING TO GET THE BACK BASIS FOR THAT. WHAT ARE WE DRAWING THOSE CONCLUSIONS ON? DO WE HAVE PEOPLE WHO ARE MISSING THEIR MILESTONES THAT ARE BEHIND ON THEIR PROJECTS? BECAUSE I JUST DON'T THINK DROPPING THEM INTO TRANS, THEIR SUCCESS RATE IS GOING TO BE MUCH LOWER THAN IF THEY WERE IN CLIN1. THE BOTTLENECKS -- THE AMOUNT OF FUNDING AVAILABLE FOR TRANS IS SO LIMITED.

DR. SAMBRANO: IF I MIGHT ADD SOME CLARIFICATION TO THIS. THE REQUIREMENT CURRENTLY TO COME INTO CLIN1 IS THAT THEY HAVE COMPLETED A PRE-IND MEETING. AND THE GENERAL REQUIREMENT AND EXPECTATION IS STILL THE SAME. SO IT HASN'T CHANGED, BUT THEY SHOULD BE ABLE TO AT THAT POINT HAVE A CLEAR PATH TO GET TO THEIR IND. BUT BECAUSE THERE'S A LOT OF FLEXIBILITY A LOT OF TIMES AS TO

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WHEN SOME FOLKS FILE OR CONDUCT THEIR PRE-IND MEETING, WHAT WE WANT IS FOR THEM TO HAVE IN THE TRAN PROGRAM WHAT WE CALL A WELL-PREPARED AND SUCCESSFUL PRE-IND MEETING WITH THE FDA. THAT MEANS ALL OF THE ACTIVITIES THAT LEAD UP TO THAT POINT SO THAT THEY HAVE A CLEAR PLAN, WHICH WE FEEL THEY CAN CONDUCT WITHIN 18 MONTHS IF THEY TRULY ACHIEVE THAT.

SO THE TARGET ISN'T REALLY MOVING SO MUCH BECAUSE THAT'S STILL A REQUIREMENT. THEY HAVE TO STILL COME IN WITH THE PRE-IND. WE WANT TO ACCELERATE THE TIME FROM WHEN THEY COME IN TO WHEN THEY DO AND CONDUCT THE FILING. AND THEN STILL ALLOWING THEM, EVEN AFTER THAT, TO DO START-UP ACTIVITIES WITH THE CLINICAL TRIAL WHICH THE CLIN1 ALLOWS. SO THAT WAY THEY DON'T EXCEED THE TWO-YEAR OVERALL TIME FRAME FOR THAT AWARD.

DR. OLSON: I GUESS THE QUESTION IS ALSO DO YOU WANT THEM TO FAIL AT THE CLIN1 STAGE AFTER YOU'VE INVESTED THE MONEY, OR DO YOU WANT THEM TO HAVE A CHANCE AT THE TRAN STAGE WHERE THEY WILL DO THE WORK THAT WILL GET THEM THE WELL-PREPARED PRE-IND. I CANNOT ARGUE WITH YOUR POINT THAT THERE IS 45 MILLION, I'M NOT EXACTLY SURE WHAT THE AMOUNT WE'RE TARGETING FOR CLIN1 PROGRAMS IS, AND I DON'T HAVE THE RIGHT PERSON HERE TO ADDRESS THAT. I KNOW

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THAT OUR FOCUS IS ON CLIN2S, LESS ON CLIN1S. BUT THAT REALLY IS THE POINT IS TO GIVE THEM A CHANCE TO GET THE ACTUAL WORK THAT THEY SHOULD HAVE DONE TO HAVE A WELL-PREPARED PRE-IND MEETING IN THE TRAN STAGE AND AVOID THAT AND THE POTENTIAL OF FAILURE AND DELAYS IN THE CLIN1 STAGE.

CHAIRMAN SHEEHY: I'M STILL TROUBLED BECAUSE I DON'T HAVE A FACT BASIS ON WHICH TO MAKE THIS DECISION BECAUSE YOU'RE SAYING THAT THEY ARE GOING TO FAIL, THAT THE PROJECTS AS THEY'VE GONE THROUGH THE GWG AND GOTTEN FUNDABLE SCORES ARE GOING TO FAIL, AND THAT'S WHY WE NEED TO CHANGE THIS, BECAUSE THEY'RE FAILING.

DR. OLSON: NO. I'M SAYING THAT THE SINGLE ISSUE THAT MOST OFTEN WILL LEAD TO DELAYS IS PROCESS-RELATED ISSUES IN THE CLIN1 STAGE.

CHAIRMAN SHEEHY: WHY WILL IT LEAD TO DELAYS? HAVE WE EXPERIENCED DELAYS IN THE PROJECTS THAT HAVE GOTTEN FUNDABLE SCORES BY THE GRANTS WORKING GROUP IN CLIN1? THERE HAS TO BE SOME FACT BASIS FOR MAKING THIS CHANGE.

DR. OLSON: I'M NOT HEAD OF THAT. I BELIEVE -- IT IS MY UNDERSTANDING THAT THERE ARE SOME PROJECTS THAT WE ARE HAVING ISSUES WITH WITH PROCESS DEVELOPMENT AT THAT STAGE.

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MR. TORRES: THAT'S WHY I TALKED ABOUT PUSHBACK.

CHAIRMAN SHEEHY: I JUST THINK WE'RE PROBABLY -- I GUESS I NEED MORE INFORMATION ON THIS BEFORE. MAYBE THAT CAN COME AT THE BOARD. BUT --

DR. MILLS: JEFF, WHAT WE'RE TRYING TO DO -- AND I THINK WE JUST GOT WAY, WAY TOO FAR INTO THE WEEDS HERE. WHAT WE'RE TRYING TO DO ON A VERY SIMPLE LEVEL, HIGH LEVEL, IS SET THE EXPECTATION FROM THE APPLICANTS THAT YOU ARE GOING TO SPEND ABOUT TWO AND A HALF YEARS IN TRANSLATION AND ABOUT ONE AND A HALF YEARS IN CLIN1, WHICH MAKES THE TRANSLATION TIME FOUR YEARS, WHICH WE SET OUT AS A STRATEGIC GOAL. AND IF OUR STATED PROGRAMS DON'T HAVE THAT AS A GOAL, THEN WE'RE NOT CONSISTENT WITH THE STRATEGIC PLAN THAT WE APPROVED, WHICH SAID THAT THESE ACTIVITIES THAT EVERYONE ELSE IN THE WORLD CAN DO IN 3.2 YEARS FOR US TAKE EIGHT YEARS. WE'RE TRYING TO GET THEM DOWN TO FOUR YEARS. IF OUR PROGRAMS DON'T AT LEAST SET THAT UP WITHOUT THE NONCOST EXTENSION, THEN WE'RE NOT EVEN AT THE OUTSET SETTING THE EXPECTATION THAT WE WANT THESE THINGS TO MOVE EXPEDITIOUSLY. THAT'S REALLY ALL WE'RE TRYING TO DO.

CHAIRMAN SHEEHY: I'M STILL CONFUSED, BUT

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I WON'T BELABOR THE POINT. I GUESS WHEN I SEE CHANGES FROM WHAT WE ORIGINALLY DECIDED TO DO, IT'S ALWAYS GOOD TO KIND OF UNDERSTAND WHY WE'RE DOING IT. I MEAN I GUESS THIS IS JUST WE'RE GOING JUST TO MAKE IT SO KIND OF IDEA, BUT I THINK WE MAY BE PUSHING PEOPLE INTO TRANSLATION WHERE THEY REALLY DON'T HAVE A GOOD SHOT. AGAIN, GIVEN THAT WE'VE BEEN APPROVING PROJECTS IN THIS SPACE THAT HAVE TO GET 1S, I GUESS -- ANYWAY. I'M HAPPY TO MOVE ON FROM THAT. I DON'T THINK I'LL BE MOLLIFIED.

NEXT. SORRY, DR. SAMBRANO.

DR. SAMBRANO: THE NEXT ITEM RELATES TO SMALL MOLECULE OR BIOLOGIC CANDIDATE ELIGIBILITY. HERE WE WANT TO CLARIFY THE ELIGIBILITY OF RESEARCH THAT INVOLVES SMALL MOLECULES OR BIOLOGICS WHERE A STEM CELL IS NECESSARY TO MANUFACTURE THE THERAPY. THIS, FOR EXAMPLE, WOULD ALLOW EXOSOME OR OTHER NOT CELL THERAPIES TO ALSO QUALIFY IF THEY ARE MANUFACTURED USING A STEM CELL. THIS WOULD APPLY TO TRAN1, CLIN1, AND PHASE I TRIALS UNDER THE CLIN2.

SO ASIDE FROM THAT CHANGE, ON THE NEXT SLIDE, THE PHASE I'S WOULD LARGELY BE THE SAME IN TERMS OF THE CANDIDATE ELIGIBILITY, BUT WE ARE PROPOSING SOME CHANGES FOR THE PHASE II AND PHASE III STAGE WHERE FOR PHASE II WE WOULD WANT TO

RESTRICT ELIGIBILITY TO CELL THERAPIES WHERE STEM PROGENITOR CELLS EITHER COMPOSE THE THERAPY OR ARE USED TO MANUFACTURE THE THERAPY. AND FOR PHASE III TRIALS, TO RESTRICT IT FURTHER BY ADDING THE CAVEAT THAT THEY ALSO NEED TO BE FOR A RARE INDICATION.

AND THE THINKING BEHIND THIS IS THAT FOR A PHASE I PROJECT, THE SMALL MOLECULES AND BIOLOGICS THAT ARE SUCCESSFUL IN ACHIEVING AND GETTING GOOD DATA FROM A PHASE I SHOULD BE ABLE TO ATTRACT FUNDING TO MOVE THOSE PROJECTS FORWARD INTO THE NEXT STAGES OF DEVELOPMENT; WHEREAS, CELL THERAPIES HAVE A MORE CHALLENGING REGULATORY ENVIRONMENT AND HAVE MORE DIFFICULTY IN GETTING FUNDING TO CARRY THOSE THROUGH. SO WE WANT TO FOCUS IN ON HELPING THE CELL THERAPIES ESPECIALLY AT THOSE LATER STAGES WHERE THERE IS THE GREATEST NEED FOR THOSE PROJECTS.

ON THE NEXT ONE WE HAVE THE CLIN3 PROGRAM, AND THE CLIN3 PROGRAM, AS IT CURRENTLY STANDS, IS A SUPPLEMENT TO CLIN1 AND CLIN2 AWARDS. AND THE REQUIREMENT WAS THAT BASICALLY IT PROVIDES FUNDS TO ACCELERATE ACTIVITIES THAT WERE ORIGINALLY PROPOSED OR THAT CAN BE PROPOSED TO ACCELERATE THOSE PROJECTS. IT HAS NOT TURNED OUT TO BE A VERY GOOD DESIGN IN TERMS OF A PROGRAM FOR US. WE HAVE HAD THREE APPLICATIONS OVER THE LAST TWO YEARS. NONE

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HAVE BEEN APPROVED FOR FUNDING OR RECOMMENDED FOR FUNDING. AND SO WE FEEL THAT WE NEED TO REFOCUS THAT PROGRAM DIFFERENTLY.

THE WAY WE'D LIKE TO DO THAT IS TO LIMIT IT TO AWARDEES THAT WOULD, IF THEY HAVE AN EXISTING, FOR EXAMPLE, PHASE II TRIAL, TO UTILIZE SUPPLEMENTAL FUNDS TO CONVERT THAT TO A REGISTRATION TRIAL; THAT IS, A TRIAL THAT WOULD BE THE BASIS FOR APPROVAL BY THE FDA FOR COMMERCIALIZING THE PRODUCT.

ON THE NEXT SLIDE, SOME ELIGIBILITY CHANGES FOR DEVICES. FIRST, FOR THE TRAN3, HERE WE WANT TO ALIGN WHAT WE HAVE IN THE CLINICAL PROGRAM WITH THE TRAN PROGRAM. SO SIMPLY BY ADDING ADDITIONAL LANGUAGE TO INCLUDE STUDIES ON THE DEVICE WHERE THE THERAPEUTIC MECHANISM OF ACTION REQUIRES THE RECRUITMENT OR INCORPORATION OF AN INDOGENOUS HUMAN STEM OR PROGENITOR CELL. THIS IS NOT CURRENTLY IDENTIFIED IN THE TRAN PROGRAM, BUT IS IN THE CLINICAL ONE, SO WE WANT TO ALIGN THOSE.

FOR CLIN2, IN THE SAME WAY THAT WE ARE PROPOSING TO LIMIT PHASE II AND PHASE III TRIALS TO CELL THERAPY, TO ALIGN WITH THAT, WE WANT TO LIMIT OUR SUPPORT OF DEVICE TRIALS TO FEASIBILITY STUDIES WHICH ARE EQUIVALENT TO A PHASE I FOR A DEVICE IN A TRIAL SETTING.

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THE NEXT SLIDE RELATES TO FUNDING CAPS THAT WE WANT TO PROPOSE FOR THE CLINICAL PROGRAM. SO THIS WOULD APPLY TO CLIN1, 2, AND 3. AND BASED ON OUR EXPERIENCE OF CLINICAL TRIAL COSTS FROM APPLICATIONS AND GRANTS THAT WE HAVE FUNDED, AS WELL AS THE CALCULATION OF FUNDS THAT WOULD BE NECESSARY TO MEET OUR GOAL OF FUNDING 50 TRIALS BY 2020, THAT IS, OUR CAPACITY OVERALL TO FUND THAT MANY TRIALS, WE'VE DETERMINED THAT AN APPROPRIATE CAP FOR EACH OF THESE PROGRAMS WOULD BE AS FOLLOWS:

FOR CLIN1 WE WOULD ALLOW PROGRAMS UP TO 6 MILLION IF THEY ARE A NONPROFIT AND 4 MILLION IF THEY ARE A FOR-PROFIT INSTITUTION.

FOR CLIN2, IN OTHER WORDS, FOR THE PHASED TRIALS, IF IT'S A PHASE I TRIAL, UP TO 5 MILLION FOR FOR-PROFITS AND 9 MILLION FOR NONPROFITS. A PHASE II TRIAL WOULD BE UP TO 12 MILLION. THIS IS WHERE THE NON-PROFITS AND FOR-PROFITS ALIGN WITH THE SAME AMOUNT IN THE SAME WAY THAT THEY ALIGN WITH THE CO-FUNDING REQUIREMENT THAT WE HAVE AT THAT STAGE. AND THEN FOR PHASE III, IT WOULD BE UP TO 15 MILLION.

AND THEN SIMILARLY, SINCE THE CLIN3 IS TO ALLOW A PHASE II OR OTHER TRIAL TO BECOME A REGISTRATION TRIAL, THAT'S EQUIVALENT TO THE PHASE

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III FUNDING AMOUNT.

CHAIRMAN SHEEHY: CAN I ASK A QUESTION ABOUT THAT? WHAT ARE THE PROJECTIONS? SO OBVIOUSLY YOU'RE EXPECTING CERTAIN NUMBERS OF 1, 2, AND 3 TO GIVE US THOSE PROJECTIONS.

DR. SAMBRANO: SO THIS IS BACK CALCULATED FROM ACHIEVING UP TO 50 TRIALS BY 2020. SO I DON'T HAVE, AND, PAT, I DON'T KNOW IF YOU HAVE, I THINK GABE DOES, HAS THE CALCULATION. RANDY, YOU MAY OR MAY NOT REMEMBER.

DR. MILLS: WE DID IT, JEFF, AND I KNOW EXACTLY WHAT YOU'RE SAYING. WE CAN GET IT TO YOU BECAUSE THIS IS OBVIOUSLY -- THESE CAPS ARE OBVIOUSLY BASED ON MODELS. AND THOSE MODELS SHOW, WITH SOME SORT OF CONFIDENCE BANDS, WHAT MIX OF TRIALS WE WOULD EXPECT TO HAVE GOING FORWARD AND THEN HOW MUCH MONEY WE HAVE TO KIND OF BACK ALL THAT UP AND YOU GET TO THIS. UNFORTUNATELY WE DID NOT BRING THAT TO THIS MEETING, BUT WE CAN GET IT TO YOU.

CHAIRMAN SHEEHY: AND THEN THE OTHER THING THAT WOULD BE INTERESTING TO SEE, FOR THE PEOPLE WE FUNDED, HOW MANY -- LIKE, I'M ASSUMING THAT THIS IS PROBABLY A MEDIAN OF SOME SORT WITH A BAND THAT HAS PEOPLE EXCEEDING AND BELOW. SO IT WOULD BE GREAT TO

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SEE WHAT THAT LOOKS LIKE.

DR. MILLS: SURPRISINGLY, WITH THE EXCEPTION OF THE PHASE IIIS, ALMOST ALL OF IT, THERE'S VERY LITTLE ALTERATION TO ANY OF THE PHASE I OR IIS THAT WE FUNDED SO FAR UNDER THESE NEW CAPS. AND DEPENDING ON THE PHASE III THAT WE'RE TALKING ABOUT, THERE'S UP TO A $5 MILLION VARIANCE THERE. BUT WE WANTED TO MAKE SURE THAT THINGS THAT WE ARE DRIVING AND INCENTIVIZING THE MOST WOULDN'T BE NEGATIVELY IMPACTED BY THIS. AND SO WE'LL GET THAT FOR YOU AS WELL.

CHAIRMAN SHEEHY: GREAT. GREAT.

CHAIRMAN THOMAS: JEFF, I'VE GOT A QUESTION. SO, GIL, THE DIFFERENT AWARDS VARIOUSLY CONTEMPLATE CO-FUNDING REQUIREMENTS, ETC. BUT WHAT SORT OF ASSUMPTIONS, PARTICULARLY WHEN YOU GET TO THE PHASE IIS AND THE PHASE IIIS, DO YOU HAVE THAT OF THE TOTAL PROJECT COST THAT OUR COMPONENT WILL COMPRISE. AND ASSUMING LEVERAGING THAT BEYOND JUST THE CO-FUNDING REQUIREMENTS, HOW MUCH OF A PIECE OF THE PUZZLE ARE WE WHEN YOU GET TO THE BIGGER TRIALS UNDER THESE CAP STRUCTURES?

DR. SAMBRANO: THE CAP DOES NOT ALTER THE CO-FUNDING REQUIREMENTS THAT WE HAVE IN PLACE. SO THOSE WOULD STILL BE THE SAME. AND THE EXPECTATION

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HERE IS THAT FOR A PHASE II TRIAL, THERE WOULD BE A 40-PERCENT CO-FUNDING REQUIREMENT FROM THE APPLICANT AND 50 PERCENT FOR A PHASE III. ANYTHING THAT WOULD THEN EXCEED THE CIRM PLUS THE CO-FUNDING WOULD NEED TO COME FROM OTHER SOURCES. BUT BECAUSE WE, IN GENERAL, ARE TRYING TO SET CAPS THAT WOULD ALLOW A PROJECT TO SUCCEED OR BE MORE OR LESS EQUIVALENT TO WHAT WE FUNDED, WE DON'T ANTICIPATE THAT THAT'S GOING TO BE A TYPICAL REQUIREMENT FOR ANYBODY COMING IN.

DR. MILLS: IN SORT OF REAL LIFE TERMS, THE PHASE II TRIALS WHICH ARE CAPPED AT $12 MILLION WILL REQUIRE THE 40-PERCENT CO-FUNDING REQUIREMENT. SO THAT PUTS US AT A $20 MILLION TRIAL. A $20 MILLION PHASE II TRIAL IS A VERY WELL-DESIGNED, VERY WELL-CONSTRUCTED, APPROPRIATE PHASE II TRIAL. SO JUST GUARDING AGAINST ALMOST SORT OF RUNAWAY. THAT AT VARIOUS STAGES AND PHASES OF TRIALS, YOU SHOULDN'T HAVE SORT OF EXCESSIVE COSTS.

WITH REGARDS TO PHASE III, OBVIOUSLY THIS IS A 50-50 REQUIREMENT, SO YOU'RE TALKING ABOUT A $30 MILLION TRIAL. AND THEN ANYTHING BEYOND THE $30 MILLION TRIAL, WE'RE JUST FUNDING $15 MILLION OF IT. AND WE LOOKED AT IT IN THE SENSE OF, PARTICULARLY GIVEN WE'RE TALKING ABOUT CELL THERAPIES FOR

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PEDIATRIC INDICATIONS, THOSE ARE GENERALLY NOT ENORMOUS TRIALS. EVEN IF THEY ARE, $15 MILLION, AND I'LL SAY THIS PUTTING ON MY HAT FROM LONG AGO AS A PUBLIC COMPANY CEO, $15 MILLION WILL GET MY ATTENTION. THAT'S A LOT OF MONEY, AND THAT IS MONEY THAT WOULD MOTIVATE ME TO DO SOMETHING. SO THAT'S HOW WE BASICALLY BASE THESE.

CHAIRMAN THOMAS: THANK YOU.

CHAIRMAN SHEEHY: DO OTHER MEMBERS HAVE QUESTIONS?

DR. SAMBRANO: I HAVE ONE MORE SLIDE ACTUALLY. JUST ONE LAST ONE. THIS RELATES TO FUNDABLE ACTIVITIES.

SO FOR THE CLIN1 AND CLIN2 PROGRAMS, WE'D LIKE TO PERMIT FUNDING FROM MANUFACTURING ACTIVITIES FOR FOLLOW-ON CLINICAL TRIAL. CURRENTLY WE ARE RESTRICTING MANUFACTURING ACTIVITIES TO ONLY THOSE WITHIN THE TRIAL THAT WE WOULD BE FUNDING. BUT IN SOME CASES, MANUFACTURING ACTIVITIES WILL ALLOW AN APPLICANT TO PRODUCE ENOUGH PRODUCT TO COVER TWO TRIALS OR MORE. AND PART OF THE EFFICIENCY IN MOVING THINGS FORWARD IS TO ALLOW THEM, IF IT MAKES SENSE, TO DO THAT.

FOR CLIN2 WE ALSO WANT TO PERMIT FUNDING FOR COMPARABILITY STUDIES AND COMMERCIAL DEVELOPMENT

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ACTIVITIES WHICH CURRENTLY AREN'T ALLOWED, ESPECIALLY IF WE ARE TRYING TO ACCELERATE AND MOVE THESE PROJECTS FORWARD INTO PIVOTAL TRIALS AND ULTIMATELY TO COMMERCIALIZE THESE PRODUCTS. THOSE ARE THE TWO THAT WE ARE EXTENDING.

AND THEN, LASTLY, WE ARE SEEKING APPROVAL FOR THESE AMENDMENTS.

CHAIRMAN SHEEHY: DO OTHER MEMBERS HAVE QUESTIONS?

DR. JUELSGAARD: I WANT TO GO BACK TO THE QUESTION YOU WERE ASKING PREVIOUSLY ABOUT THE TRANSLATIONAL GRANTS. SO THE TRANSLATIONAL GRANTS COVER A VERY BROAD SPECTRUM, FROM PROJECTS THAT ARE JUST BEGINNING TRANSLATION TO THOSE THAT ALREADY WOULD BE QUITE A WAYS THROUGH. SO IF WE HAVE A PROJECT THAT'S QUITE A WAYS THROUGH TRANSLATION, BUT THERE'S PROCESS DEVELOPMENT WORK, ETC., THAT THEY MAY NEED TO DO TO GET TO THAT NEXT LEVEL, IN OUR SCORING OF THE GWG, DO WE GIVE ANY CREDIT FOR THE STAGE OF TRANSLATION THAT AN APPLICANT MAY BE? THAT IS, THE FURTHER ALONG THEY ARE IN THEIR TRANSLATIONAL EFFORTS, THEY GET A BONUS FOR THAT. THAT'S A QUESTION.

DR. SAMBRANO: WE DO NOT GIVE EXTRA CREDIT IN THAT WAY. ON THE OTHER HAND, THE TASK OF

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REVIEWERS IS TO ASSESS WHETHER THE PROJECT BEFORE THEM IS ONE THAT WILL ULTIMATELY SUCCEED IN GETTING TO THE EXPECTED OUTCOME. SO ONE THAT HAS DEMONSTRATED ALREADY THE ABILITY TO HAVE COMPLETED A LOT OF THE KEY TASKS TO GET THEM TO THAT OBJECTIVE WILL LIKELY DO BETTER THAN ONE THAT HAS NOT.

DR. JUELSGAARD: SO IT'S BUILT INTO THE SYSTEM, THAT THE ONES THAT I JUST ASKED ABOUT, ASSUMING THEY'VE GOT A GOOD PROJECT, WOULD GET A HIGHER SCORE THAN SOMEBODY MUCH EARLIER EVEN THOUGH IT SOUNDS LIKE A GREAT EXPERIMENT?

CHAIRMAN SHEEHY: YOU KNOW, I GUESS THAT COULD GO EITHER WAY DEPENDING ON WHAT A REVIEWER'S BIAS IS, FROM MY EXPERIENCE, BECAUSE SOME OF THESE THINGS ARE FAIRLY MUNDANE. I DON'T THINK THAT THAT CREATES THE SAME LEVEL OF ENTHUSIASM NECESSARILY IN SOME REVIEWERS. SO I THINK, SHORT OF DIRECTION FROM THE REVIEW TEAM, THAT ACTUALLY COULD CUT BOTH WAYS.

DR. MILLS: AS A FORMER REVIEWER, IT WOULD BE A FACTOR I WOULD CONSIDER. SO I WOULD CARE A LOT ABOUT WHETHER I BELIEVED THEY COULD DO WHAT THEY SAID THEY WERE GOING TO DO. AND CLEARLY THE FURTHER YOU ARE DOWN THAT ROAD, THE MORE LIKELY YOU ARE TO SUCCEED. BUT I WOULD THEN BALANCE AGAINST WHETHER I CARE AND HOW MUCH I CARE THAT EVERYTHING YOU SAID

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CAME TRUE. AM I HAPPY?

SO IT'S NOT -- IT'S CERTAINLY NOT THE ONLY CONSIDERATION. IT'S A FACTOR, BUT IT'S NOT QUITE THAT BLACK AND WHITE.

DR. JUELSGAARD: SO, RANDY, IN THAT REGARD, SO HARKENING BACK TO WHAT PAT WAS TALKING ABOUT, WHICH SOUNDED A LOT LIKE PROCESS DEVELOPMENT ISSUES WHERE IN THE BACKGROUND THERE ARE A NUMBER OF THESE. SO WHEN YOU HAVE A GWG MEETING TO CONSIDER TRANSLATIONAL PROJECTS, HOW MANY PEOPLE ARE IN THE ROOM THAT ARE CONVERSANT WITH PROCESS DEVELOPMENT LEADING TO AN APPROVABLE PROCESS? BECAUSE IF YOU DON'T HAVE PEOPLE THAT ARE CONVERSANT WITH THAT, THEN THEY MAY NOT UNDERSTAND THAT, AND THAT MIGHT IMPACT THE SCORING.

DR. MILLS: SO WE COMPOSE -- AND, GIL, JUMP IN HERE AND CORRECT ME WHEN I GET THIS WRONG. BUT THEY COMPRISE OR MAKE UP THE GWG ON A REVIEW-BY-REVIEW BASIS, PARTICULARLY FOR TRANSLATION. SO THE COMPOSITION OF THAT GWG, PARTICULARLY IN TRANSLATION, THEY'RE SELECTED FOR EXACTLY THAT SKILL SET. SO IT'S WELL REPRESENTED.

DR. SAMBRANO: AGREE.

DR. OLSON: THEY'RE ASSIGNED TO EVERY PROJECT.

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MR. TORRES: BUT NOT ALL OF THEM.

DR. SAMBRANO: IT DEPENDS -- ART TORRES WAS JUST ASKING IF IT'S ON ALL OF THEM. SO FOR TRAN, WE HAVE A BROAD SPECTRUM OF TYPES OF CANDIDATES FROM THERAPY TO A TOOL. BUT WE DO ASSIGN AND MAKE SURE THAT FOR EACH APPLICATION WE HAVE SOMEBODY WHO UNDERSTANDS THE PROCESS DEVELOPMENT AS WELL AS HAS A PERSPECTIVE FROM THE CLINICAL SIDE, OR IF IT'S TOOL, WHAT THE RELATIVE VALUE OF THAT TOOL WOULD BE IF THEY ARE SUCCESSFUL. SO THAT WE HAVE A WELL-ROUNDED SET OF INDIVIDUALS WHO ARE ASSESSING EACH OF THESE PROJECTS.

MR. TORRES: NOT ALL OF THE INDIVIDUALS ARE PROCESS ORIENTED.

DR. SAMBRANO: NOT ALL OF THEM ARE.

CHAIRMAN SHEEHY: DO WE ACTUALLY ALWAYS HAVE A MANUFACTURING SPECIALIST THAT REVIEWS EVERY APPLICATION?

DR. SAMBRANO: WE HAVE SOMEBODY WHO HAS EXPERTISE IN CMC THAT WILL REVIEW EACH OF THE APPLICATIONS WHERE IT'S RELEVANT.

CHAIRMAN SHEEHY: I STILL -- I STILL HAVE QUESTIONS ABOUT THAT PARTICULAR ONE. DOES THAT ANSWER YOUR QUESTION, STEVE? DO YOU HAVE MORE QUESTIONS?

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DR. JUELSGAARD: NO. IT DOES ANSWER IT. I THINK WHAT WE'RE GOING TO DO IS SEE HOW THIS WORKS OUT, IF ULTIMATELY THIS IS THE WAY THE LINES GET DRAWN. I'LL BE CURIOUS, PARTICULARLY IN THE TRANSLATIONAL AREA, TO SEE HOW PROJECTS GET SCORED BASED ON WHERE THEY STAND IN TERMS OF -- ALONG THE LINE IN TRANSLATION. BECAUSE FOR ME, IF YOU'RE QUITE A WAYS DOWN THE ROAD IN TRANSLATION, AND YOU'RE TRYING TO DEAL WITH PROCESS DEVELOPMENT ISSUES, THAT IN AND OF IT ITSELF, ASSUMING ALL THE OTHER SCIENCE IS SOUND, DOESN'T NECESSARILY HAVE TO BE STELLAR, BUT IF IT'S SOUND, I PERSONALLY WOULD MOVE THAT PROJECT FURTHER UP THE CONTINUUM IN TEREMS OF WHERE IT STANDS VERSUS OTHERS, BUT WE'LL SEE.

CHAIRMAN SHEEHY: I ALSO WONDER IF THERE SHOULDN'T BE -- MAYBE A BETTER WAY TO ADDRESS THIS ISSUE IS MORE OF A ROBUST INTERFACE WITH THE TRANSLATION CENTER THAT WE JUST BROUGHT ON. I JUST DON'T KNOW IF THIS IS THE BEST THING, FROM MY PERSPECTIVE, FOR THIS PROBLEM. I DON'T HAVE A GOOD EVIDENCE BASIS, FACT BASIS, ON WHICH TO KIND OF GO ALONG WITH THIS PERSONALLY. IT WOULD BE GREAT TO HAVE THAT FOR THE BOARD ALONG WITH THE OTHER ISSUES THAT I HAD, THE MODELS FOR PHASE I, II, AND III, AND IF WE COULD GET THAT TO THE BOARD BEFORE WE DECIDE

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THIS.

FOR THIS ONE, I STILL THINK THAT I'M NOT -- IT'S NOT CLEAR TO ME THAT THIS IS THE BEST SOLUTION TO THE PROBLEM WHEN WE JUST INVESTED IN A TRANSLATING CENTER. WHY NOT ENCOURAGE FOLKS TO PARTNER UP WITH THEM TO WRITE THEIR APPLICATIONS FOR THE CLIN1S AS OPPOSED TO DROPPING THEM BACK DOWN IN TRANSLATION, WHICH IS ALREADY A POT THAT'S OVERFLOWING. I WONDER IF ANYBODY HAD THOUGHT ABOUT THAT.

DR. MILLS: GILL, I THOUGHT WHAT WE'RE TAKING ABOUT HERE AND THE SPECIFIC ISSUE IS JUST SAYING THAT WHEN YOU'RE IN CLIN1, WE EXPECT YOU TO GET YOUR WORK DONE IN 18 MONTHS. IS THAT THE TOPIC ON THE TABLE?

DR. SAMBRANO: YES.

DR. MILLS: THIS HAS NOTHING TO DO WITH DROPPING ANYONE DOWN TO TRANSLATION. THIS DOESN'T AFFECT TRANSLATION IN ANY WAY. IT JUST SAYS WE'RE RUNNING OUT AN EXPECTATION THAT OUR CLIN1 APPLICANTS DO 18 MONTHS OF WORK IN 18 MONTHS AND NOT DRAG IT OUT LONGER. HAVING LOOKED AT THIS, JEFF, A LOT OF THESE APPLICANTS VIEW OUR APPLICATION AND OUR CRITERIA AS IF THEY WERE A GAP, MEANING THEY WILL TAKE THE SHAPE OF ANY CONTAINER WE ALLOW THEM TO

TAKE.

AND WHEN WE HAD -- IT'S FUNNY. DR. JUELSGAARD MADE THIS POINT. I WAS READING THROUGH TRANSCRIPTS OF LONG AGO. WHEN WE HAD GRANTS FOR A CLINICAL TRIAL THAT WAS FOUR YEARS, THEY WOULD TAKE FOUR YEARS EVEN THOUGH THE AVERAGE LENGTH OF A PHASE I TRIAL IS 19 MONTHS, OUR APPLICANTS WOULD PROPOSE FOUR YEARS OF WORK. SO ALL WE'RE DOING HERE IS SAYING THE EXPECTATION IS THAT YOU GET FROM YOUR SUCCESSFUL PRE-IND MEETING, WHICH YOU'VE HAD PRIOR TO EVEN APPLYING, GET FROM THERE TO YOUR IND IN 18 MONTHS. IF YOU NEED TO, YOU CAN JUSTIFY AND GET A COST EXTENSION AND OTHER THINGS. STUFF COMES UP AND WE UNDERSTAND THAT. BUT WE'RE SETTING OUT AN EXPECTATION THAT YOU DO YOUR WORK IN A TIMELY FASHION. THAT EXPECTATION IS NOT BENDING THE TIME SPACE CONTINUUM. IT IS WHAT EVERYONE ELSE IN THE WORLD DOES AND CONSISTENT WITH WHAT IT SHOULD BE.

THAT'S ALL WE'RE REALLY TRYING TO DO HERE IS SAY OUR OVERALL EXPECTATION FOR HOW LONG THAT DEVELOPMENT SHOULD TAKE MEET WITH OUR ACTUAL INDIVIDUAL PROJECT GOALS.

CHAIRMAN SHEEHY: IF I CAN MAKE A COUPLE OF POINTS, AND I'M JUST TRYING TO ALIGN INFORMATION THAT I'M GETTING. SO I WAS ORIGINALLY TOLD THAT THE

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REASON WE'RE DOING THIS IS BECAUSE WE HAVE PROJECTS IN CLIN1 THAT REALLY SHOULD HAVE BEEN IN TRANSLATION, AND THAT WAS WHAT WAS SUGGESTED, IN THAT THEY WOULD BE BETTER OFF BEING IN TRANSLATION BECAUSE ALL THEY HAVE TO DO IS GET A PRE-IND.

THE SECOND THING IS I AGREE WITH YOUR PROBLEM. IF WE SAY FOUR YEARS AND PEOPLE TAKE FOUR YEARS, BUT I THOUGHT WE HAD ADDRESSED THAT PROBLEM WITH OUR MILESTONE, THE WAY IN WHICH WE DEVELOPED OUR MILESTONES WHERE PEOPLE BENEFIT FOR ACCELERATING FASTER THROUGH THERE. IF THAT DID NOT DO THAT AND WE NEED TO DO THIS, THAT'S FINE.

DR. MILLS: THE FIRST PART IS JUST WRONG BECAUSE I WAS PERSONALLY INVOLVED WITH SAYING WE NEEDED TO MAKE THIS CHANGE. AND WE NEEDED TO MAKE THIS CHANGE BECAUSE IT WAS THE ONLY WAY FOR US TO HAVE OUR TRANSLATION TIME GOAL, WHICH IS TRAN1 PLUS CLIN1 PUT TOGETHER, BE CONSISTENT WITH OUR STRATEGIC GOAL. IF WE DIDN'T DO THIS, THEN WE WOULD SAY WE HAVE PROGRAMS THAT SAY YOU CAN TAKE MORE THAN FOUR YEARS, BUT WE HAVE A GOAL THAT SAYS WE HOPE IT GETS DONE IN UNDER FOUR YEARS.

THE MILESTONE GOALS HAVE BEEN INCREDIBLY EFFECTIVE AT MAKING PEOPLE HIT THEIR MILESTONES WHEN THEY'RE EXPECTED, BUT IT DOESN'T DRIVE URGENCY.

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BASICALLY JUST DRIVES TIMELINESS. SO WHAT WE'RE TRYING TO DO HERE IS SAY WE WANT YOU TO REALLY PUT YOUR BACK INTO IT, AND WE WANT YOU TO GET THIS DONE, PARTICULARLY AT THAT STAGE, QUICKLY. I DON'T VIEW THE MILESTONE PIECE AS ONE OR THE OTHER. IT'S VERY HELPFUL. AND IT'S ALSO VERY HELPFUL TO HAVE TIMELINES THAT SAY WE DO EXPECT YOU TO DO YOUR WORK ON TIME.

CHAIRMAN SHEEHY: OKAY. THAT WORKS. SO DO WE HAVE ANY OTHER QUESTIONS FROM FOLKS OR CAN I TAKE A MOTION?

DR. STEWARD: I HAVE A QUESTION.

CHAIRMAN SHEEHY: SURE. PLEASE.

DR. STEWARD: SO I'D LIKE TO ACTUALLY GO BACK TO ONE OF THE EARLY POINTS, AND THIS IS WITH REGARD TO THE PI PERCENT EFFORT. AND THE QUESTION IS CONSEQUENCE OR PROCESS. SO THE IDEA, I BELIEVE, WAS THAT THE GRANTS WORKING GROUP WOULD REVIEW THIS FOR APPROPRIATENESS AND THEN MAKE A DECISION OR DETERMINATION. THEN WHAT? AND I'M SPECIFICALLY ASKING SUPPOSE THE GRANTS WORKING GROUP SAYS, NOPE, THAT'S NOT ENOUGH TIME. DOES THAT IMPACT ON THE SCORE?

MR. TORRES: FOR THE PI.

DR. STEWARD: YEAH, FOR THE PI. DOES THAT

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IMPACT ON THE SCORE? DOES THAT MEAN A RENEGOTIATION? IS IT A REQUIREMENT? I'M JUST NOT CLEAR WHERE THIS IS GOING.

DR. SAMBRANO: SO THE EXPECTATION HERE IS THAT IT WOULD BE PART OF WHAT THE GWG SCORE WOULD BE. SO IT WOULD IMPACT ON OVERALL FEASIBILITY. IF THE GWG FEELS THAT THE PI IS NOT DEDICATING SUFFICIENT EFFORT -- AND THIS IS EVEN TRUE WHEN WE HAVE A MINIMUM PERCENT EFFORT DESIGNATED. SOMETIMES THE GWG WILL SAY THEY'RE REALLY NOT DEDICATING SUFFICIENT EFFORT FOR THE ACTIVITIES THAT ARE PROPOSED. BUT JUST TO ALLOW FOR FLEXIBILITY FOR THE PI, WE WANT TO NOT RESTRICT IT TO SIMPLY 30 PERCENT AND ALLOW THEM TO PROPOSE WHAT THEY FEEL IS MOST APPROPRIATE AND HAVE THE GWG INCORPORATE THAT INTO THEIR ASSESSMENT OF FEASIBILITY OF THE PROJECT.

DR. STEWARD: JUST TO POINT OUT THE CONSEQUENCE OF THAT. AS A REVIEWER, WHAT I WOULD DO IS SCORE THE GRANT LOWER IF I DIDN'T FEEL THAT THE PI WAS DEVOTING ENOUGH TIME. THAT MEANS THAT IT GETS PUSHED AT LEAST TO THE NEXT ROUND. SO IF THAT'S OKAY, ALL RIGHT. I'M NOT COMPLETELY SURE THAT'S OKAY.

AND I THINK HAVING A SET AMOUNT IS, AT LEAST, A SIGNAL THAT THAT'S EXPECTED. SO THOSE ARE

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MY CONCERNS. I'M NOT QUITE SURE. I'D LIKE TO HEAR OTHER COMMENTS ON IT. THANK YOU.

MR. TORRES: ON THAT POINT, OS, I THINK YOU'RE RIGHT. WHEN WE REVIEW THE VARIOUS APPLICATIONS, EVEN THOSE OF US WHO ARE LAYMEN AND HAVE NEVER WORKED IN A LAB WERE KIND OF AGHAST SOMETIMES WHEN A PI SAYS IT'S GOING TO BE 50 PERCENT ON THE PROJECT. AND GIVEN ALL HIS OR HER OTHER RESPONSIBILITIES, THERE'S NO WAY THAT PERSON CAN SPEND 50 PERCENT ON THAT PROJECT. SO I THINK THIS IS A GOOD MOVE FOR THE GWG TO GIVE A REVIEW OF THE PERCENTAGE. AND IF IT DOESN'T COME WITHIN WHAT THEY THINK IS APPROPRIATE, THEN THAT'S UP TO US TO DECIDE.

CHAIRMAN SHEEHY: IT DOES SEEM LIKE A VERY SUBJECTIVE STANDARD, THOUGH. I DO TAKE YOUR POINT, OS. GIVEN THE OBJECTIVENESS OF MANY OF THE THINGS THAT WE REVIEW, THAT ONE SEEMS TO BE PARTICULARLY SLIPPERY.

DR. MILLS: GIL, CORRECT ME IF I'M WRONG, BUT THE WAY I UNDERSTOOD THIS ONE IS THIS. THAT IT'S REALLY MORE OF A KINETIC THING. SO LET'S SAY WE HAVE A CLINICAL TRIAL AND WE HAVE AN INVESTIGATOR THAT'S WORKING ON THAT CLINICAL TRIAL DURING THE CLINICAL ENROLLMENT AND TREATMENT PHASE WHERE HE'S

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SPENDING OR SHE'S SPENDING A TREMENDOUS AMOUNT OF TIME ON THAT. THEN YOU GET TO EVALUATION PART OF THE TRIAL WHERE A CRO IS WORKING VERY DILIGENTLY COMPILING DATA. THE PI REALLY DOESN'T HAVE A ROLE. AND SO WE GET INTO THESE SITUATIONS WHERE WE DON'T WANT TO BASICALLY OVERLY PAY SOMEBODY TO WATCH GRASS GROW.

DR. SAMBRANO: PART OF THE ISSUE ACTUALLY ALSO RELATES TO ALLOWING WHAT WOULD BE AN APPROPRIATE PI TO SERVE AS A PI. MANY OF THEM HAVE CLINICAL DUTIES WHERE THEIR OWN INSTITUTION, IF THEY ASSIGN THEMSELVES 30 PERCENT EFFORT, ARE JUST NOT PERMITTED TO DO SO BECAUSE OF THEIR CLINICAL DUTIES. SO PART OF IT IS ALLOWING FLEXIBILITY IN LETTING THE GWG DETERMINE IS WHAT THEY ARE ABLE TO DEDICATE TO THIS PROJECT SUFFICIENT TO GET THE TASK DONE? IF IT'S NOT, THEN IT SHOULD BE REFLECTED IN THE OVERALL SCORE. BUT IF IT IS, THEN WE COULD ALLOW SOMEBODY WITH 20 OR 25 PERCENT IF THE GWG FEELS IT'S OKAY.

CHAIRMAN SHEEHY: STILL SEEMS VERY SUBJECTIVE.

DR. STEWARD: I ACTUALLY HAVE TO AGREE WITH JEFF, AND I THINK OBJECTIVE IS EXACTLY THE RIGHT WORD OR SORT OF RANDOM, I GUESS. I JUST DON'T THINK THAT THE GRANTS WORKING GROUP AS CONFIGURED

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RIGHT NOW HAS AN ABILITY TO MAKE THOSE KINDS OF JUDGMENTS ON THE FLY. I'M PRETTY SURE THAT THE ABILITY TO DO THAT DIFFERS BY REVIEWER, AND THAT IT JUST PUTS THINGS IN A LITTLE BIT OF A MORE FUZZY SITUATION THAN WE'VE HAD IN THE PAST. SO I'M NOT COMFORTABLE WITH THIS YET. I'M NOT COMFORTABLE. THANK YOU.

CHAIRMAN SHEEHY: MAYBE WE SHOULD THINK OF ALTERNATIVE MECHANISMS TO ADDRESS THIS ISSUE. IS IT JUST WAY OFF BASE TO SAY THAT THIS COULD BE A PREREVIEW ELEMENT ALONG THE LINES OF SOME OF THE OTHER THINGS THAT WE REVIEW, LIKE THE BUDGET? IF THIS IS AN ISSUE, IT SEEMS LIKE THE INFORMATION THAT THE REVIEWERS WILL HAVE PROBABLY ISN'T SUFFICIENT AND THERE ISN'T ENOUGH TIME -- LIKE, I CAN UNDERSTAND IF THEY WERE TALKING TO THE PI AND THEY CAN WORK THIS OUT; BUT IF IT COMES IN, IF IT'S BELOW THE 30 PERCENT, WHY CAN'T WE HAVE AN ITERATIVE THING THAT THE TEAM DOES TO KIND OF DETERMINE IF THAT'S SUFFICIENT? THAT ALMOST SEEMS LIKE THAT'D BE BETTER THAN ASKING THE REVIEWERS TO KIND OF FIGURE OUT WHETHER THE PERCENT OF EFFORT IS APPROPRIATE WITHOUT KNOWING LIKE THE CLINICAL DUTIES OVERHANG OR THE KINETIC-NESS THAT RANDY EXPLAINED.

DR. TORRES: REVIEWERS OFFER THEIR OPINION

ON THAT ISSUE.

DR. SAMBRANO: THEY DO. THE CHALLENGE FOR US IS JUST SIMPLY THAT WE DON'T WANT A MINIMUM ELIGIBILITY THRESHOLD WHERE WE'RE GOING TO BE THINKING OF IMPLEMENTING EXCEPTIONS TO. IT REALLY SHOULD BE THE BARE MINIMUM THAT WE'RE WILLING TO ACCEPT IN ORDER TO MOVE FORWARD. WE THOUGHT THAT THE BEST FOLKS POISED TO MAKE A DECISION BASED ON THE ACTIVITIES THAT ARE PROPOSED AS TO WHETHER IT IS SUFFICIENT TO ACCOMPLISH THEM OR NOT WOULD BE THE GWG. AND THAT'S WHY WE DIDN'T PROPOSE A MINIMUM. WE DECIDED THAT THAT IS SOMETHING THAT SHOULD ALIGN WITH THE TASKS THAT ARE PROPOSED. DO THEY HAVE A TEAM AND A PI THAT ARE SET UP TO ACCOMPLISH THESE APPROPRIATELY OR NOT?

DR. JUELSGAARD: JUST A QUESTION. SO HOW IS IT THAT AT THE CURRENT TIME WE KNOW WHAT PERCENTAGE OF THEIR TIME A PI IS INVESTING IN A TRIAL? SO IMAGINE THEY SAID, I'M GOING TO INVEST 30, 35, 40 PERCENT OF MY TIME, AND THAT'S WHEN THE APPLICATION COMES IN. HOW DO WE KNOW THAT THAT'S ACTUALLY TAKING PLACE ON AN ONGOING BASIS?

DR. SAMBRANO: SO ASIDE FROM THEM CERTIFYING THAT THAT IS THE PERCENT EFFORT THAT THEY WILL DEDICATE OR IN THEIR IN PROGRESS REPORT, THE

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AMOUNT BASED OUR SUPPORT AND OTHER SUPPORT THEY HAVE AND SIGNED OFF BY THE INSTITUTION, THAT'S ALL WE HAVE. WE DON'T DO AN AUDIT OF THEIR TIME.

DR. MELMED: THE LAST POINT YOU MADE ABOUT THE INSTITUTION IS VERY IMPORTANT BECAUSE THE INSTITUTION IS ALSO CONCERNED ABOUT TIME AND EFFORT. AND THEY'RE RIGOROUSLY AUDITED TO ASSURE COMPLIANCE WITH TIME AND EFFORT. IF THEY HAVE A 30 PERCENT TIME AND EFFORT ON A GRANT, IT'S HIGHLY UNLIKELY THAT THE INSTITUTION WOULD ALLOW THEM TO DROP THAT 30 PERCENT UNLESS THERE'S A PREAUTHORIZATION. ONCE THE INSTITUTION APPROVES THE TIME AND EFFORT, THAT GOES ON THE BOOKS AS AN INSTITUTIONAL COMMITMENT.

DR. STEWARD: JUST TO SAY, AT INSTITUTIONS OF HIGHER EDUCATION AND PROBABLY MOST OTHER PLACES AS WELL, PI'S ARE ASKED TO CERTIFY THEIR TIME EXPENDITURES PERCENT EFFORT UNDER PENALTY OF PERJURY. SO IT'S TAKEN SERIOUSLY.

DR. MELMED: YES, ABSOLUTELY. THAT'S MY POINT.

CHAIRMAN SHEEHY: SO DO WE HAVE ADDITIONAL QUESTIONS FOR DISCUSSION? I THINK WE'VE FLAGGED SOME ISSUES THAT I THINK, WHEN WE BRING IT TO THE FULL BOARD, HAVE A LITTLE BIT MORE INFORMATION ABOUT. BUT DO OTHER FOLKS HAVE QUESTIONS? SO HOW

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DO WE WANT TO MOVE THIS FORWARD? IT SEEMS LIKE THAT IT OBVIOUSLY SHOULD GO TO THE FULL BOARD. I THINK THAT'S THE PLAN, RIGHT? WHAT ARE OPTIONS? I DON'T KNOW -- I PERSONALLY WOULD PROBABLY ABSTAIN PENDING MORE INFORMATION ON WHETHER OR NOT I APPROVE THE CONCEPT. THAT DOESN'T MEAN THAT I WOULDN'T BE LIKELY TO DO IT AT THE BOARD.

MR. TORRES: WE CAN MAKE A RECOMMENDATION TO MOVE THIS PROPOSAL WITH RESERVATIONS HIGHLIGHTED BY THE ISSUES THAT HAVE BEEN RAISED HERE FOR FURTHER CONSIDERATION WITHOUT HAVING TO ABSTAIN.

CHAIRMAN SHEEHY: IS THAT YOUR MOTION, SENATOR TORRES?

MR. TORRES: I THINK SO.

MS. BONNEVILLE: I THINK IT WOULD HELP THE TEAM IF YOU COULD ADDRESS SORT OF THE QUESTIONS THAT YOU WOULD LIKE SPECIFICALLY ADDRESSED AT THE BOARD MEETING SO THAT WE CAN PUT THAT INFORMATION TOGETHER.

CHAIRMAN SHEEHY: I'D REALLY LIKE TO KNOW MORE ABOUT THE TIME FRAME ISSUE BECAUSE I'M STILL CONFUSED ABOUT THE RATIONALE FOR IT. I HEARD TWO DIFFERENT RATIONALES.

THEN THE MODELS FOR THE FUNDING. AND ALSO FOR THE PEOPLE WE FUNDED, WHAT THAT LOOKS LIKE. AND

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THEN THE PI ISSUE, WHICH WAS JUST RAISED, AND MAYBE SOME CLARIFICATION ON HOW THAT WOULD WORK. YOU MIGHT WANT TO REACH OUT TO DR. STEWARD OR DR. MELMED AND KIND OF GET A SENSE OF WHAT MIGHT BE OTHER ALTERNATIVES, IF THERE ARE ALTERNATIVES, OR WHAT KIND OF DIRECTION MIGHT BE GIVEN TO THE WORKING GROUP SO THAT THERE'S CLARITY ON THIS AND IT DOESN'T BECOME JUST A SUBJECTIVE METRIC.

ANY OTHER THOUGHTS PEOPLE HAVE? THOSE ARE THE ONES THAT KIND OF JUMPED ON ME.

DR. STEWARD: I TOTALLY AGREE. I WOULD RECOMMEND SOME VERY SPECIFIC REVIEW CRITERIA FOR THE PERCENT EFFORT ISSUE. AND THE REVIEWERS COME FROM VERY DIFFERENT BACKGROUNDS. AT NIH THIS IS SORT OF THERE AND REALLY NOT. IT'S ONE OF THESE THINGS THAT IS ALMOST A CHECKED BOX ON NIH REVIEWS; WHEREAS, WE'RE REALLY ASKING THE REVIEWERS TO TAKE THIS SERIOUSLY. SO I THINK THERE NEEDS TO BE SOME VERY SPECIFIC CRITERIA. THANK YOU.

DR. MELMED: WITH RESPECT, I KNOW THAT NIH DOES TAKE IT SERIOUSLY, AND REVIEWERS -- WE'VE SEEN MANY GRANTS WHERE REVIEWERS HAVE QUESTIONED TIME AND EFFORT ON THE PI. I THINK THAT'S A VERY IMPORTANT QUESTION. I DO THINK NIH REVIEWS DO TAKE INTO ACCOUNT, AND THESE CRITIQUES OR PRAISES DO COME OUT

IN THE NIH REVIEWS, IF TIME AND EFFORT IS APPROPRIATE, TIME AND EFFORT IS INAPPROPRIATE, OR INSTITUTION COST SHARING FOR FACULTY SALARY OR FACULTY PI IS VERY APPROPRIATE. I THINK IT'S A VERY IMPORTANT QUESTION, AND IT'S A COMMITMENT, AGAIN, OF THE INSTITUTION. WE SHOULDN'T ALLOW CIRM TO BE EXPLOITED BY THE INSTITUTIONS TO SUPPORT TIME AND EFFORT OF FACULTY WHO ARE OTHERWISE UNFUNDED.

CHAIRMAN SHEEHY: SO I HAVE A MOTION. DO I HAVE A SECOND? IF THERE'S NO OTHER ISSUES THAT PEOPLE WANT TO EXPRESS.

MR. TORRES: MY MOTION ENCAPSULATES THIS PREVIOUS DISCUSSION.

CHAIRMAN SHEEHY: EXACTLY. IT CAPTURES THE RESERVATIONS. DO I HAVE A SECOND?

DR. HIGGINS: I'LL SECOND THAT.

CHAIRMAN SHEEHY: GREAT. ANY PUBLIC COMMENT ANYWHERE? CAN WE HAVE A ROLL CALL PLEASE.

MS. BONNEVILLE: DEBORAH DEAS. ANNE-MARIE DULIEGE. DAVID HIGGINS.

DR. HIGGINS: YES.

MS. BONNEVILLE: STEVE JUELSGAARD.

MR. JUELSGAARD: YES.

MS. BONNEVILLE: BERT LUBIN. SHLOMO MELMED.

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DR. MELMED: YES.

MS. BONNEVILLE: JEFF SHEEHY.

CHAIRMAN SHEEHY: HERE.

MS. BONNEVILLE: OS STEWARD.

DR. STEWARD: YES.

MS. BONNEVILLE: JONATHAN THOMAS.

CHAIRMAN THOMAS: YES.

MS. BONNEVILLE: ART TORRES.

MR. TORRES: AYE.

MS. BONNEVILLE: KRISTINA VUORI.

DR. VUORI: YES.

MS. BONNEVILLE: MOTION CARRIES.

CHAIRMAN SHEEHY: MOTION CARRIES. AND I THINK THAT IS IT FOR BUSINESS. SO WE CAN ADJOURN. THANK YOU, EVERYONE.

(THE MEETING WAS THEN CONCLUDED AT 11:08 A.M.)

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REPORTER'S CERTIFICATE

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