Megan Columbus: All right. With that, I'm going to go ahead and get started. Welcome to the NIH Peer Review: Live Mock Study Section. This is a great follow-on session to the last one we just had, which gave the basics of our peer-review process. This one is going to be live. It's going to be interactive with a lot of people on the screen to give you a great sense of what's going on. Your emcee for today is Brian Hoshaw. He is the Chief of Review of the National Eye Institute, and I am Megan Columbus. I am Director of Communication of Outreach for the Office of Extramural Research, and I'll just be coming back in at the end to help with some Q and A. With that, take it away, Brian.

Brian Hoshaw: Hi, everyone, and welcome to the live mock study session. For most of you, the review meeting is really black box. You submit your grant. You wait some time. You get a score, a summary statement. We don't really know what happens in-between. This presentation will give you a peek inside, so you'll get an idea of what happens during the review, during the discussion, what topics might come up. This is a mock presentation. None of the applications are real, and also keep in mind, everything is abbreviated. Most review meetings are half a day, whole day. We used to have sometimes a day-and-a-half in-person meetings, so it's a little bit abbreviated version of what you might see. This is interactive. At two points during the presentation, we'll pause. A question will be addressed to the audience, and then we'll do a quick poll just to see what the answers are, what people are thinking, if you're able to guess the right answer as part of the review. It's a good follow-up to the peer review talk before this. Okay. So we'll be assessing three applications today. In between, I'll give a short summary, touch on some main points. During the talk, as Megan said, you can enter questions into the Q and A. We have some review chiefs and senior SROs behind the scenes who will be answering them. And then if we have time at the end, if there are certain questions that keep coming up during the meeting, we'll try to address those if we have some time. So let's just jump right in. I'm going to turn the meeting over, and we'll have the presentation started. Okay. Take it away.

Jessica McKlveen: Hello. My name is Dr. Jessica McKlveen, and I am the scientific review officer and designated federal official for this meeting. Most of my work is done before the meeting happens, arranging the logistics, recruiting and preparing the reviewers. At the meeting, I make sure that NIH regulations and procedures are followed and take notes for the final summary statement.

So we can go ahead and get started with introductions. Please give your name, university and a brief description of your area of expertise. We will start with our chair, Dr. Peter Kozel. And, Dr. Kozel, I believe you're muted.

Peter Kozel: Thank you. Good afternoon. My name is Peter Kozel. I'm from the University of Europa, and I will be the chair for this meeting. My job is to guide the discussion and ensure that it stays on topic. I will introduce each application and the assigned reviewers and will direct the committee when it is time to discuss specific topics such as the budget or to give final scores. And if we could have the rest of our reviewers, please.

Lana Shekim: Him everyone. I am Lana Shekim. I'm a professor at the University of Florida, and my area of expertise is in pharmacology.

Debbie Hodge: Hello. I'm Debbie Hodge. I am a professor at the University of Maryland, and my background is in biochemistry.

Shardell Spriggs: Good afternoon, everyone. My name is Shardell Spriggs. I'm a professor at the University of Maryland School of Medicine with a background in behavioral neuroscience.

Nishadi Rajapakse: Hi. I'm Nishadi Rajapakse. I'm a professor of chemistry at Duke University.

Faye Chen: Hi. I'm Faye Chen. I'm calling from UCSF, and my expertise is in alternative medicine.

Anil Wali: Hi. I'm Anil Wali. I'm Associate Professor at the Wayne State University Karmanos Cancer Center, and I [Indistinct] oncology program.

Jessica McKlveen: Brian?

Brian Hoshaw: Yes, Danielle. If you were talking, I think, is your microphone on? You were trying to talk, but you weren't. Okay, maybe we'll come back to her.

Philippe Marmillot: Okay, so I'm Philippe Marmillot. I am a professor at George Washington University, and my expertise is in biostatistics and clinical trials.

Grace Shen: Hi. My name is Grace Shen. I'm a professor at Imperial College, and I work in the department of neuroscience, and my expertise is in biology of addiction.

Jessica McKlveen: Thank you all for introducing yourselves. We also have another NIH employee that's observing the meeting. Would you like to go ahead and introduce yourself?

Shawn Gaillard: Yes, thank you so much. Hi, everybody. My name is Shawn Gaillard, and I'm a program officer in the National Institute of Drug Abuse, NIDA. I wrote the request for applications, also called an RFA, that you will be reviewing. Before the discussion starts, the SRO has agreed to allow me to give you a description of the RFA and to answer any general questions. My main role at this meeting is to observe and to take notes on the discussion, and I will be available for the duration of the meeting to address any questions that you might have about the RFA if the SRO finds appropriate.

Jessica McKlveen: Thank you. Before I turn the meeting over to the chair, I'd like to first go over some legal issues. In terms of confidentiality, the discussion of the applications is confidential. Anything we discuss here should not leave the room. In terms of conflicts of interest, thank you for identifying your conflicts prior to the meeting. If you're in conflict with an application, you will leave the virtual room during the discussion of that application. In terms of scientific misconduct, if you suspect any type of misconduct in the applications, please contact me privately prior to the discussion. We want to give the principal investigators the benefit of the doubt before this topic comes up during a discussion since the application may have to be deferred if there really is an issue. Here is a summary of the review format for the meeting. The chair will introduce the applications and the reviewers. Then the assigned reviewers will give the preliminary scores before part reviewer one gives a brief overview of the application. Each reviewer will state the main score-driving issues for the application. You don't have to repeat what was already said by a previous reviewer. Next, the discussion is open to the whole panel. You can participate in the discussion of any application for which you are not in conflict. After the discussion, the reviewers will state if there are any issues with the production of human subjects, the inclusion of women, minorities and across the lifespan or the use of vertebrate animals all where applicable. Then the assigned reviewers will give their final scores. Then after final scoring, we will discuss any issues with the budget, resource sharing plan and/or the authentication of key biological and chemical resources. Are there any questions before we begin the review?

Danielle Carlin: Yes, I have a question. I apologize. I'm reviewer seven, and my sound, now, is finally working. So I have a question about scoring. What is the cutoff for funding? That is, can you tell me what score I should give the application if I want it to be funded?

Brian Hoshaw: Okay. Everybody stop now. This is our first interactive question, so if we could put the first poll question up, and that is, "Should the SRO let the reviewers know what score to give if they want the application to be funded?" So it's a yes-or-no question. I will give maybe 20 seconds or so. Okay. I think that's good. Okay, so 88 percent said, "No, they should not." We'll go back to the SRO for this.

Jessica McKlveen: All right. Good job. In review meetings, we do not discuss the F word, or funding. We are here to assess and score the scientific and technical merit of the applications, and we do not make funding decisions. At the second level of review, the advisory council considers recommendations and scores in light of institute goals and priorities. The two stages of review are a cornerstone of the NIH peer-review system. Next, I would like to ask the program officer to briefly discuss the purpose and goals of the RFA.

Shawn Gaillard: Sure, so you will be reviewing applications from an RFA that NIDA named Discovery of Novel Treatments for Opioid Use Disorders. The RFA is meant to support research on novel therapies that have not been approved for clinical use. The applications can focus on pharmacological, behavioral or alternative treatments. At NIDA, we decided to allow for a broad range of applications, so this RFA is clinical-trial optional. What that means is that we can accept applications that either involve or do not involve the clinical trial.

Jessica McKlveen: Thank you very much for that helpful summary. I'd like to remind everyone that there are separate review criteria listed in the RFA for clinical trials, and so for these applications, please be sure to address the correct review criteria during the discussion. I will now turn the meeting over to our chair, Dr. Kozel.

Peter Kozel: Before we start our discussion, I'd like to remind everyone to limit their evaluation to the review criteria published in the RFA, and also, please focus your discussion on the issues in the applications which drove your score. So let's begin with our first application. Dr. Marmillot is in conflict if we could put him in the waiting room briefly. Okay. I'm going to assume Dr. Marmillot has left. Our first application is from Dr. Jane Johnson. She's an early-stage investigator, and the title of her application is IGF-1 as a Potential Treatment for Opioid Use Disorders. The assigned reviewers are doctors Shekim, Hodge and Spriggs. Could the assigned reviewers please give their preliminary scores?

Lana Shekim: My score is two.

Debbie Hodge: I gave a three.

Shardell Spriggs: I gave a five, but after reading the preliminary critiques, I will most likely adjust my score based on the comments from the other reviewers.

Peter Kozel: Thank you. Dr. Shekim, can you lead us off?

Lana Shekim: Sure. So, as you said, this is an application from an early-stage investigator. The application proposes to leverage some recent and very exciting discoveries with insulin-like growth factor one, IGF-1, to see if it can be used as a treatment for opioid use disorder. The first two aims involve biochemistry and pharmacology-based experiments to develop IGF-1 as a therapeutic, and the third aim will examine the effects of IGF-1 in preclinical studies. I'm very excited about the potential impact of this study. The application clearly addresses the rigor of the prior research by pointing out the strengths and weaknesses of the published research that support the project. In addition, the use of male and female rodents and the animal models of aim three is a strength. The approach section is detailed, and all of the necessary information needed to assess the experiments is clearly presented. Therefore, the scientific rigor is strong as well. The application is innovative, and the environment is stellar. I had some concerns with the design of one of the aims, but these concerns are minor. I also gave the PI the benefit of doubt as far as strength of her publication record since she is an early-stage investigator. That's it.

Debbie Hodge: Okay, I will jump in and first say that I agree with all of the first reviewer's comments, so I'm not going to repeat all of the strengths, but I just want to add that I'm impressed with all of the expertise such as the biochemistry, the pharmacology that is really required for the aims, so it's represented on this research team. I just think they're wonderful. This increases my confidence that the PI will be able to accomplish the aims. That's all I have.

Shardell Spriggs: So my focus was on the preclinical behavioral test in aim three. This aspect of the application has some flaws in the design. I personally do not agree with the control the PI chose. For the one aim, this is an issue, but hearing the comments from the other reviewers on the potential impact of the research, I will adjust my final score, so it reflects the whole application.

Peter Kozel: Thank you all. Let's now open the discussion up to the full committee.

Nishadi Rajapakse: So I have a question about the pharmacology expertise. Does the application have expertise ... specific growth factor because it can be tricky to work with.

Shawn Gaillard: Oh, this is Shawn again. I'm the program officer. Can I address this issue since I've been advising the PI on this particular application?

Brian Hoshaw: Okay, I will stop the presentation here for a second interactive poll question. The question is, "During the discussion, can the program officer jump into the conversation and answer a question?" Okay. I think that's enough time. We'll see what the poll answer is. Okay 70 percent. A little closer, but 70 percent say no, 30 percent say yes. So we'll turn it back over to the SRO.

Jessica McKlveen: Thank you for asking, but no. This would not be appropriate. Program staff are here to observe the discussion, and they can answer general questions about the RFA if the SRO finds it appropriate, but they should not be involved in the discussion of specific applications. It is important that we keep the two levels of peer review separate.

Debbie Hodge: So I think I can step in and answer that question about the expertise. There is a coinvestigator with extensive expertise with insulin-like growth factors, so that area is covered.

Peter Kozel: Thank you, so this application does involve the use of vertebrate animals. We heard a little bit about that before. This is a scorable issue. Could the assigned reviewers tell us a little bit more about the use of animals?

Shardell Spriggs: Yes, the PI adequately addresses the questions relating to the use of vertebrate animals.

Lana Shekim: I agree.

Debbie Hodge: I also agree.

Peter Kozel: Okay, good. Thank you. I'm going to summarize the discussion. This application is from an early-stage investigator. The goal of the project is to explore the potential for IGF-1 to be used as a therapy for opioid use disorder. The application addresses a clear need in the field, and reviewers agreed that the potential impact is high. Both the rigor of the prior research and scientific rigor have been well addressed. There were some concerns about the controls selected for the behavioral studies in aim three, but this was considered to be a minor point, and I think that we're ready for our final scores from the three reviewers.

Lana Shekim: My final score is still a two.

Debbie Hodge: My score is also a two.

Shardell Spriggs: I'll move to a three.

Peter Kozel: Thank you. Our range is from two to three. I'm going to ask all reviewers to enter their final overall impact scores. Remember to hit save. Are there any budgetary comments?

Debbie Hodge: No, I think the budget is appropriate for the proposed work.

Lana Shekim: I agree.

Shardell Spriggs: I also agree.

Peter Kozel: Excellent. How is the resource sharing plan?

Lana Shekim: The resource sharing is very detailed, and all of the appropriate areas have been addressed.

Debbie Hodge: I agree.

Shardell Spriggs: I agree as well.

Peter Kozel: Fantastic, and finally, how about the authentication of key biological, chemical resources?

Shardell Spriggs: Authentication plans for the grow factor are appropriate.

Lana Shekim: I agree.

Debbie Hodge: I too agree.

Peter Kozel: Excellent. Thank you, all. Let's bring Dr. Marmillot back in for the next application.

Brian Hoshaw: Okay. I'm going to jump in again and give a little recap. So there are a number of questions about ESI applications. So ESI applications, if you qualify for that, it is just for R01 applications, so it's not just a stage of your career for any application, just R01s.

Most R01s are reviewed in CSR Study Sections, and the ESI applications are clustered together so that way, the ESIs are giving a little consideration on preliminary data and publications. It really helps reviewers get in the mindset of, "We're reviewing ESI applications." And generally, they do discuss at least half of that cluster. So for this application, also, you noticed most the applications we see are multidisciplinary, so it's possible that one reviewer will be there just for an aim or two, and this is why the discussion is so important. They review the applications, give their preliminary scores, but then when they look at the critiques and have the discussion, they can see all the different aims and all the expertise, and then the score comes together. We also note that certain aspects of the grant will affect the score. Other parts like budget or authentication, they're discussed after the scoring, so it won't affect the overall score of the application. And then finally, program officer there to take notes, to observe the application so the reviewers can help out the PI, and I'll say they really do their best to attend the meeting and observe and listen to discussion, but they generally don't participate in the discussion. It's possible at the beginning if it's an RFA, the SRO might ask the program officer to give some background on the FOA or the RFA, but the point there is, they're making general comments and not comments about a specific application. Okay, and with that, we will move onto to the next application.

Peter Kozel: Thank you. Our second application this afternoon is from Dr. Tom Wilson. It's entitled Novel Alternative Treatments for Opioid Use. There are no conflicts. The assigned reviewers are doctors Rajapakse, Chen and Wali, and could those assigned reviewers please give their preliminary scores?

Nishadi Rajapakse: Two.

Faye Chen: Two.

Anil Wali: One.

Peter Kozel: Thank you. Now, these scores are very close and indicate that there are many strengths with this application, and I'm going to ask the reviewers to focus on what factors led to such favorable scores. Dr. Rajapakse, if we could start with your review.

Nishadi Rajapakse: Yes, thank you. So this application proposes to test alternative treatments, especially plant extracts, as a novel form of treatment for opioid use disorders. The PI is a renowned medicinal chemist who has experience developing plant-based medications. The rigor of the prior research is addressed based on the review of the literature in this field. A weakness is that he does not have access to the plant extracts that they propose to use, and it does not appear that they will have time and have access any time soon. Overall, even though there are a number of weaknesses with the approach and the level of innovation is marginal at best, the PI has a good working knowledge in this field, and I'm sure that he can figure out how to solve any potential design flaws and overcome any technical challenges as the study gets underway. Overall, I really like the application, and I'm very confident of the PI's ability to get the work done. Thank you.

Faye Chen: Okay, so I'm the second reviewer for this application. I agree that the PI is very talented, but as I was reading the application, I realized that he hasn't published in the last few years, maybe a decade or so. In addition, I am not sure from the application that they have the resources and the personnel to conduct the experiments. Well, and I also have another concern about the novelty of the plant-based medications. I think that's low because they are similar to the ones that are already being tested in clinical studies, so based on that, I thought the innovation suffers a bit. But overall, I do agree with the first reviewer. This is a good application. I'm going to stop here.

Anil Wali: Thank you, I'm the [Indistinct] reviewer, and I agree with my both colleagues, primary and secondary reviewer. The PI is very well-known, a person of this field, and while I was in graduate school, he was published in the high-impact scientific journals, but lately, I have come across that he hasn't been publishing in high-impact scientific journals, and besides that, I have additional concern that they are proposing to utilize animal models in this application and will be only using male mice. So I do not agree with the rationale for excluding female mice in the design. So I have a question for the SRO. Should this affect my score?

Jessica McKlveen: Yes. According to the guidelines for rigor and reproducibility, sex as a biological variable should be addressed in the approached section of the application. If the PIs will not be using both sexes, they need to provide a justification, and this issue can affect the score.

Anil Wali: Well, in that case, I considered this additional weakness with this application.

Peter Kozel: Okay, I think that concludes the comments from our three assigned reviewers, and we're now going to open up our discussion to the full panel.

Lana Shekim: Hey, I'm not an assigned reviewer, and I didn't really read the application. Can I comment on the discussion?

Brian Hoshaw: Okay. We're going to have our third poll question here. One of the reviewers asks if they have not read the application, they're not assigned, are they able to participate in the discussion? Again, yes or no. Now, I'll say as an aside, some of our sound issues weren't scripted, but they really are part of any review meeting these days. It makes it more realistic-feeling. Okay, this split. This is a good question. Can they participate? Fifty-five said yes, and 45 percent no. I will turn it over to the SRO for the answer.

Jessica McKlveen: Yes. Anyone who is not in conflict with an application can participate in the discussion. Since everyone will be submitting final votes, everyone can participate in the discussion.

Lana Shekim: Right, so what I'd like to say is that I'm hearing a number of weaknesses: lack of access to the compounds, little current work by the PI and failure to address sex as a biological variable that seem inconsistent with the scores and the high-impact range that the assigned reviewers gave. Perhaps the assigned reviewers could speak a little bit more about how they came up with the initial scores?

Jessica McKlveen: Your assessment in scores should be based on what is presented in the application, not what the PI did years ago. In addition, the qualifications of the applicant are only one of the five reviewed criteria. If there are weaknesses in the approach, we should not assume they will be fixed based on the comments in the summary statement.

Peter Kozel: Could someone address Dr. Shekim's comment, question?

Nishadi Rajapakse: Yes, you make a valid point. The application does have issues in the research plan, and the PI has not done a good job in discussing potential pitfalls or giving any alternative approaches. And after hearing additional weaknesses from the other reviewers and realizing that my score might not reflect the number of weaknesses, I will adjust my score.

Faye Chen: Yeah, I also agree with the first reviewers, and I will also adjust my score.

Anil Wali: Ah, sorry, my apologies. Since this is my first meeting, I'm still calibrating my scores. So now, I see there are a number of weaknesses, so I will be adjusting my score as well.

Peter Kozel: Okay, thank you. That was a great question. Are there any concerns about the use of vertebrae animals aside from the issue with the justification for the use of only male mice which we've previously talked about?

Nishadi Rajapakse: So this aspect is acceptable. All points have been addressed adequately.

Faye Chen: Yeah, I agree with that too.

Anil Wali: I agree wholeheartedly, yes.

Peter Kozel: Okay, thank you. So I'll summarize our discussion. The goal of this application is to develop new plant-based therapies for the treatment of opioid use disorders. The reviewers acknowledge that the PI has an in-depth knowledge of the topic, although he has not published in almost a decade. There were also concerns about the availability of resources and personnel to conduct the experiments, the novelty of the approach, the use of only male mice without an adequate justification for excluding female mice as well as a lack of discussion on the potential pitfalls and alternative approaches. We've heard that our assigned reviewers are going to change their scores. Could we have those final scores, please?

Nishadi Rajapakse: Yes. Based on the discussion, I will raise my score to four.

Faye Chen: I will change my score to a four, too.

Anil Wali: I will also move to four.

Peter Kozel: Okay, thank you. I'm going to ask all reviewers to please submit their final scores. Remember to hit save. Are there any comments on the budget?

Anil Wali: I think budget is quite acceptable.

Nishadi Rajapakse: I agree.

Faye Chen: I agree.

Peter Kozel: Okay, thank you. How about the authentication of key resources?

Nishadi Rajapakse: So the topic has been addressed, and also the resources-sharing plan is thorough and acceptable.

Faye Chen: Yeah. I agree on both topics.

Anil Wali: I agree as well.

Peter Kozel: Okay, thank you.

Brian Hoshaw: Okay. I'll jump in for a little debrief. So in that application, so, yeah, people are usually surprised by this. Each application, they are assigned at least three reviewers, often more, based on how complicated the application is, how large it is, what type of research they're doing. All of the panel members who aren't in conflict, they have access to the application. They can read it. They often do if there's overlap with their field, but everyone is able to participate in the discussion, and this is an example. It seems far-fetched, but it's not that uncommon where a reviewer sort of focused in on the application. They only see a couple of weaknesses. They give it a pretty good score, but then each reviewer has nonoverlapping weaknesses. So when someone sits back and hears a discussion, it's like, "Wow, you're saying two and three. That really sounds like a five," and this is very important for score calibration, and it's another reason that we have the discussion, and everybody will vote on the application as well, but you see that the assigned reviewers give their final score, and that sets the voting range. If the final scores are two to four, that's the scoring range all the reviewers will use. There is a process where they're able to raise their hand to say, "I'm voting outside the range." They're often asked to give a reason why. Nine times out of 10 is because the comments don't match the scores that they're hearing. We didn't want to go to that today because of time, but there is a process where assigned reviewers set the range. Other reviewers can vote outside the range.

Megan Columbus: Brian, could I just ask you to comment really quickly on the extent of the discussion for each application?

Brian Hoshaw: Yes.

Megan Columbus: Did we abbreviate it for this session, or is this really what people are getting?

Brian Hoshaw: Yes, good point. Yeah, the number of questions that I have. This is an abbreviated version. I would say for R01 applications, anywhere from 15 to 25 minutes depending on the score range. If the score ranges are very close, it will be quick. Sometimes you'll have two, two, seven. There will be a long discussion of that. So this is a very abbreviated version. They go into more complexity. They go into a lot more depth not just for R01s, but if it's a clinical trial or program project, they'll have a lot more time allocated to that. Yeah, a number of questions on that. This is an abbreviated version. Okay? So for the sake of time, I will turn it back over to the chair for the third application.

Peter Kozel: Okay. We now have our third and final application. It's from Dr. George McFee. It's entitled A Clinical Trial Examining Cognitive Behavioral Therapy for Opioid Use Disorder. The assigned reviewers are doctors Carlin, Marmillot and Shen. And could those assigned reviewers please give their preliminary scores?

Danielle Carlin: Ah, yes, I gave it a three.

Philippe Marmillot: I gave it a six.

[ Chatter ]

Peter Kozel: I think we have ...

Philippe Marmillot: I gave it a six. Yeah, I gave it a six.

Peter Kozel: And I think we should have one more reviewer. Well, in any case, we have a bit of a range. Carlin, could you please start your review.

Danielle Carlin: Sure, can you hear me, okay, first of all?

Peter Kozel: Yep.

Danielle Carlin: Great, thanks. So this application proposes what I consider to be a highly novel use of cognitive-behavioral therapy, also known as CBT, to treat opioid use disorders. In the design, CBT or a sham treatment will be administered to participants at a single clinical site who meet the DSM-5 criteria for opioid use disorder. The participants will have follow-up interviews at 6 months and 1 year to assess opioid use. They have been ... There have been other studies that have examined the effects of CBT on opioid use, but this application proposes what I think to be a novel treatment plan that is based on a recent paper that has some very exciting results. The paper also indicates that longer CBT sessions maybe have a longer-lasting effect on opioid use. The application is clearly written, and the PI is a leader in the field. All of the review criteria in the RFA that are specific to clinical trials have been addressed, and the study protocol has been included, and it is clearly written. The study time line is feasible and well justified. Challenges and proposed solutions were adequately discussed. The experiments are sufficiently powered, including detection of sex-based differences. And ... But my score would have been better, but I have concerns with the control sham procedure that they will be using, and I thought that they could've included more information on the training of personnel at the clinical site. Thanks.

Philippe Marmillot: Okay, and thank you. So I agree with most of the strengths and weaknesses stated by Dr. Carlin. However, I gave a less favorable score because I believe that the investigators have misinterpreted the results from the key paper they are citing. My concern deals with the rigor of the prior research. So the investigators interpret the results of this paper to show that the new treatment has a longer-lasting effect. However, I do not agree with this interpretation because it's my opinion that it's really unlikely that a new treatment procedure will have any added benefits. Therefore the hypothesis is flawed, and this was a major score-driving concern for my review.

Grace Shen: All right. I'm just a reviewer, sorry. I was muted just now. So I actually agree with the first reviewer, Dr. Carlin, and I also gave an initial score of three, and I respectfully disagree with the comments of Dr. Marmillot. I believe that the rigor of the prior research appears to be very solid.

Peter Kozel: Okay, in the interest of time, I'm going to open this up to the full panel.

Lana Shekim: So while I wasn't assigned this application, I did read it out of curiosity. So I agree with Dr. Marmillot that the intellectual foundation of the application is extraordinarily weak. PI didn't understand the results and the implications of this paper.

Peter Kozel: So we had a fairly substantial range on this preliminary impact scores. Would the assigned reviewers like to address the issue of rigor of the prior research? We've sort of been dancing about this.

Grace Shen: So I saw the comments and the critiques from the other reviewers, and I even went back and looked at those papers. I think that the PI's hypothesis is still based on scientifically rigorous arguments even if there are some concerns that this experienced PI and team will be able to address the issues and move forward based upon the pitfall and backup strategy. I still think that this application sufficiently will be productive.

Philippe Marmillot: Yes, thank you, but I respectfully disagree with your assessment.

Peter Kozel: Okay, it appears as though that our reviewers are not going to be able to come to a consensus. Dr. McKlveen, do we need to keep going, or can we reach a consensus, or can we stop here?

Brian Hoshaw: Okay, now for our final poll question. The reviewers cannot come to a consensus on the merits of the application. Does the review continue, or can the chair cut it off? So the question ... Yeah, I'll phrase that better, sorry. Do they have to come to a consensus on the merits of an application, yes or no? Yes, they have to. No, the reviewer can stop at this point. Okay. So a little more clear here. So 76 percent said they do not have to come to a consensus. We'll see what the SRO says.

Jessica McKlveen: The review panel does not have to come to a consensus on the merits of an application. The objective of peer review is to identify an application's strengths and weaknesses and how those individual strengths and weaknesses are balanced to arrive at a final overall impact score. Reviewers may weigh each strength and weakness based on their individual expertise and thus may arrive at different final overall impact scores. The objective is not to reach a consensus evaluation of the merits of an application, and all reviewers not in conflict should submit a score that is based on the discussion.

Peter Kozel: Thank you for clarifying this. Now, I think the scientific rigor has been discussed thoroughly. It appears that reviewers are not going to come to a consensus, so let's continue along with our evaluation of this application. Can the reviewers please comment on the protection of human subjects and the inclusion criteria?

Grace Shen: Yeah, I can do that. They have trained therapists that will implement the CBT protocol, and all the necessary precautions are in place to ensure the safety of the participants. They also plan to recruit an equal number of men and women, and the projected minority recruitment is acceptable. Children will not be included in this study, but their plan, they have a plan in place to recruit their participants from 18 to 85.

Peter Kozel: Okay, thank you. I'm going to now summarize the discussion of this application. The application aims to study the effects of cognitive- behavioral treatment on opioid use disorders. The application proposes a randomized clinical trial for participants over the age of 18. All the clinical trial review criteria listed in the RFA have been addressed. The rationale for this study is based upon a recent paper which may indicate beneficial effects of longer therapy sessions. However, the reviewers do not all agree on the interpretation of the results of this key paper and how much they support the application's hypothesis. Therefore, the evaluation of the merit appears to be varied widely between the assigned reviewers for this application, and with their final scores, I think we're going to find out just how wide a reception that is.

Danielle Carlin: So for my final score, I'm going to stick with a three.

Philippe Marmillot: For me, I still have major concern with the concept of a flawed hypothesis, and thus, I'm still at six.

Grace Shen: And I am going to stay at a three.

Peter Kozel: Okay! Thank you, all. There are two very different perceptions on the merit of this application. As each of you votes your conscience, I would encourage you not to split the difference but to rather be decisive and align your scores towards the perception you found most convincing. Are there any comments about the budget?

Philippe Marmillot: Yes. I feel that the budget is excessive for the amount of work proposed, and the percent of work from the personnel is too high, and they overestimated the costs. Can we lower the budget in this application?

Jessica McKlveen: We can make recommendations on the budget for NIH staff. Do you have specific recommendations that you would like to make?

Philippe Marmillot: Yes. In this case, I would like to recommend that the personnel requests for one of the technicians be eliminated and that the supply budget be reduced by $50,000 a year.

Jessica McKlveen: Do the other reviewers agree?

Danielle Carlin: Yes.

Grace Shen: Yes.

Jessica McKlveen: Okay, I will make note of this in the final summary statement, and please make sure that those comments are included in your final critiques as well.

Peter Kozel: We have some comments about the authentication of chemical and biological resources.

Grace Shen: Yeah, authentication is not really applicable for this application. There are no biological or chemical resources that need that.

Peter Kozel: Okay, thank you, and can the reviewers address the resource-sharing plan?

Philippe Marmillot: Yes. This application does not address this topic, and it's not acceptable.

Peter Kozel: Okay. Do the other reviewers agree with this?

Grace Shen: Yeah. The resource-sharing plan is not addressed in it.

Danielle Carlin: And, yes, I agree with the other two reviewers.

Jessica McKlveen: Okay. I'll make a note of this on the final summary statement. Please be sure that these comments are in the appropriate section of your critique for this topic. And so this will conclude our review meeting today. Thank you very much to our chair for moderating the scientific discussion and to each of you for serving as reviewers. After all, we cannot accomplish peer review without you. Please ensure you securely dispose of all confidential material, update final critiques and criterion scores if your enthusiasm has changed as a result of discussions today and ensure that we receive any information pertinent to receiving your reimbursement and honorariums.

Brian Hoshaw: Okay, a minute or so left. There were ... Thank you to the panel, first of all. Hope that was very informative. A number of questions about not-discussed applications. So very quickly, if ... Sometimes, the applications, only the top half will be discussed at the meeting. That is based on the preliminary, the average preliminary score from the reviewers. They submit their critiques and scores before the meeting. A line will be drawn. About the top half will be discussed. Reviewers do have an opportunity to rescue an application if it's on the not-discussed list. The ones that are not discussed do not get a final score, do not get a summary of discussion. However, they will get the full written critiques and criterion scores from the assigned reviewers, so it's not discussed. It's not just you won't get any feedback. You will get all the critiques. You will get criterion scores, very valuable feedback, you just won't get an overall score, and there won't be discussions. And this is to save time so that the top half can get discussed. Another question, "So enhancing reproducibility and rigor through transparency," you see that was discussed here with rigor, prior research and scientific rigor, sex as a biological variable. These things are really embedded in review now, and it's not just something that was brought up as part of NIH and fell by the wayside. It really is part of every review of every application, so make sure your own application you address rigor, scientific rigor, rigor of previous research and then aspects such as sex as a biological variable. So as you can see, the committee does not have to come to a consensus. They'll discuss ... get to a certain point in the interest of time, and this is where the whole panel voting really matter because we asked them not just to sort of give the average scores of the difference, but really vote based on the discussion that you heard.

Megan Columbus: All right. I'm afraid that that's the time that we have for today. I thank you. I think people really appreciated seeing the review in action aspects of this, so thank you to all of our panelists and everybody behind the scenes who is answering the many questions that came in. If people have additional questions, please, all the institutes and centers have booths out there. We do have a central ask-a-review-officer booth. Please feel free to go ask your questions tomorrow. I think it's the end of the day for the booths today. Your feedback is important. Let us know how the session went for you back on the screen that you got here and entered the session on with the description, and when you're finished with the conference, please let us know how it went. Thanks again for interacting.