Cate Pritchard: Thank you for joining this session, Animals in Research: Tips to Keep Out of the Doghouse. My name is Cate Pritchard, and I am an Animal Welfare Program Specialist at the NIH Office of Laboratory Animal Welfare, otherwise known as OLAW, and I'm your moderator for this 45 minute session. Now I'd like to present our panel for today, Dr. Jacquelyn Tubbs, a Veterinary Medical Officer in the OLAW Division of Compliance Oversight, and Dr. Brent Morse, the Director of the Division of Compliance Oversight at OLAW. Jacquelyn Tubbs, DVM joined the Division of Compliance Oversight as a Veterinary Medical Officer in September of 2019. She received her DVM from Tuskegee University School of Veterinary Medicine. She was the first person to complete a post doctoral fellowship in laboratory animal medicine at the National Toxicology Program at the National Institutes of Environmental Health Sciences. Prior to joining OLAW she established the Gnotobiotic Core at Duke University and served as the Technical Director. She's also a diplomat of the American College of Laboratory and Animal Medicine. Brent C. Morse, DVM is a Director of the Division of Compliance Oversight at OLAW. He's a 1987 graduate of Washington State University's College of Veterinary Medicine, and he completed his residency in laboratory animal medicine with US Army. His previous positions included Acting Chief of the Veterinary Medical Branch of the Division of Veterinary Resources at NIH while serving as a Commissioned Corps Officer within the US Public Health Service. And he also completed several management positions as a Veterinary Corps Officer in the US Army. So welcome to you both. All right, the format for today's session includes a short presentation followed by Q and A with our presenters. During the presentation we have Q and A staff to answer questions in the Q and A box. So let's get started. Your first presenter is Dr. Tubbs.

Brent Morse: Actually I think it's Dr. Morse.

Cate Pritchard: Oh, my apologies. Dr. Morse.

Brent Morse: That's all right. Welcome, everybody, and thank you for joining us. I want to thank Dr. Jai Tubbs for assisting me in this presentation. Dr. Tubbs and I both work in the Division of Compliance Oversight, but she also works in the Division of Assurances at OLAW. So she has a great experience in both sides of how research is funded and also dealing with problems when things go wrong. So our presentation is in two parts today. I'm going to be giving you a few slides to orient you to the basis for our talk, and then we're going to go over some real life scenarios to put things in perspective and to put into play some of the issues that I'm going to cover in the first few slides. So let's first look at the regulatory basis for OLAW's oversight of funded research using animals. Thank you. The Public Health Service policy on Humane Care and Use of Laboratory Animals, or what we'll call the PHS policy, or the policy, was established by the Health Research Extension Act of 1985. OLAW has responsibility for the general administration and coordination of the policy. These are the three general categories under which institutions must report noncompliance to OLAW, listed here. Any serious or continuing noncompliance with the PHS policy. Any serious deviation from the provisions of the guide for the care and use of laboratory animals, and any suspension of an activity by the IACUC. Next slide, please. Although OLAW works directly with institutions, and not individuals, we understand that our actions often directly impact investigators and the research team .. .

Person: You're back, you can just unmute yourself.

Jai Tubbs: Okay, I have no idea what happened. Is my screen still being shared?

Person: No, it's not, you can share your screen, and Mr. Morse, there you are.

Brent Morse: There we go I think.

Person: Yep, you're back.

Brent Morse: Okay, I'm just going to proceed here, at least through this slide that was up there, and we'll see how things go. There it is. OLAW will provide assistance and guidance when things go wrong, and the incident is reported to our office. Institutions must demonstrate that corrective actions are being implemented, and we will evaluate whether or not those corrective actions are expected to be effective, and we want to make sure that everybody understands that self reporting is part of enforced self regulation. The PHS policy is based on the institution overseeing their research program, and then taking actions to correct when incidents go wrong, and notifying our office. Next slide, please. Thank you. So just to put this all in a little bit of perspective, this chart illustrates the types of reportable incidents that OLAW received in 2020. We'll have 2021 available in a few months. Almost 90 percent of protocol issues, which are listed as animal study issues, almost 90 percent of those incidents relate to not following or not being familiar with the protocol. For example, animal users aren't reading the protocols, they're not properly trained on protocols, and may not even have access to current protocols. So let's look a little closer at the types of animals involved in noncompliance reports to OLAW in 2020. Next slide, please. And it should be no surprise that the vast majority are rodents. I call your attention to the involvement of fish, especially since incidents that involved fish often result in significant animal welfare issues and high mortality. And we'll talk about that a little bit later in the presentation. Birds, amphibians, reptiles, they make up the remaining 4 percent there listed here. Next slide, please. So who is responsible for the issues that are reported? This data again, refers to issues for 2020. We at OLAW, and also those who oversee the Animal Care and Use Program at your institution understand that performing research with animals is very complicated. Investigators often perform complex and intricate procedures with animals, and may be involved with their research animals on a daily basis, and this chart reflects that involvement and the opportunity for things to go awry. So you can see usually when things go awry it is related to the protocol and to the investigative team. Next slide, please. The goal of the PHS policy and its underlying authority of the Health Research Extension Act, and OLAW regarding noncompliance, is that the entity has been given a reasonable opportunity to take corrective action. It's a very general statement, but it's at the core of self-monitoring and self-correction. Some of the more common tactics for institutional self-correction are listed here. And you can see that retraining personnel is probably the most common action that's taken. Counseling of those personnel that are involved in the noncompliance. Occasionally reprimands. Terminating employment fortunately is quite rare. Modifying institutional policies. Sometimes things go wrong because there is not an effective institutional policy to guide people when it comes to specific issues with using animals in research. And then repair or modify the facility if it's a facility issue. Enhancing PI and study oversight, that can be either by other personnel in the Animal Care and Use Program or by the Institutional Animal Care and Use Committee themselves. They may need to modify or suspend, or in rare circumstances, terminate the animal study protocol. Some of the other things that can be used by the institution are temporarily appointing a co-PI who is experienced with animal research, especially if they're experienced with the species that's being used or with the procedures being employed. Improving environmental monitoring of the animals, or increasing IACUC oversight and monitoring of the lab if there is repeated noncompliance. OLAW and the PHS policy does expect increased intensity of the corrective actions for repeated noncompliance, because of the negative implications of repeated issues with animals, and the impact on animal welfare. So our goal here today is to hopefully keep you out of the doghouse, and especially keep you away from repeated noncompliance. Next slide, please. So what are some of the implications of reportable issues? So OLAW gets called, what happens? Well, hopefully what happens is the first bullet on this slide. Corrective actions and improved systems with better research outcomes. That involves not only input from the IACUC and the attending veterinarian and the administration at the institution, but also input from the researchers. Make sure that those corrective actions allow the research to proceed. There can be special terms and conditions of the award, enhanced reporting requirement that is usually from the institution to OLAW. Like I said, we deal with institutions, but that doesn't mean that it won't impact the researcher. There can be cost disallowance regarding the NIH funding. Unable to use the data to publish or for grant proposals. Suspension or termination of the award and possible repayment of funds. Damage to reputation, not only of the institution, but of the individual researcher because of the assessment of peers and collaborators. May need to retract or withdrawal the scientific publication, or the journal may need to issue a corrigendum or errata for the article. And in obviously, the very extreme cases, there can be criminal prosecution. So we're starting out with the top one, which is by far the most common. Corrective actions and improved systems, down to something that is much more rare, and that is any kind of criminal prosecution. So let's take a break from the slides, see if anybody has any questions so far.

Cate Pritchard: We don't have many questions so far. There was one question about how are violations generally brought to your attention, if you'd like to expand on that?

Brent Morse: Yeah, that's a very good salient point here. As you know, it's going to be self-reported in most cases from the institution, by the vast majority, well over 90 percent of the reports come from the institution. And in many of those cases, it is self-reported by the research personnel to the IACUC or to the veterinary staff, and brought to the IACUC. So we do get some reports from other sources, such as the USDA, when they do their walk through and do their inspection, if they see something that should be reported to OLAW, they'll usually inform the institution that they should report that specific noncompliance to OLAW as well as to USDA. And it can also .. . Incidents can also be reported by the funding component to OLAW, and of course we do get allegations from animal rights organizations and from employees or disgruntled, former employees. So there are many different avenues for us to receive reports of incidents. Two things that we look at when we receive a report. One is OLAW's jurisdiction. Is it an activity that we do have jurisdiction over because of the PHS policy? And the second thing we look at, is it reasonable? Is this allegation or is this report something that falls within the issues that we normally have reported to our office. So there are the two things that we look at.

Cate Pritchard: Thank you. We have another question. This is a good one. If a university decides to voluntarily apply its assurance to all animal work, regardless of funding, so not limited to PHS, for example, then any suspension or serious noncompliance becomes reportable, even if it is not supported by the PHS?

Brent Morse: That's correct, and that .. . OLAW oversees approximately 890 assured institutions domestically, within the United States. It's a small handful of those institutions who have voluntarily written into their assurance document with our office that they will report all incidents related to animal welfare regardless of the funding origin. So it does happen, but it is .. . It's a small subset of the institutions that report to OLAW.

Cate Pritchard: Great, and another question, at a recent OLAW webinar, I thought that a presenter stated that NIH OLAW cannot prevent data from being published when it's involved in a reportable event. Can you clarify this?

Brent Morse: I can, I think. That is a true statement. When the data is gathered, it belongs to the institution. It does not belong to OLAW, it does not belong to NIH. So it is the institution's data, but it would be rare for a journal to accept data that was gathered from an animal use protocol that was not gathered and approved for use by the Institutional Animal Care and Use Committee, the IACUC. So the idea of having to put some sort of a statement that some of the data was approved by the IACUC and some of the data was not, most journals don't want to do that, but it's up to the institution to decide if they want to approach a journal. And same thing goes for future grant proposals. I can only think of one example, but there's one example of unauthorized data gathered from animals that was used in a grant proposal to an institute at NIH, and it was rejected, and the student had to go back and re-perform the study, recollect the data, with an approval from the IACUC, and then resubmit. And in that case they were successful the next time around, but in general, you don't want to use data that has not been approved by the IACUC for a grant proposal.

Cate Pritchard: Thanks. And the last question that we have right now is that one of your previous slides indicated that 1 percent of noncompliance does not specify the species. So could you give some examples of reports of noncompliance that doesn't involve a particular species?

Brent Morse: Sure. Normally what happens is the compliance does .. . The report of the compliance is not dependent on any specific species of animals. So for example, if there is a general program failure with their occupational health and safety program, and we've had these in the past, it would be reported as a programmatic failure, but it doesn't affect any specific animal, it affects the program at the institution. So that's where those type of issues fall.

Cate Pritchard: Awesome. All right, you're good to go with questions for now.

Brent Morse: Okay, can we go to the next slide? Great. Thank you. So sometimes all lab members do not know what's approved in the protocol. I mentioned this before, and they assume certain procedures and techniques are approved, and this can lead to noncompliance. So make sure that anybody who's working with animals in your lab is properly trained, but also has access to the protocol or at least understands the procedures that they're going to be performing relative to the protocol. Sometimes a noncompliance is related to less experienced lab members and their performing procedures and techniques which result in noncompliance. Such as maybe they do a dosing miscalculation, that can result in animal death. Maybe there are post surgical complications because they either haven't been properly trained in the surgery, the post-op is not being properly monitored by the person. There are .. . These first two are fairly common reasons why noncompliance occurs, and is reported to OLAW. It's not uncommon to receive reports of expired drugs. Corrective actions for this type of noncompliance usually includes creation of an internal audit system to keep track of expiration dates. Sometimes individuals assume procedures are approved on the protocol or perform approved procedures on animals that are assigned to a different protocol. Each circumstance still results in the conduct of activities that have not been reviewed and approved by the IACUC, and therefore, are not compliant. And whether the error is made by the husbandry or the research staff, missing food or water is commonly reported to OLAW. And this of course is an animal welfare issue that can result in the death of animals. The other one is inadequate monitoring of animals, and these last two can be grouped together when we're talking about food or water restriction in a research study. It's very important that the responsibility for those animals, for providing food and water is clearly stated, and that whoever is responsible for that understands what they are to do and who they can notify if something goes wrong. Next slide, please. Okay, we're going to shift a little bit here and talk about some of the hot issues in compliance oversight. The first one, and the most common issue that we hear with animals in general, whether it's rodents, primates, canines, is post procedural analgesia. Okay, missing, providing that analgesia at the proper time after a procedure or a surgery. So the suggestion is to make sure to remove ambiguous language from protocols or SOPs. You don't want to have things like professional judgment or when required. You want to have a specific time or timelines for when analgesia is to be administered. These types of procedures, usually it's pretty well known what the pain levels are going to be and what type of analgesia's going to be given, and when it should be given. So just animals can hide pain very well, and we don't want to be relying on professional judgment or trying to determine when it's required. We also want to assist the research team by allowing them to create records or charts to document administration. Make it easy for them to document that and pass it on to other people who would be in charge of providing that analgesia. So this is probably the number one issue with reports to OLAW, missing analgesia or documentation of administering analgesia to animals. The other very common one is failed CO2 euthanasia in rodents due to insufficient exposure time or lack of appropriate post-exposure observation. So animals may look like they're dead, but they can go into a narcoleptic state for quite awhile, and what we don't want is for them to recover in a freezer or refrigerator. This can usually be prevented by applying a secondary physical mean after the CO2 euthanasia. Of course, this has to be documented in the protocol and approved by the IACUC. Another reason, they may not have proper flow meter or instructions for the use of CO2 euthanasia chamber. That should be posted nearby so that anyone who is to use the chamber, even though they will have been trained on using the chamber, can refer to the instructions to make sure they're following all of the steps. Some institutions are more closely monitoring the CO2 euthanasia areas, and/or the carcass disposal freezers. In some cases, they're doing a regular check, a physical check of those areas, and some institutions use closed circuit or video monitoring of those areas, to make sure that the procedures are being followed. I mentioned earlier about fish, and the use of research fish. Physical plant or husbandry failures often lead to catastrophic losses, and many fish species are exquisitely sensitive to multiple environmental parameters, such as water temperature, the salinity, the PH, the nitrates, chlorine level, oxygen level, whether that's too high or too low, water flow, and ozone. I have received reports of animals dying in response to each of these being out of the proper level. So make sure that if you are going to be working with fish .. . Well, let me just say, we highly recommend monitoring and remote alarm systems for parameters appropriate to the species of fish that you're going to use. Okay, next slide. And to wrap things up here with this slide set, lack of food and/or water. We talked about that earlier, especially when we're talking about food or water restriction studies, to make sure that the responsibility for feeding or providing water is very clear. Whether it shifts from the research staff to the husbandry staff or back, or whether it goes from one member of the research staff to the next for, say, a weekend. It needs to be clear and people need to understand what their responsibilities are. And the last comment I have regards atmospheric or testing chamber failure. I just had a report on this a couple of days ago, where animals died in a testing chamber because someone forgot they were in there and left for the weekend. There was no monitor, no alarm, and the animals were found dead on Monday morning. So please, whether you're using it for a hypoxia study, a smoke inhalation, UV exposure, or some sort of a behavioral study, please make sure that those chambers are treated like small rooms, and a small animal room needs to be monitored, and it needs to have an alarm in case life threatening parameters go out of whack. So we hate to see this type of report when it's probably preventable with an inexpensive monitoring system. Okay, I think we can go ahead to the next slide and see, Cate, do you want to take any more questions? Or do we want to proceed to the scenarios?

Cate Pritchard: We definitely want to hit some questions.

Brent Morse: Okay.

Cate Pritchard: Okay. So the first one is a little bit more about guidance and communication. It says in the past I've personally been a victim of scapegoating by multiple PIs. What protections or routes of reporting are available to techs that are outside of the internal IACUC process? Often techs are not informed or even involved in the IACUC reporting process.

Brent Morse: Okay, this is probably something that OLAW would not be able to assist, other than just advise. The technician would .. . If it is a veterinary technician, probably the best thing is to talk to your supervisor, whether it's the veterinarian or if you have a technician supervisor, talk to them about not only the specific issue you're concerned with, but it sounds like you may have an issue with the culture in your institution. As I mentioned, OLAW deals with the institution as a whole and not with individuals, but we do understand that where communication fails, animal welfare can be impacted as well. So good communication from everybody in the program is vital, you want not just the vet techs but the animal care techs, you want them to be able to communicate up through the chain. Make sure that what they see is being reported, and that there is a proper response. But that's about as far as I can go today answering that question.

Cate Pritchard: Great, thank you. And I think this one may be a little bit more in the weeds and maybe better directed towards the AVMA, but do you know why CO2 is recommended for rodent euthanasia and not N2?

Brent Morse: And I'm sorry, not what?

Cate Pritchard: N2.

Brent Morse: Yeah, I don't. I know that CO2 has been very effective and has been used for a long time. And it's obviously very wide spread. So I'm sure that is a part of the reason why the AVMA has been very observant of changes in the use of CO2 for euthanasia, and coming out with better guidance on that. But again, yeah, that's probably more of an AVMA question.

Cate Pritchard: Yeah. Can you talk about our guidance and our oversight of agricultural animals?

Brent Morse: Sure. One question that came up earlier had to do with the use of .. . I'm sorry, had to do with whether reporting of animals that are not necessarily PHS funded, maybe not even in the biomedical research arena at an institution, whether or not those needed to be reported. And in that case, dependent on whether the institution wanted to report. But where agricultural animals are used in biomedical research, and they are commonly used, they are considered of course laboratory animals at that point. They need to be kept under the auspices of the "Guide for the Care and Use of Laboratory Animals," and make sure that the PHS policy does apply to those agricultural animals if they're being used for biomedical research. So in that case, the PHS policy and the guide would both apply and the guide does have some instruction in there for agricultural animals.

Cate Pritchard: Excellent. Those are all the questions we have at this time.

Brent Morse: Okay. Thank you. Then I think what we're going to do now is go to the next slide. We do have some real life scenarios and we're going to give you something to chew on for your environmental enrichment, and I'm going to turn over the remainder of the presentation to Dr. Tubbs. Jai?

Jai Tubbs: Thank you. I recognize we only have 10 minutes, so hopefully we'll get through two scenarios and maybe one polling. So the first case scenario starts with investigator Aaron Rodgers at Green Bay University conducted a protocol approved surgery on mice and the animals recovered successfully. During veterinary rounds, the surgery cards on the cages indicated the animals were administered an opioid. In this case, buprenorphine SR, and the mice exhibited no signs of pain and distress. However, the protocol states an opioid and a nonsteroidal anti-inflammatory drug, in this case meloxicam, will be administered as the analgesic regimen. So the question for the audience is, is the administration of one of two approved analgesics considered a noncompliance? Keep in mind, these animals showed no signs of pain, no signs of distress. Please vote. All right, so first place appears to be the choice yes, second place appears to be choice no, and third, unsure. So the answer is .. . Got to use my mouse. Yes. This is considered a noncompliance. So while I stress that the animal showed no signs of pain or distress, the investigator or animal user must adhere to what is described or written in the protocol. So to be in compliance, animals would need to have been administered both buprenorphine and meloxicam. So let's consider some ways scenario one could be avoided. One, always, which has been previously stated, ensure that all lab members are familiar with the protocol, especially if amendments were recently approved and added to the protocol. Also going back to what Dr. Morris said about access, is there a hard copy of the protocol in the lab in a notebook where individuals can easily access it? Or do they know how to access it online? And if there is a hard copy, when amendments are approved, are they added to that notebook? That can also help increase compliance. Another method could be assigning roles and designating which individuals will perform the post-op care or administer the drugs. Decide if it will be the surgeon, the lab manager, or the person performing the evening checks. Also a laboratory could consider utilizing a post-surgery form or a checklist that they've created internally to ensure that action items had been completed. So for the next scenario, it says during morning husbandry checks, a cage of mice was discovered lacking an appropriate amount of special diet. The mice were found in poor condition, but recovered with supportive care. Discussions with the Rodgers Lab revealed the lab was responsible for providing a special diet and the mice had not been monitored as frequently as described in protocol. So question for the audience, would you consider the decreased frequency of monitoring to be a noncompliance? And the majority selected choice yes, second place is no, and third place is unsure. So survey says yes. This would be considered a noncompliance. So again, must adhere to whatever's written in the protocol, in this case the frequency of monitoring was not adhered to, and by adhering to that monitoring it's very likely that the food would have been replenished in a timely manner. So some ways to avoid case scenario number two, one could consider creating a schedule for the weekday and the weekends among the lab members that are going to be feeding the animals. Document. On that schedule could have lab members provide their initials so it's clearly documented who has performed the AMs, the PMs, or the Saturday or Sunday responsibilities. And the suggestion of keeping this document in the husbandry room if possible. One, the documentation isn't traveling back and forth between the lab, and two, if husbandry staff members are in there, they can easily see if these animals are being fed the special diet by the lab as required. Another key is communicating with the husbandry team that services the animal room, and providing them with contact numbers so that lab members can be readily reached. This is important for scenarios such as, maybe there's a lab that's providing a special diet, a conference is coming up, there's going to be a skeleton crew in the lab, and they would actually like husbandry staff to actually provide the special diet. Or it could be an instance where husbandry staff member comes in in the morning to service the room and notices that the Sunday PM or Monday AM has not been checked. And they can contact the lab members through the contact information that has been provided. And again, we've emphasized this before and before, review the protocol with the lab members. And absolutely stress the importance of adhering to the monitoring plan and the lab's responsibilities. For example, the protocol could state that animals would be monitored four days post surgery, and the individual goals looks at mice on Monday and Tuesday, they look great. They're running around, their incisions are completely healed, so they don't want to do Wednesday and Thursday, but the protocol says 4 days post surgery. So Wednesday, Thursday would have to keep that monitoring if that's how it was described in the protocol. Just kind of adhere to what's written. Now the third .. . Oh, I'm sorry.

Cate Pritchard: Can I stop you?

Jai Tubbs: Yes.

Cate Pritchard: Yeah, we have a question, and this has to do with flexibility in protocols. So we're going back to scenario one.

Jai Tubbs: Okay.

Cate Pritchard: And they're asking, once the noncompliance has been addressed, could the protocol be amended to read something like post surgery animals will be administered an opioid, which may be supplemented with an NSAID if pain or distress is recognized or observed.

Jai Tubbs: Absolutely. So if it's recognized that an individual had approved multimodal, they're going to give an NSAID and buprenorphine. Determine that buprenorphine is sufficient enough. As long as that language is approved by the IACUC amendment, absolutely can be submitted. Because when research occurs, different results are seen, and you know you can make adjustments as needed to the analgesic regimen pending IACUC approval. Okay?

Cate Pritchard: Mm-hmm.

Jai Tubbs: All right, so scenario three. A lab member performs CO2 euthanasia involving a cage of mice. The individual did not perform a secondary method of euthanasia as required by the euthanasia SOP referenced in the protocol. Mice that recovered from the incomplete euthanasia were found alive in the carcass refrigerator later that day. So a question for the audience, would you consider the lack of conducting a secondary method of euthanasia to be a noncompliance?

Cate Pritchard: While we are waiting for those answers, we will need to wrap up in just about 1 minute.

Jai Tubbs: Sure.

Cate Pritchard: Thank you.

Jai Tubbs: All right. All right, overwhelming majority is yes, second place is .. . Oh, second and third place are tied. And the answer is yes. Yes this would be considered also not only a noncompliance, but an animal welfare issue as well. So ways to avoid scenario three. One, determine if the training is appropriate, review the lab SOP, review the protocol training that's described. Does it need to be updated? Is it consistent with the institutional policy on euthanasia? From an institutional standpoint, it must be determined that the policies are clear and well disseminated. When updates are made to the policy, are they disseminated via e-mail, posting or appropriate signage that is clearly understood? Regarding the euthanasia equipment, is the equipment considered easy to use, or are investigators and animal users constantly troubleshooting or reaching out for feedback or assistance in using the equipment? Is an automated euthanasia system available for use? Regarding location, is the location of the euthanasia station in a central location? Is it near animal resource personnel? So when individuals do need assistance with euthanasia, do they have quick access to someone that can help them? Also, use of a security camera or a card reader at a euthanasia station may be beneficial. So when those animals are found in a refrigerator they can be properly, humanely euthanized. The appropriate supervisor or point of contact is informed, maybe they can look at the card reader, see which individuals were in there the past couple of hours, or review security camera footage for accountability purposes. And since we're running out of time we'll skip past. No polling here. Very quickly, doctor Gilligan is a researcher, does research with fish. Some fish are NSF funded, other fish are not NSF funded. Unfortunately 600 fish died because the biofilters failed due to lack of maintenance. Now...and 600 fish died before a 4 month period. While none of the fish that died were NSF funded, the question of is the loss of 600 fish reportable? Okay, top choice is yes. Second choice is unsure, third choice is no. And the answer is yes. This is considered reportable. So any animal, regardless of funding, when you have an unexpected death should be reported to the veterinarian and the IACUC, and regarding non-PHS funded projects, there are certain circumstances or events that occur that should be reported to OLAW, and absolutely, when in doubt, give us a call at OLAW to discuss those scenarios, and see if it's reportable or not. And I hope I did not talk too fast, I hope some of the information was retained, and now we have time for additional questions and answers for the Q and A.

Cate Pritchard: All right, at this time we actually are going to have to be tying this up, but you can always leave us an e-mail. Send us an e-mail at OLAW@mail.NIH.gov and we'll respond to you as quickly as possible. So we'd like to thank the presenters and participants for such an informative session. If you have additional questions, go ahead and contact us at our exhibit booth or via e-mail, and you can always find contact information in the help section of our grants.NIH.gov site. Your feedback is always so very important, so please take a moment to let us know how we did and what you thought by clicking on the session feedback button located within the description and presenters on the auditorium list of sessions. So thank you again to everyone, and have a great day.