TRANSCRIPT
Module 2: Regulations in Clinical Trials

- Hello, and welcome to module two where we are going to be having a close look at the regulations in clinical trials in Australia. Our outline for module 2 covers an introduction to both the ethical framework and also the governance framework that looks after clinical trials in Australia and the key documents to ensure safe and successful clinical trials. So this will involve looking at the Therapeutic Goods Administration, also known as the TGA, the Human Research Ethics Committee, also known as the HREC, and the governance assessment, and we'll look at how they work side by side to complement each other through the process. And to do this, we're also going to look at something called the National Statement, and that is the full name is the National Statement on Ethical Conduct in Human Research in Australia. And we'll look a little bit more closely at how that document helps underpin all of the processes together. At the end of this module, we're gonna have two terrific video discussions. In the first we're going to be talking to a former chair of a Human Research Ethics Committee about the ethics and governance processes in place. And in the second video discussion, we're going to talk to a research manager about the ethics process and the importance of having a lay member of the community on an ethics committee and the value that they bring by representing consumers of research in the community. So first up, we are going to take a closer look at regulations in clinical trials, the basics of ethics and governance processes. So the first thing we're going to look at when we cover these processes is the Therapeutic Goods Administration, also known as the TGA. Now, I think in recent years, particularly through COVID, everybody's heard the term the TGA when discussing new drugs or vaccines being approved. And we heard that very commonly through COVID. But the TGA is Australia's government authority which is responsible for evaluating, assessing, and monitoring products that are defined as therapeutic goods. And most often we think of these as drugs and medicines, and that's one part of it, but things like devices such as pacemakers are another part. And all up, the TGA tries to ensure that Australians stay healthy and safe. And you might have heard overseas the FDA in America, which is the Food and Drug Administration, or the EMA in Europe, which is the European Medicines Agency. So the TGA is our Australian equivalent of those organisations. So clinical trials conducted in Australia are subject to various regulatory controls to ensure the safety of participants. And we regulate the use of therapeutic goods supplied in clinical trials in Australia under something called the Therapeutic Goods Legislation. So this ensures that all clinical trials in Australia involving medicines and biologicals are regulated under this. And paperwork needs to be filed with the TGA so that they're aware of the clinical trial and the use of the unapproved drug in Australia within that clinical trial. And there's something called the Australian Clinical Trials Handbook, which we'll have as well in the end listed under resources and references, and that document and handbook provides guidance to assist clinical trial sponsors, Human Research Ethics Committees, investigators, and institutions to understand their roles and their responsibilities under the TGA legislation. So you can read a little bit more about that in more detail if you like at the end. So the next assessment we're going to talk about is the Human Research Ethics Committee, or the HREC assessment. So this process looks at any type of research, so clinical trials is part of that, but all research that is looking to be performed in Australia must be approved by Human Research Ethics Committee before any participant has any trial related procedures performed. And it looks not just at the ethics of a situation or a trial or a process, but also at the scientific

methodology to ensure that that is sound and it has merit, because we don't want to be putting participants through research that is not any of those two things. So the composition of a HREC is regulated, and it must have a minimum of eight committee members. And the membership must include a chairperson, it must include two laypeople with no affiliation to the institution, a nurse or allied health professional, a pastoral care representative, a lawyer, and two researchers or scientists with current research experience relevant to the proposals being considered at a meeting. So the types of things that they review in the application has strict guidelines, and there's many different subcategories with questions that need to be adequately answered by the investigators for the proposal to be considered. For example, how many people will be recruited? How will consent be obtained? What the study involves in terms of visits and time commitment. What's being asked of the participants? How confidentiality and privacy will be maintained. And many more subcategories. They look at a review as individuals and also as part of that wider group, so proposals that are being considered are circulated to all members of the committee and then they're presented for a group discussion. And usually there is a lead discussant or two who presents to the group the intricacies of the trial, and potential or actual issues are all discussed. And often this is in great detail. So the final assessment occurs after review of all of the documents that are required by legislation to be submitted for a clinical trial proposal. Then a formal letter is sent back to the investigator advising of the outcome of the review from the Human Research Ethics Committee and any questions that need clarification or further information. So all approved documents are itemised, including the very important participant information sheet and consent form, which we will talk about in later modules in great detail. And as well, it's important to note that multiple sites across different states in Australia may come under one submission. For example, Westmead Hospital may provide approval for other sites in New South Wales from an ethical point of view. However, it's important to note that each site will still need to examine its own governance structure, and we'll talk about this a little more in the next slide. So, and that brings us to the third element in the ethics and governance processes, which is the governance assessment. So this is looking more at the institution to give assurance that the investigators and the institution are able to conduct the trial properly. Like we said, ethical approval can be given to multiple sites, but governance will be assessed individually at every institution. So there will be a local governance officer to ensure that key regulations are followed, and they're things like the local capacity to conduct the trial, that the study site has the capacity to do the work, and it has the resources to do them properly and according to the protocol. They also look at whether the researchers have the necessary expertise. They look at support from other departments to ensure that it's a true collaboration. For example, that everybody knows they're taking part in the study, they're all on deck, and they all understand their role in the process. For example, in an MS clinical trial, that might involve the MRI department being able to take the right pictures and have the necessary time available to do that well. And finally, they'll look at the finances and ensure that they support the work, that they're fair, and they'll also ensure that all of the contracts are properly executed so that everybody's protected. Now we're going to have a closer look at something called the National Statement on Ethical Conduct in Human Research Australia. Now, this document is so important. I've been a former member of a Human Research Ethics Committee, and this National Statement guided everything that we did in that committee, and it formed an important framework so that we knew that we were looking at the right things, in the right order, and that we were protecting the safety of the participants as much as humanly

possible. So it really is a key document in clinical trials. So it was developed jointly by the National Health and Medical Research Council, the Australian Research Council, and Universities Australia. It was launched in 2007 and updated in 2018. A new update is currently underway, and it should be adopted from the beginning of 2024, so watch this space. Now, the purpose of the National Statement is to promote ethically good human research. It's the Australian ethical standard against which all research involving humans, including clinical trials, are reviewed. So it sets up the ethical issues specific to clinical trials in Australia, including important aspects such as the use of a placebo in research, looking at payments to participants, attention to specific patient groups who are prone to vulnerability. Now, by this, I just don't mean those with cognitive issues or children or from a minority group, but those that may be pregnant and those people that are in potentially unequal relationships with investigators. And that includes patients who are under the care of the investigator for their normal disease management. So the National Statement assists any researcher conducting research with human participants to help them follow the Australian guidelines. It assists the members of the Human Research Ethics Committees when they're reviewing research. And it also helps assist potential participants to understand a lot of the terminology and what they should expect in a clinical trial. So it's essentially the framework and guidance for the Human Research Ethics Committee, and usually the meetings I've been involved in, it really does sit right in the centre of the meeting. And as I mentioned before, it guides everything that's done. And very importantly, there's gonna be a link to the National Statement provided at the end of this module, so if you wanna delve into that a little bit more deeply, you can do so. Next up, we're going to have a discussion with the Human Research Ethics Committee executive officer and research manager on the importance of including consumers in the ethics process and the value that they bring to the committee to ensure that clinical trials stay focused on the individual and that important aspects of the National Statement are considered. And this includes protecting clinical trial participants. Hi, and welcome again to module 2, where today we're going to be speaking about the ethics processes in Australia, and particularly the Human Research Ethics Committee. And we're going to be be touching on some of the processes that underpin all of that in Australia and the types of things that keep us at a very high standard in terms of clinical research. So today I have a very special guest. I have Associate Professor Helen Mitchell. So welcome, Helen. Helen is from the University of Sydney, and specifically in the School of the Sydney Conservatorium of Music, which is very interesting. Helen also lives with multiple sclerosis and has done for a long time now. And she's a singer, a music scholar, a music performance researcher, and also the chair of the Human Research Ethics Committee at the University of Sydney. So welcome, Helen.

- Thanks, Therese.

- Before we get started on talking about some of the processes, as a music professor, how did you get involved with the Human Research Ethics Committee?

- Gosh, it's been a while, well over 10 years, Therese, and I, at the time I was at the Conservatorium, my boss put me forward. They were looking for a new member of the committee from The Con. And I was the person that they recommended. So I turned up to see what it was all about.

- And how has that been for you? Have you enjoyed it?

- It's been one of the most fascinating jobs I do at Sydney University, and it's been such a pleasure to see so many research projects from every different discipline from all levels, from honours students through to the professors, to see all sorts of different things happen at the University in all different areas. I worked my way through. I'm so delighted to have been part of so many different committees, and I now chair one of the committees at Sydney University. So I get to meet a lot of the researchers and find out more about their research as we go through that process.

- Wow, that's just incredible. I just find that whole story incredible. But let's get back to basics now. So Helen, if you wouldn't mind, I know this is a huge question, but just so that we're all at the same starting point, what is human research?

- That's a great question, Therese. What is human research? So human research is conducted with or about humans, so that might be humans as in a person, it might be with their data, and it might be their tissue. So we can work with humans in a number of different ways. It might be something like taking part in surveys, taking part in interviews, thinking about undergoing some kind of medical testing treatment, being observed by the researchers, or giving researchers access to our data or our documents or other materials. So it can be a variety of things all about human interactions.

- Yeah, and I guess we're focusing on clinical trials in these modules, but clinical trials almost come under that huge umbrella of human research, don't they? They're just one tool that we can use to answer the questions. Okay, now, I'm also thinking that most people in our community probably would not be aware of what a Human Research Ethics Committee actually is, so can you give us some background information on that?

- Perfect. Research ethics committees are a big operation. So my research ethics committee, there are about 15 people. We have researchers from across the University. We have members of the community, we have laypeople as part of our team, we have a lawyer, we have someone who's involved in pastoral care. And together we sit and think about research projects that come in. We evaluate alongside the National Statement. So that gives us our tips. It's not a rule book, but rather it gives us values and principles that help us evaluate each proposal as it comes through to us.

- So Helen, now that we know that we've got this amazing group together from all different backgrounds, what happens practically at a Human Research Ethics Committee?

- So everyone's had a chance to read through the application, all those extra documents, the ones you might read, those information statements and consent forms. And we think through what we're reading and all the kind of questions that we might ask of the researchers. We're guided by the values and principles of the National Statement, so we've got four things to think through as we work our way through the document. First of all, we're thinking about the research merit and integrity of the project, and we're thinking very much that the project is justifiable by its potential benefit to the community. We're thinking about things like justice to make sure that the process of recruitment is fair and reasonable

and it's not overburdening potential participants. We're also thinking about beneficence, whether the benefit of the project outweighs any risk. And we're also thinking about respect and whether or not the project respects the human beings taking part and giving their time to take part in the project.

- Wow, I mean, and it's so great to know that the National Statement gives that guidance to underpin all of this, because that must make it not easier for you as the Human Research Ethics Committee, but it gives you the tools that you need, doesn't it, to be able to perform your job well, in addition to all the other things you've gotta look at.

- Absolutely, and it's not a rule book. We're not trying to assess it according to a set of rules, but rather we're trying to understand the project and see the merit and try to understand what the researchers want to do.

- And because you're looking at so many different projects, Helen, like you mentioned right at the beginning with human research covering such a huge gamut of potential projects from simple surveys to really complex phase one early clinical trials of a new drug or a new biotechnology project. There must be some robust discussion, I'm imagining, within a Human Research Ethics Committee about some projects.

- Absolutely, and I would expect there to be robust discussion. We really want to tease apart anything, the things we do understand, the things we don't understand, and to make sure that the project itself is robust and can go forward and is ready for participants to take part.

- Yeah, so thank you for sharing all of that. I think that's been really helpful for me and hopefully for our MS community as well, just to understand what goes on behind the scenes so that by the time a clinical trial is ready to be presented to somebody when they're seeing their neurologist or nurse in the MS clinic, that it's been through this incredibly robust and systematic process to ensure that it's as safe as it possibly can be. And we know that for some very early phase studies, there's no guarantee of complete safety, but as much as we can humanly do, with as much expertise as we get together on those committees, to just ensure the safety for the participants, but also for the researchers and for the organisations as well. So you've just brought that together beautifully. Helen, thank you so much for your gift of time today.

- It's a pleasure. Thank you.

- Hi again, and welcome to our video discussion for Module 2. So today we're going to talk about the ethics and governance process which protects clinical trial participants in Australia. We're going to have a little overview of the process and the processes that underpin clinical trial approval and how the ethics and governance works in Australia. But we're going to particularly dig a little bit deeper into the role of what was previously called the layperson. And now Kelly will let us know exactly where that's up to, but I believe it's consumers and individuals in the community. So welcome to Kelly Hanson. Hi, Kelly. She's the manager of the research office at the Western Sydney Local Health District. And Kelly's also the executive officer of the Human Research Ethics Committee for the Western Sydney Local Health District.

- Hi, Therese. Thanks for inviting me to do this today. I've worked in the research office since 2009. I've been in the health system since 1988, so been around a while. Research is a rapidly changing space, and one of the wonderful things about it is every week brings something new that, you know, that you don't know despite the years in the work. And that allows me to spend time with dedicated, passionate, highly intelligent, wonderful people who I can go to and discuss these things so we make sure we do the best for the researchers and for the participants in the research. So it's a very wonderful, exciting space that we work in. And our goal is making sure participants are well protected, understand what they're agreeing to, and benefit greatly from their experience.

- So we've previously touched on in other Modules how the Human Research Ethics Committee is made up of all different groups of people and from different walks of life. But today I wanna dig a little bit deeper about a really important role that sometimes gets overlooked, and that's of laypeople, so people from the community on the Human Research Ethics Committee, which now we refer to as consumers, I believe. But you can fill us in a little bit more on that. So what role do these people play in the process? And what exactly do they do?

- Okay, from my perspective, the consumer rep on the committee is the most important person there. They are the members who ask the questions that are most relevant to the experience of the participant. They consider the vulnerability of the participant and the coercive power in the unequal relationship between the doctor and the patient, especially someone who's been very unwell and will do anything for the doctor who's been so good to them. And they force the committee to have the conversation that ensures that informed consent is what really happens. They are invaluable to the process.

- Right, that's so important. We're going to talk about informed consent a little bit later on in some of the Modules. But almost like they're the devil's advocate, aren't they, in just making sure that that participant is going to be protected.

- Absolutely. You know, I never ceased to be amazed by the courage these people have to sit in a room of highly educated, learned people and ask a really basic question. Say, "Well, yep, hang on a minute. That's fine. It might be all ethical by the rules and regulations, but what about this?" And when they first start, it takes a little bit of courage to do that because they feel a bit uncomfortable. But we have some wonderful consumer representatives who are very courageous in their questioning of, you know, of what's going on in the project. And I just absolutely admire them so much because they're so important. I don't think most of the people who access health services know much about, if anything about, human research ethics and, you know, the importance of the voice that the consumer rep gives to each and every one of them in the research that's conducted. It's just so, so very important. We have one lay member in particular who has not fallen into the trap of becoming too highly educated, as a lot of them do after many years on the committee, and he recently reviewed a very complex, very onerous oncology drug trial. And he made some really wonderful points. You know, he talked about, you know, the schedule of activities and how gruelling that would be on patients who had failed every line of treatment and were at end of life. He, you know, asked questions about, "Okay, they're going to come this frequently. What are you

doing about cab vouchers and meal vouchers and support people and, you know, getting them to and from and looking after them in this time?" And also, he also questioned, you know, "These people are so ill and been cared by this team for such a long time, a lot of them are going to say yes out of gratitude. How's the team going to navigate that to ensure that their best interests are served?" And he also made this wonderful comment. He said, "I wouldn't like to be poked and prodded like this if I was ill, but I can see that if I, you know, had been so ill and I was grateful to these people how I might do something I wouldn't ordinarily do." But he also questioned how they were going to accommodate the fears and concerns of the family who wouldn't understand if their relative's at end of life, has been so, so sick, you know, why are they going to go and do this when they could be spending time with family when they have limited time left? And, you know, his question was, "How do you resolve that?" And that really forced a wonderful conversation in the committee of learned people who, you know, yes, this is ethical, this is normal for this patient group, but oh, how do you resolve that? How do you account for that? And that "how do you resolve that" question from the consumer rep is the most important question in the room.

- And I imagine, as you said, that would take a lot of courage to do that, but at the end of the day that's the most important thing because if we're doing a trial and all of the expense and all of the time commitment, not just from the participants but from the researchers, and then they don't consider these things that will support and underpin the trial to be successful, it will just all fall apart. So in some ways, like you say, they're the most important questions, but I also wonder, Kelly, the people that that's been spoken back to, the experienced researchers, scientists, specialists, how receptive are they to those comments?

- We're very fortunate that the people on our committee have great respect for that, and it creates such a rich conversation and consideration of the project because, you know, everyone's there to look at the project from their expertise. The expertise of the consumer is those questions.

- So Kelly, just to wrap it all up, how does our process of ethics and governance approval ensure both safe and effective clinical trial for potential participants?

- Okay, so at Western Sydney Local Health District, we operate with a three committee process. A lot of other LHDs don't have that. Locally, we feel the level of robust review is very essential, particularly for a drug trial. So every study that comes through our door has scientific review and ethics review from two different committees, but if there's a drug, the study is also presented to our area drug committee. And that committee is made up of pharmacists and researchers who have specialist knowledge in drug effect and interaction, storage, dispensing, TGA regulations, and all that very crucial information about drugs, especially drugs that aren't registered yet. For all the others, they go to the Scientific Advisory Committee, and that is a group of career researchers, doctors, scientists, who look at the study for its scientific validity, and then they make recommendations to the Human Research Ethics Committee, who then consider the study for ethical acceptability. And that gives us a very robust review to ensure that we're making sure we've checked every aspect of the study and that we're going to protect the participant, which is our primary goal. The other side of the review process is the research governance process, and that is risk management for the organisation, essentially. That looks at that the people conducting the

trial have an appointment with the health service, that they have the skills and qualifications to do what they're proposing, and that they have the resources to do that, budget, staff, and all the other things they need because it's unethical to start a project that you can't complete because you haven't prepared properly. The other thing governance looks at is contracts and agreements and insurances and indemnities. So while all these things are very focused on protecting the organisation and the researcher, they're also another layer of protection and insurance for the participant. And that's our main goal, to make sure that we're looking after those people and giving them the best possible outcome.

- Oh, thanks for tying that all up together, Kelly, because I think it can be really confusing and I don't think a lot of people also until now might have realised that the ethical approval for a study also takes into consideration that scientific validity, because as we know, it's not ethical to conduct a study that hasn't had that rigorous look at it. So that process is actually much bigger than what we were previously thinking. And also to know on the flip side that we've got the governance side, which is looking after the participant by making sure that the researchers are all well qualified and they've got everything in place that they need to, to have a successful and safe trial.

- Yeah, absolutely.

- So thank you for tying that all together for us today. It's been wonderful having you here.

- My pleasure. Thank you for having me.

- [Therese] Thank you for completing this Module. A list of Resources and References is also available if you would like to explore these concepts in more detail. I encourage you to please take the quiz to check your level of understanding before moving on to Module 3, where we are going to talk about informed consent and the participant information sheet in greater detail. Thanks for joining us today, and we'll see you next time.