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Proof Committee Hansard

**HOUSE OF
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STANDING COMMITTEE ON LEGAL AND CONSTITUTIONAL
AFFAIRS

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HOUSE OF REPRESENTATIVES
STANDING COMMITTEE ON LEGAL AND CONSTITUTIONAL AFFAIRS
Friday, 11 May 2001

Members: Mr Andrews (*Chair*), Mr Bilson, Ms Julie Bishop, Mr Cadman, Mr Griffin, Mr Kerr, Mr Murphy, Ms Roxon, Mr St Clair and Mrs Danna Vale

Members in attendance: Mr Andrews, Ms Julie Bishop, Mr Cadman, Mr Griffin, Mr Murphy, Ms Roxon and Mr St Clair

Terms of reference for the inquiry:

To review the the report of the Australian Health Ethics Committee of the National Health and Medical Research Council entitled *Scientific, Ethical and Regulatory Considerations Relevant to Cloning of Human Beings* dated 16 December 1998.

WITNESSES

KING, Ms Catriona, Operations Manager, ES Cell International Pte Ltd..... 169

KLUPACS, Mr Robert, General Manager, ES Cell International Pte Ltd..... 169

Committee met at 9.34 a.m.

KING, Ms Catriona, Operations Manager, ES Cell International Pte Ltd

KLUPACS, Mr Robert, General Manager, ES Cell International Pte Ltd

CHAIR—I declare open this public hearing of Legal and Constitutional Affairs Committee inquiry into aspects of human cloning. I welcome all those who are present here today, in particular Robert Klupacs and Catriona King from ES Cell International Pte Ltd. This is probably one of the final public hearings of the committee's inquiry, although the field continues to develop, as we have seen with cloned pigs and developments in the US with material from various individuals finding their way into the genetic make-up of children. It remains a topical issue and no doubt will continue to do so. We are interested today in looking at gaining some insight into the work of privately funded organisations that are undertaking embryonic stem cell research, so we welcome you here today. Although the committee does not require you to give evidence under oath, the hearing today is a legal proceeding of the parliament and warrants the same respect as proceedings of the houses themselves. The giving of false and misleading evidence is a serious matter and may be regarded as a contempt of the parliament. I invite you, if you would like to, to make some opening comments.

Mr Klupacs—Thank you, Mr Chair. We have prepared a paper giving our major corporate position on some issues of cloning. I thought I might just talk through that with you in a somewhat informal way and then I suspect we will take questions after that. If I just work through the paper with you I can summarise it as we talk.

Firstly, I will give you a bit of background about our company. ES Cell International, as you will see, is a Singapore registered company, but it came from work performed by Professor Alan Trounson and colleagues at Monash University, in collaboration with people in Singapore. ESI has two major shareholders: one is the Singapore government—through a venture capital fund—and the other is a group of Australian investors. It is effectively a joint venture between Australia and Singapore. The company is incorporated in Singapore but the management operations are in Melbourne.

As we have outlined in the paper, we are funding quite a deal of research around the world, in Singapore, Australia, Israel and Holland. One of the big issues for us as a corporate organisation is to ensure that that is done according to the correct ethical guidelines and medical research guidelines. Perhaps later on in question time Catriona may take you through some of the work we have done in attempting the NIH approval of our compliance cell lines.

Part of our mission is to try to take the undoubtedly important discovery of embryonic stem cells and turn them into things which can have a major impact in human medicine, either as cell transplantation or in the area of discovering the genes and controlling factors that turn these cells into these things in the body, developing those genes and proteins as therapeutic agents, as you would any other pharmaceutical product. That is our corporate mission and that is what we are doing. I think we, as a company, have been brought into the debate, like a lot of other people in the area, and asked: are we in cloning, as that term is defined? Are we looking to grow embryos to make new cell lines, et cetera? There are a couple of key points I want to make in my opening address.

With regard to reproductive cloning—and this committee probably knows more about it than I do—there is a very clear position in that we are not doing, and do not believe in, reproductive cloning at all. I think that puts us in the same position completely as every other major company and every other major well thought through argument which says reproductive cloning is absolutely abhorrent.

In terms of therapeutic cloning, of which I think there has been quite a lot of debate about the obvious medical implications, and the possibility of using therapeutic cloning as something that can help mankind, yes, there is no doubt that is true. From a commercial and even from a scientific angle, though, you have to think about how hard it is going to be if you want to make a big impact in medicine. Is therapeutic cloning the way it is going to work? Our position as a company is: probably not.

The idea of taking the chairman's cells, for example, and creating an embryo, isolating the embryonic stem cells and then treating them with the technology we have to put back into one individual—notwithstanding the scientific difficulties—from an economic sense is a very difficult way to actually make money. While we think theoretically and potentially in certain disease states it may be very important, from our perspective it is not something we see as having a major impact in our business. While ethically we can see the reasons for it, commercially we see it might be a very difficult thing to actually develop. We are not for or against it, but we just think commonsense needs to prevail. In 20 years time, perhaps it is something we can look at.

As we said also in point 4, under carefully regulated conditions, with very carefully selected disease states as well, it may have a place. Our view as a company is that we would like to take the initial starting material—embryonic stem cells, which we now have—learn how they function, what controls them and use that material downstream as the therapeutic component.

The other point I would like to make in the opening statement is that we see ourselves as becoming universal donor cells. It is the differentiated cells, the new neurones, the new heart cells and the new liver cells that we will be able to grow from the starting material which will be the ultimate product. Linked to that, people have actually written to me and said, 'You people are abhorrent. You create embryos in the laboratory to make stem cells. You're a killer.' The point I would like to make is that obviously the embryonic stem cells came from embryos, from surplus embryos from IVF, originally located in Singapore.

We have now grown six cell lines within our research laboratories. The commercial reality is that it is very unlikely we will ever have to go back to another embryo source again to grow a new line. The lines we have were obtained in compliance with the NIH guidelines. Catriona can talk about that. You may or may not be aware that Monash University, which we are backing, put an application to the NIH to get us approved and that process has been on hold pending legal review of the NIH statutes regarding embryonic work.

Our position is that we do not think we will ever have to go back to derive another embryonic stem cell line. The traditional way pharmaceutical companies work is that you have a master seed bank which is locked away and then everything derives from that. That is pretty much where we are. We have no further work ongoing on the derivation of cell lines and do not intend to in the short to medium and probably long term. All our company's interest is in now focusing

on what controls those cell lines, what are the genes that are expressed by those cell lines, and how we can use that genetic information to take our original starting material, convert that into other material and then transplant it back into animal models to see whether it can cure disease.

That is our whole business focus. If we are successful in that we think we will have two things: yes, we will make money, we hope; and, secondly, we will be curing some very nasty diseases such as multiple sclerosis, Parkinson's disease and stroke. More recently we have been able to grow heart cells in the dish. If you have a major heart attack it is very likely you will die within three to six months after that because your heart muscle is damaged. It is theoretically possible now, from what we have done recently, to potentially regrow a heart cell by transplanting back cells. That is a key area of our research. That is probably all I would like to say as opening remarks. I would like to have my note tabled, if I can. Then I will be very comfortable taking questions.

CHAIR—Thank you very much. Can I just pick up on the point about the embryo position? You understand that is a matter of major contention in this whole area. This inquiry has been going for some time and developments occur, but my recollection was that when Professor Trounson first came to speak to us he said—if I can paraphrase it accurately—that, whilst you had sufficient stem cell lines at that stage, they had not been derived according to the National Institutes of Health protocols and that it would be necessary to derive further cell lines according to the NIH protocols. Do I understand—as I said, this may be a product of the transmission of time—that that has now been done and so that is why you are saying this?

Mr Klupacs—That is right. Exactly.

CHAIR—I will just explore this a bit further. Have the stem cell lines that you use been derived from Singapore and brought to Australia?

Mr Klupacs—Yes, for passaging and culturing.

CHAIR—And it was because of questions about the Victorian law and whether you could do that here or not. Are they used only by those associated with you? Or do other researchers elsewhere have access to them? Are you envisaging they might?

Mr Klupacs—The answer to the question is they are in such small quantities at the moment that the only people who have access to them are our initial collaborators. But we are very clearly on the public record as saying to every group in the world, 'Once we can grow them up we will make them available to you for your research applications.'

Ms ROXON—At a cost.

Mr Klupacs—No, that is free of charge. Obviously any commercial material transfer that we expect is. For instance, if I gave the cells to you in a research laboratory and you made a discovery with the cells, you would come and talk to me about it, but they would be free of charge. Our competitor does sell the cell lines. To be honest, it is a very fine line between being academic and commercial here. If we took the moral high ground and said everyone in the world could have the cells, I think we would find that our competitors might get the advantage of it. If we said everyone had to pay for the cells, everyone would be up in arms about how we

are not treating science correctly. We have walked a middle line. All the academics that come to us can have access to the lines. Their institutions have to accept that if they make a discovery they will talk to us, but there is no guarantee that we can agree terms and they are free to do whatever they like. But, yes, they are free of charge.

CHAIR—Is your competitor the Wisconsin project—

Mr Klupacs—That is right.

CHAIR—Thomson?

Mr Klupacs—That is right.

CHAIR—If, as you say, it is unlikely further embryos would ever be required—I am just hypothetically trying to tease this out—what would be your attitude to some form of regulation? I will put two scenarios to you. What would be your attitude to a regulation that said, on the basis that it is unlikely any would be required, ‘What is there is available and work can continue with that, but we should prohibit any more’? That is the first scenario.

Mr Klupacs—There are two comments there: you can think of a worst case scenario, after all this time, if for example the freezers break down and the cells are gone. So you would hate to think there was a statute that said, ‘Well, you’ve done it, they’re gone. You can never do it again.’ That is the worst case scenario.

The only other reason we could think of for growing new lines is that we are not quite sure of the background of our cells. There may be differences about genetic backgrounds, say if it is Caucasian versus negroid versus Asian. Maybe there is some genetic difference. I am not sure about that. I have heard arguments from a number of people. My reaction, as an individual having had some scientific advice from the people I have spoken to, is that it probably would not be a big deal if you could not make any more lines with what we have. But the other side of the question is that I do not actually know for certain whether there will be differences from genetic people and, if I am trying to create universal donor cells and I am putting all that effort in, the last thing I want to do is to only be able to treat all the people from an Anglo background, for example.

While my tendency would be to think it was not a big issue, because of the unknowns I would be a bit worried about having a statute that said you could not. We do not have any problem with having very stringent regulations about how you go back to creating new embryos. I do not think that is an issue for us at all, but it is just the unknown quantity, that is all.

CHAIR—My second scenario is what you are leading to: to say hypothetically what if there were not an outright prohibition but there were a series of hoops that had to be jumped through before some regulatory authority in order to justify why there was a need to create more embryos for this purpose or use embryos for this purpose. In a sense I think you have answered or you are answering that second scenario.

Mr Klupacs—Yes, I think I just answered it. To be fairly emphatic, from our perspective at ESI we have no problems dealing with government regulations about having to get further

embryos, because that is what we have dealt with in the past and that is what we expect to deal with in the future. I think it is a good thing because it keep all the cowboys out of the game, to be quite honest. I would hate to think of a situation where people are growing embryo factories. That terrifies me. I think if you are going to do it you have to do it properly. We have done it under the law at present. There is a chance, albeit incredibly small, that we could lose them all and we would like to be able to go back again, but our expectation is if we went back again we would do it under the laws at the time. Governments will always regulate. I just hope they are realistic, that is all.

Ms ROXON—It might be helpful for us if you give us your view on what would be realistic because, whilst you say it has not been a difficulty for you and you have worked within the regulations, I would think that a lot of people would have the view that really you went offshore to do what you could not do here and then complied with somebody's regulations but not ours, or complied with ours because you did not do it here and brought it in at a stage when you were going to comply.

Mr Klupacs—Yes, I have heard that.

Ms ROXON—I think it would be useful for us to know what sort of regulation would be workable for you so that, if you were in a position where you wanted to create new stem cell lines, you could do it in Australia and you could be confident about the process, the background of the cells and all those sorts of things that you were saying, where you do not necessarily know about the ones that you produced in Singapore.

Mr Klupacs—There are two points there. I have heard the point expressed to me, 'You went offshore to get them.' The reality was that Alan Trounson could have gone to Sydney or Brisbane or somewhere else in Australia, it is just that he had a collaborative link with a guy in Singapore and that is what he built on. I just wanted to put that on the record.

The other thing I would say about the regulations—and this is from a company perspective—is that I thought the NIH guidelines worked through and complied with were very well thought through and very cognisant of people's rights. I think we would be quite comfortable having exactly the same set of guidelines here. The third thing we would be quite happy with would be to have some type of registration system. In particular, I think that is what we as a corporate organisation would look at to say that, if you wanted to get funded, let's say by the NHMRC, to work on embryonic stem cells—and that is a policy decision—the only way you could do that would be if you had a registered line and then maybe an ITA or a genetic manipulation authority committee that would govern who had access to that.

I have no problem with that and I like the fact that there is an independent body that would look at those applications, like we did with the NIH. Firstly, it gives me confidence as an individual that I have done it the right way as a company and, secondly, it gives me a corporate comfort that potential investors think we are not cowboys and doing something ethically immoral. It can point to the fact that, yes, we have done it against published guidelines and, yes, there is another body that has looked over our application and given us a tick in the box.

Frankly, from a commercial perspective, that makes a lot of sense. If we are going to do that in Australia I think it behoves us to do something like that. As I said, I think it is unlikely that

we would ever go back and isolate new lines, but there are other people who want to do it. I think if they want to do it, they have to do exactly what we have done and be open to public scrutiny. That is all I would say.

Ms ROXON—I want to ask a question which is sort of related. You said in passing that you were incorporated in Singapore. Why is that?

Mr Klupacs—I think that was one of the commercialisation requirements. We needed to get money very quickly. We went around Australia looking for investment in this from various venture capitalists and, irrespective of the ethics and the area that we are in, they all said, 'It's way too early to get an investment.' A group in Singapore said, 'We think it's fantastic technology. Can we invest? Our only requirement is we can only invest in Singapore companies.' So from a pragmatic view that is what they did. Fortunately for me we were able to bring on an Australian group who were able to, if you like, balance out the Singapore investment. That is the only reason. It was because the venture capital community at the time in this country did not want to invest in it.

Mr MURPHY—Mr Klupacs, I notice in your opening submission—and picking up on what Ms Roxon just said about funding—that you have Singaporean and Australian investors. Can you give us any details of the origins of those investors, what their line of business is and their motivation for getting involved in this?

Mr Klupacs—Yes, I can tell you about both. The Singaporean government have an economic development board and underneath the economic development board they have venture capital groups, one in particular for life science. One of those groups, Life Science Investments, is the group that has invested in our company. That is public. It is also public that the group invested from Australia is a group called ESL Australia. Back then, ESL Australia had seven high net worth individuals and we have publicly disclosed two of those people: they are Carl Strachan and Mr Peter Williams. They have told me what their motivation was and I will pass that on. It may be different.

We have the Monash Institute of Reproduction and Development. Carl is a good friend of Alan Trounson. He sat on the advisory board for approximately 10 years. He had heard about this technology for a long time and when we were having problems getting money he thought he would put some money in and got a group of mates together. So there are seven high net worth individuals. Obviously they hope to make money, but if you ask him directly I think he had two reasons—because we had a major dinner when we announced this. The philanthropic benefit here that one day they may be able to cure mankind of some very debilitating diseases—and some of the people in the group's parents have suffered from those—I think was a major driving force. The second driving force, because of the friendship of Carl and Alan Trounson in particular, was that here was one of the great discoveries of the world with a great benefit that could potentially die because of lack of funding. Carl put his hand in his own pocket and convinced some of his friends to become involved as well. Carl and Peter are publicly disclosed. I would be uncomfortable in telling you who the other five are without their consent. ESL Australia is a publicly registered company. I think the directors may even be published. If they are then they are publicly available. I have not checked that out so I would not be able to tell you, Mr Murphy.

Mr MURPHY—Do those investors have any expectation that in their lifetime the research that your company is doing might contribute to a cure for Parkinson’s disease, multiple sclerosis or even heart disease, as you have mentioned in your submission?

Mr Klupacs—Yes, they are all very hopeful. They are not young men any more—they are 55 or 60—so I think they are hoping that we will. To be honest, Carl is 65.

Ms King—It depends how close you get to it.

Mr Klupacs—Carl said to me, ‘Buddy, you’ll cure my Alzheimer’s when I get it,’ and I said, ‘I hope so, mate.’

Mr MURPHY—If you can cure ‘old-timer’s disease’ that would be a good thing.

Mr Klupacs—Yes, exactly.

Mr CADMAN—If what you did in Singapore is illegal in Victoria, isn’t it just a matter of somebody turning their back when you bring the product home? If I were to commit a crime in another country which was a crime in any state of Australia, what would be the legal position when I returned and the crime was known here? Say, for example, I escape the authorities in Singapore for drug running and that is known by the authorities here. I will put it in stark terms because I think there is an issue in that you say you could have gone to Sydney. You could not have gone to Sydney because the technology was not available in Sydney.

Mr Klupacs—No, that is not quite right.

Mr CADMAN—Why didn’t you go to Sydney?

Mr Klupacs—It is like everything: scientific collaborations occur for a number of reasons.

Mr CADMAN—Where were stem cells available in Sydney at that time?

Mr Klupacs—No, it was not the stem cells. The issue here was embryo sources. I will ask Catriona because she is the expert in this area. We are not lawyers so we cannot comment on the legalities of it. The bottom line was to obtain embryonic stem cells you needed to have access to embryos. The rules in Victoria were different from the rules in Sydney or Brisbane in that, if you wanted to get embryos for embryonic stem cells, you could have gone to Sydney or Brisbane. At the time we went to Singapore. That is a fact. The reason we went to Singapore was that Alan Trounson had just finished a sabbatical with an embryologist up there, had a close personal link and did reciprocal work in Singapore.

Mr CADMAN—Was raising finance part of that process as well?

Mr Klupacs—No. That was 1995; we did not incorporate this company until July 2000.

Mr CADMAN—It is very interesting. I would like to understand from you who the owners of the technology are.

Mr Klupacs—The owners of the technology are three universities: Monash University, the National University of Singapore and Hadasit Medical Organisation in Israel.

Mr CADMAN—In equal shares?

Mr Klupacs—Yes.

Mr CADMAN—Any patent rights or benefits from findings are equally shared?

Mr Klupacs—That is right.

Mr CADMAN—So the financial inducement that you have talked about is a shared result. I wanted to make that clear because I did not understand how the patents applied. The patents are to the university. Is that to the individual or to the institution?

Mr Klupacs—The way the patent law works is that the owner of the patent in the Australian tertiary sector in most cases is the university—other than Melbourne University now—but the inventors are the individuals who work within the university. If I am a Monash University employee, under common law if I make an invention my employer owns the title to the invention. That is the way it works. Monash University has a policy guideline so that, when inventors make inventions which Monash University then licences or transfers and gets money for, that money flows back in various formulas to their department, to the individual and to the university as a whole. That is pretty similar across most Australian universities.

Mr CADMAN—There is no direct benefit to the individual—or is there some direct benefit?

Mr Klupacs—There is. Ultimately, if this makes money and the university makes money, the university will allocate some money to the inventors, to the actual individuals who created it.

Mr CADMAN—On page 2 you talk about the need for possible access to IVF excess embryos, but in your opening statement you felt you would never have to go back. I read that as you almost saying, ‘We would like to have access.’

Mr Klupacs—I am not sure that that is what we wrote.

Ms King—No, what we meant was that that is how they have been derived.

Mr CADMAN—That is a description, but you say, ‘Our aim is to produce.’

Mr Klupacs—No, we say that our ‘aim is to produce stem cells which can be used as universal donors’. What we are saying there is that you start with an embryonic stem cell. Our goal as a company is to create a neuronal stem cell, from that a cardiac stem cell, a liver cell and so on. That is the universal donor, not the human embryonic stem cell per se. We want to learn how to turn that into a cell lineage—that is, the universal donor.

Mr CADMAN—I understand that. That is descriptive of what has occurred rather than an explanation of what you are actually doing.

Ms King—That is right. We are trying to differentiate the issue of using therapeutic cloning in a clinical modality. That would mean, for example, that if you needed treatment we would take perhaps a skin cell from you and then have an egg donated by somebody, transfer the genetic material from your skin cell to create an embryo and then use the stem cells from that specific embryo to create a therapeutic cell line. It is a patient-by-patient process. We are saying that we do not believe that is what we want to do. We do not believe it is necessary and so we have created this bank of stem cells from 12 anonymously donated embryos, which hopefully we can then use to treat anybody who needs treatment for a variety of diseases.

Mr CADMAN—You said earlier there were six lines.

Ms King—Yes.

Mr CADMAN—Wouldn't 12 embryos produce 12 lines?

Ms King—It would not. It is not an easy technology. It does not always work for every embryo.

Mr Klupacs—If you look at the people in Wisconsin, I think they refer to 40 or 50 embryos produced in one line. Our original line was probably about 20.

Ms King—They certainly got better at it. The first two cell lines probably needed about eight embryos and then the next four cell lines were pretty much from about four embryos.

Mr CADMAN—Where does 12 come in then? I do not understand that.

Ms King—From one embryo, a blastocyst—have you seen pictures?

Mr CADMAN—Yes, we have our heads around that.

Ms King—You have probably seen it ad infinitum. They put the embryo through a special process whereby they remove the outer ring of cells—which are the cells, if the embryo were implanted, that would form the placenta—then what is called the inner cell mass in the middle, the stem cells themselves. It is a fairly difficult technical procedure and that is one of the main reasons why Alan wanted the group in Singapore to do it—because they have an excellent embryology laboratory.

Mr CADMAN—Could it not have been done in Australia?

Ms King—There are good embryology laboratories as well, but they have not developed the expertise. They have not been asked to. There is no reason why they could not, but they are not doing that. They are not able to isolate the stem cells every time.

Mr CADMAN—I think you said something about 20, and Wisconsin was 50 or something. Could you explain the relationship between 12 embryos and six lines?

Ms King—The number is 12 embryos. They needed 12 embryos—

Mr CADMAN—To get six lines.

Ms King—Correct.

Mr CADMAN—Thank you. That is all I needed to know.

Mr GRIFFIN—The first eight did two and the next four did four?

Ms King—That is right.

Mr CADMAN—That is clear.

Mr Klupacs—Our process became more efficient as we learnt how to do it.

Mr St CLAIR—If there were regulations to stop collecting embryos in the future, what role would that have in a natural evolution, if you like, of staying with what you had 20 years ago, for example, and not being able to collect anything that has happened since through embryos? Is there any relationship there?

Mr Klupacs—That is a good question. I have not thought about that.

Ms King—What is the issue?

Mr St CLAIR—The issue is that you are using an embryo of two years ago, for example.

Mr CADMAN—Do genes get added?

Mr St CLAIR—There is a regulation brought in and 20 years down the track you still have all your lines, which is fine, but it may have all moved on.

Mr Klupacs—In terms of genetic evolution?

Mr St CLAIR—Yes. Is it an issue?

Mr Klupacs—I do not think so. In 20 years, I do not think it will be. For example, in the pharmaceutical industry, monoclonal antibodies is probably a good analysis. They came out in the seventies. Some of the original hybridonal lines, if people are aware of them, are still being used today. That is 20 years down the track, from mice that are now 30 or 40 years old. Three thousand years into the future perhaps it might be an issue because you could see some genetic evolution, as in the carcinogens and all the other stuff. We mutate to evolve. But over 20, 50 or 100 years, I think that is very unlikely.

Ms King—I think the answer is that we do not know.

Mr St CLAIR—That is all right. Neither do I, but I thought I would ask.

Mr Klupacs—It is a very good question. I have not even thought about it.

Ms JULIE BISHOP—I want to understand a little more about the arrangement between ESI and the universities. What sort of legal relationship is there between the private company, ESI, and Monash, the University of Singapore and Hadasit? There are also universities in the Netherlands?

Mr Klupacs—Yes.

Ms JULIE BISHOP—What sort of relationship is it? Is it a memorandum of understanding between them?

Mr Klupacs—It is a contract research agreement. Obviously its original owners are licensees of the technology. The universities have a benefit there from the company. As any company does, we have let contract research agreements to research laboratories, three of which include the original founders plus the Netherlands, plus there are two other research contracts that we are putting in place now.

Ms JULIE BISHOP—What has the Netherlands university got to do with it?

Mr Klupacs—As a company we are trying to find the best technology and the best groups in the world to develop our technology. I spoke before about cardiac cells. The group in the Netherlands are world leaders in taking mouse embryonic stem cells and turning them into mouse cardioscience. We are attempting to do that with humans now.

Mr CADMAN—You used the word ‘we’ there. You did not make it clear that it was being done outside of Australia.

Mr Klupacs—We the company.

Mr CADMAN—We understand now, thank you.

Mr Klupacs—We are incorporated in Singapore and managed from Melbourne, but we are very global and we are trying to bring as many research groups into bed to accelerate our research and our activities. The Netherlands is one of those.

Ms JULIE BISHOP—What would be in it for the Netherlands group?

Mr Klupacs—We pay them, so we get to fund their positions. Obviously scientists would love to make some money, but by and large scientists like to get very large publications in very prestigious journals. If you can get access to human embryonic stem cells and do this really incredible stuff, like create human hearts, what is in it for them is that we fund the research they would otherwise not have funded, and the likelihood is they will get some very large publications they would not have otherwise got which will increase their profile in the scientific community. That is obviously a major part. The subpart for them is that if they are successful we will be paid in success fees and royalties for any products that we make and in any profits we generate.

Ms JULIE BISHOP—What about the government regulation in, say, the Netherlands? Is there an issue at all? Does the government have any interest in this?

Ms King—They are just debating the bill in their parliament at the moment, which will be a similar bill, I think, to the UK one. It is just going through now. There is nothing at the moment.

Ms JULIE BISHOP—Is there any direct relationship between ESI and the individual researchers?

Mr Klupacs—Some of the founders have options and shares in the company directly. Any new scientist that gets brought on may, as part of the package, get options in the company as well in a traditional sort of buyer to company sense. So, yes, there is, but not all the scientists that we fund will get those and not all the universities that we fund will get those either.

Mr CADMAN—Thank you very much for that. You said something about creating a human heart. I do not think you really meant that, did you? Are you talking about the creation of material? Human hearts comprise, as I understand it, a number of different types of material and you would need to go into reproductive cloning to do that.

Mr Klupacs—No, actually the human heart, when you think of organs—and if you think bioengineering of organs is going to be the way of the future—in some respects may be the easiest thing to start with because it is made up of two things: tubes and muscles. A pancreas, for example, has a whole number of other things. It has to be able to secrete things in a biological sense. The heart, by and large, is just a pump.

Mr CADMAN—Yes, but you are talking about creating heart tissue, I think, are you not?

Mr Klupacs—Yes, what we are trying to do—

Mr CADMAN—Rather than a human heart?

Mr Klupacs—Heart muscle cells.

Mr CADMAN—I needed to clarify that. The other thing is that when you receive funding from, say, the National Health and Medical Research Council—

Mr Klupacs—We do not, the universities do.

Mr CADMAN—Okay, the university does and it applies this research. Does the National Health and Medical Research Council become a shareholder in the product or the thing?

Mr Klupacs—No.

Mr CADMAN—So we are funding nationally private research?

Mr Klupacs—I think if you look at the NHMRC guidelines and the NHMRC's published policies on how they provide funds, they have very clearly told NHMRC recipients, 'While it is

important that we are funding you because your peers have said you are the best’—and they are on record, this is their policy—‘we do not want you just to do science for science’s sake. Where appropriate, and if at all possible, we would like you to commercialise your results.’ The NHMRC is the ultimate seed capitalist, as is the ARC in the Australian community for technology. So what happens is that all the universities receive grants as one way to keep the research going. They sometimes get topped up by companies and they make inventions with those. The current policy in Australia and Singapore is that, if you make money with government grants, the government is quite happy to vest that title in the university and commercialise it. That is the government policy.

I know there is another committee looking at those other issues. In other countries of the world they say, ‘If we give you a government grant we will keep some equity in that if you make an invention.’ That happens in the United States, for example. But the current situation in Australia is that the government has said, ‘We will give you grants. We expect you to raise some other infrastructure requirements. We sincerely hope that you don’t just do science for science’s sake. We do hope that this turns into product so we can generate some economic wealth for the country.’

Mr CADMAN—I would not expect you to necessarily agree with the approach in the United States where the government holds some sort of a share, but it is an interesting concept.

Mr Klupacs—With other hats on, I think it is a very interesting situation.

Mr CADMAN—Yes.

Mr Klupacs—I guess you could debate it for a long time. The question is whether government really wants to get involved and mandate how commercial and entrepreneurial it becomes. That is another debate. The reality is: could a lot of the work that has been done in Australia over the last 10 or 20 years, some of which has been commercialised and some of which has not, have occurred? The answer is probably not, without government assistance.

Ms JULIE BISHOP—Does it not come down to where the wealth is going to be generated?

Mr Klupacs—Yes, in some cases. This is another debate, but Australia has a fairly poor record of underpinning some exciting research and then having it all go offshore. The great advantage of saying, ‘Yes, this company is incorporated in Australia,’ is the people it has employed—Catriona and myself are Australian so we pay taxes here. Also, Australian investors have a chance to keep the technology in Australia and Monash University, as a shareholder, keeps that back in.

I think it comes back to commercial expertise. I personally would love to see Australians own more of their technology, but you have to accept where you are in the value adding curve. If you want to develop a drug and you do not have the infrastructure in this country, you have to go offshore to get it done. As long as you can negotiate a significant equity return in it, that is probably okay. I am always worried when people make a discovery, try to raise money in this country, cannot do it, sell out to someone in the United States or Europe and there is no equity kept in Australia. That always concerns me. But that is the capitalist world. You just have to accept it.

CHAIR—Are you satisfied that the immortality of the cells is going to continue to maintain this multipotency?

Mr Klupacs—My insurance policies would be very interesting. So far they have been passaged. They have been continuously passaged to remain immortal. They have only been growing for a year and a half, I think, so you cannot definitively say these things are immortal; but to date there has been no deterioration. They have been passaged nearly a hundred times now.

Ms King—The experience in mouse embryonic stem cells shows that they are certainly immortal. They have been going for 20 years.

CHAIR—Some of the other submissions have suggested that new therapies will be available in five or six years. What does your crystal ball say?

Mr Klupacs—Five or six years? Our business plan says we will be in clinical trials with a new therapy by the middle of 2004. That is somewhat ambitious. If we are not in clinical trials in five years we will be out of business. Our view would be that 2004-2005 is when we will be in clinical trials.

CHAIR—Are you doing any work on adult stem cells?

Mr Klupacs—Yes, we are.

CHAIR—Can you outline that for us?

Mr Klupacs—What has been shown now, as from where we were 12 months ago, is that adult stem cells seem to have the capacity to be able to differentiate from the other cell types, but it is still not that common—and quite difficult. With adult stem cells, no-one has been able to show yet that they are immortal. But we are aware that because these things are available we need to be in that game as well, because we are a stem cell company, not just an embryonic stem cell company. We are a stem cell company. We have small research collaborations ongoing at Monash University looking at adult stem cells and we are about to sign up with a company two larger deals with people in that area. I think there is an overlap of the underlying technology anyway which we would like to get access to. Embryonic stem cells, adult stem cells—who knows? In 10 years time you might get one cell image from an embryonic stem cell and be able to take an adult stem cell for something else—and we do not know what that is, so we have a fairly large and diverse discovery budget which includes both.

Ms ROXON—You talk about your aim being focused on the development of the universal donor cells or lines. We have heard evidence about the different types of methods, and I might be confusing two things here, so please do not hesitate to tell me if I have them all mixed up. One of the processes we have been hearing a lot about is the development of cells to a particular level and then the need to put those cells, rather than straight into a patient if you like—as I think you describe here—through another embryo in some way. My understanding is that there are two different ways you might do it. Am I right in saying that if you are successful in creating these universal donor cells you would not use extra embryos at some other stage; you

would actually be hoping to produce nerve cells which are going to be compatible to put into any type of—

Mr Klupacs—Absolutely.

Ms ROXON—So the only point at which the embryos become an issue is at the original establishment of the line.

Mr Klupacs—Exactly.

Ms ROXON—So it does not use this other process?

Mr Klupacs—From an absolutely commercial perspective, I hope I never have to go anywhere near another embryo again. I have got them down. It is a very expensive, time consuming and risky process.

Ms ROXON—I just wanted to be sure that I understood that properly. Thank you for that.

Ms King—Just to elaborate a little bit, the issue—which I am sure you understand—is that people talk about the need for therapeutic cloning because of potential rejection by the body of foreign cells that have come from somebody else. We believe we have other ways of dealing with that, apart from therapeutic cloning. There are a number of strategies that our research is working on to avoid that.

Ms ROXON—That potentially confuses a little bit more, only because the use we have all been making of therapeutic and reproductive cloning blurs it. If you can explain that to me in another way, that may be clearer for everyone. Perhaps you can describe it without saying ‘therapeutic cloning’.

Mr GRIFFIN—Do you think you can create a generic stem cell which basically splits them all across—

Ms King—Correct, yes.

CHAIR—That will not pose rejection problems for individuals?

Ms King—That will not be rejected. Yes, that is right.

Mr Klupacs—And if it does, we would like to get anti-rejection drugs or approaches that will be given alongside that.

Mr GRIFFIN—So you are looking at it like the analogy of a blood bank with different blood types which are—as long as I am a A-plus or an O—

Ms King—Hopefully it will not even be that compartmentalised. Hopefully our stem cell lines can be used for anybody.

Ms ROXON—You will just have a bank of nerve cells and a bank of some other type of cells?

Ms King—That is right.

Mr GRIFFIN—Using the blood bank analogy, when you have an A-negative or a B-positive or whatever, essentially you will be producing a blood, in effect, that can be used for anybody regardless of their blood type.

Ms King—That is right.

Mr Klupacs—Universal blood. Yes, that is right.

CHAIR—The other problem, as I understand, is if you are using the individual embryos, as the deputy director of the Roslin Institute—which is not doing human work but doing animal work—said to me, there simply would not be enough embryos available to be able to go down that track. There is a practical limitation to it.

Ms King—It is very inefficient. It is a technically difficult procedure. For example, if we were needing to treat you, it would take some time. We would need to find an egg donated from somebody, create the embryo, and then grow the cells and multiply them in the laboratory for several weeks to get enough cells. The whole process has technical problems along the way, so it would not be a feasible way of operating.

Mr Klupacs—They do it with haemopoietic stem cell treatment associated with cancer, but the advantage is they can take the blood, isolate the cells and put them back. It is still not widely used because it is so labour intensive. When you have to multiply that 10 times in the therapeutic cloning sense, I do not think it is ever going to come off.

CHAIR—I have a question about safety. How do you know that the stem cells that you have derived do not carry genetic or metabolic disorders themselves? Is there some procedure?

Ms King—They are karyotyped. We use karyotyping chromosome analysis in the laboratory before they start a line.

CHAIR—I take it you are reasonably confident that that is efficient.

Ms King—Yes.

CHAIR—What is the current status of indemnity for scientists working with the company?

Mr Klupacs—The company, as part of its contract research, has indemnified all the universities in a traditional sense for things that may go wrong. If we go downstream and make a product out of this based on their work, and they have done it with all care and responsibility and it goes wrong—as it does occasionally go wrong—the company has indemnified all our research partners. Obviously if someone has fraudulently played with the cells and we do not

know about it, and that is the reason it goes wrong, indemnities will not hold there. But we have indemnified those people.

CHAIR—The company is not insured with HIH?

Mr Klupacs—No. HIH was a major sponsor of the institute and put up the money for my original salary at the institute, so it was given in a very convoluted way.

CHAIR—Presumably the intellectual property opportunities are in the applications.

Mr Klupacs—Yes.

CHAIR—What you said before essentially in answer to Julie is—

Mr Klupacs—Yes, our intellectual property policy is to protect the discoveries. We would like to know the genes and proteins that cause an embryonic stem cell to turn into a nerve cell.

CHAIR—The trigger?

Mr Klupacs—The trigger points would be major IP.

CHAIR—In differentiation and—

Mr Klupacs—De-differentiation. Then the other side of the equation would be the delivery systems. Theoretically you should be able to inject the cells back, but I think that could be quite difficult. For example, in learning how to put cells back into someone's brain, I think there is a whole slew of intellectual developments that need to occur to do it properly. We are not funding anyone there at this point but we will have to downstream.

CHAIR—Is it fair to say that that is why you are basically prepared to give the cells away? I am trying to look ahead to the big picture. Obviously you are a commercial company. The potential commercial advantage you see is in the techniques of things like differentiation that will render a financial return.

Mr Klupacs—Yes. We are not arrogant enough to think that we will ever know it all. A lot of discoveries need to be made by the scientific community, some of which we might get access to, some we will not. But we have taken the view internally that this needs to move very quickly, because ultimately it is about improving mankind, and we need to give it to as many people as possible. There are some smart people out there and serendipity will play a major role. If we sit on it and try to control it internally, all we are going to do is, firstly, piss off the scientific community and, secondly, not advance science. That is of no value to us.

CHAIR—Does that also have an advantage in that if you are not doing that then others may well be tying it up in a way that means some of the necessary inventions are tightly commercially owned by certain major pharmaceutical companies and the like?

Mr Klupacs—Yes. One of our major competitors is the Roslin Institute, for example. They have patents and they are working. The whole game in intellectual property development is to get as much as you can early to trade off with the other pieces you do not have. But if you have no tools to trade with you may as well give it up. The pharmaceutical area, as you know, is the most highly patented area in the world for exactly that reason. People like to get the monopoly to justify their investment, but more importantly it is to trade off intellectual property pieces of enabling technology so they can grow. If we do not move quickly and get access to intellectual property, particularly the regulation side, the gene side, our company will not survive, or we will be taken over, or someone else will just put us out of business. My investors do not want that to happen.

CHAIR—In terms of the future, where do you see the commercial advantage coming from?

Mr Klupacs—For us—and our business plan says this—if we can own the intellectual property over the genes that can turn an embryonic stem cell, or even an adult stem cell, from that phenotype into something else, and I can licence that perhaps non-exclusively to everyone in the world, that is fantastic. Maybe I keep it for myself and then I have got a monopoly that I could say is worth X amount in value. That is the real driver for me. Obviously downstream, once I get to that point, drug development and therapeutic development is relatively routine but expensive and risky. But if you own the intellectual property at least you trade that and that will have a value.

CHAIR—In that regard there is probably no one major competitor; it is depending on what sort of collaborative efforts you can undertake with a whole range of scientists. Hopefully the discovery will come from someone within your stable, if I can use a racing analogy, rather than the Wisconsin stable or the Roslin stable.

Mr Klupacs—Yes, that is right. Ultimately in this game you place a lot of bets and you hope your bets come home. I have been involved, in other lives, in situations where we have done that. We funded probably 20 groups and it was the 21st that made the discovery. That is the risk you run. We think in this area there are some very good scientific groups. We cannot fund them all, we cannot collaborate with them all but we hope the people we have backed will help our company grow.

Ms ROXON—In answer to one of the questions from Kevin, you said there were a lot of smart people out there and, hopefully, somewhere or other the answers will come up. Going back to this universal donor concept, I understand why that would be your aim; what I do not understand is what sort of tools you are using or why it is that you have such confidence that you would be able to achieve that when it seems to be one of the things all of the other scientists have for a very long time been working on as well. Can you tell me why you have the confidence that that will be achievable in this particular time frame, or what sorts of tools are being used. What are the indicators that that is likely to happen? It does seem to make quite a difference to the way we might view the need to regulate.

Mr Klupacs—Our confidence—if that is the right word, because this is high risk—is based fairly much on the mouse field. There are mouse embryonic stem cells, there are mouse adult stem cells and people have learned how to manipulate certain needs. There was a paper published a month ago on people producing pure mouse islets or pancreatic cells and putting

them back into diabetic mice, effectively curing diabetes in the mice. What we want is to be able to do that in the human. The problem is there are a couple of quite idiosyncratic things. The major factor that is used in the mouse field to hold the stem cells in a certain state does not work in the human setting. You cannot guarantee that because it worked in a mouse it will work here, but there is enough overlap in some of the results to give us a level of confidence. If we work hard enough we will make the same discoveries that have been made in the mouse and modify them for the human setting. But there are no guarantees. That is the reality, unfortunately.

Ms ROXON—But you think, in creating these universal lines, the potential for immunological rejection would be treated by some sort of other medication that you think can be provided at the same time? Is there work being done in that area as well?

Mr Klupacs—There is a huge amount. There are some fantastic antirejection drugs. The only problem with cyclosporin, which is the major antirejection drug, is that it will actually kill an embryonic stem cell, or that type of cell. We need to develop other types of antirejections. I could point you to another series of literature in the antirejection field. There are probably 30 drugs in phase 1 and phase 2 clinical trials. There are other approaches to immunise people with their own antigens to protect them against those sorts of things. We are not funding that per se, other than that we have immunological consultants. Our business probably would be to link up. You give our cells, plus another company's cells, and that is the ultimate treatment. That is often what happens in cancer medicine at the moment, for example.

Ms King—In this brief paper we were trying to focus just on the cloning issue rather than the stem cell derived medical treatments, but it is quite likely that we may not even need to use cells as the therapy themselves. We will instead, as Robert was describing, discover the factors that turn those cells into a nerve cell and then commercialise that factor, which can just be injected or taken as a pill.

Ms ROXON—It will turn the cells that are already in your body into—

Ms King—Exactly, yes.

Mr Klupacs—We might find, for example, that if you put erythropoietin in a dish it turns that cell into a blood cell—that is the treatment. Erythropoietin is a known factor and people could use that for the same purpose.

Mr MURPHY—The cell lines you have now have been derived from those 12 embryos. You say it is unlikely you will require further embryos. Do you have a bank of stored embryos in addition to those 12 which you have already?

Mr Klupacs—The company does not, no. IVF clinics around the world do, but we do not.

CHAIR—Thank you very much. It has been very interesting. I suspect it raised some things for all of us that we had not contemplated before you came along. I thought we were going to be dealing with the sort of nitty-gritty of legal relationships between companies and that sort of thing, but you certainly raised some very interesting things for us. Thank you for your submission and for coming along today.

Resolved (on motion by **Ms Julie Bishop**):

That this committee authorises publication of the proof transcript of the evidence given before it at the public hearing this day.

I thank everyone for their attendance and declare this meeting of the committee closed.

Committee adjourned at 10.32 a.m.