COMMISSIONER: Good morning. This morning we move to a new topic, Opportunities in Nuclear Medicine, and I welcome Professor Eva Bezak from the University of South Australia and Mr Prab Takhar from the South Australian Health and Medical Research Institute. Counsel.

MR JACOBI: Radiopharmaceuticals are now an established and integral part of modern medical practice. Radiopharmaceuticals are used for diagnostic procedures through the introduction of particular radioisotopes into patients mainly by injection in order to identify conditions such as cancers and heart diseases. Separately, radiopharmaceuticals are used in the treatment of disease. There are a range of existing therapeutic techniques using radioisotopes such as those using an isotope of iodine, as well as a range of prospective and potential techniques which are the subject of well-developed research and inquiry.

Depending on the particular isotope required, radiopharmaceuticals are generated either in reactors, or in the case of typically smaller elements, by using accelerates such as a cyclotron. Radioisotopes currently used for medical purposes in South Australia are produced both at ANSTO's research reactor in Sydney and also in South Australia's cyclotron located at the South Australian Health and Medical Research Institute, or SAHMRI. Locality of production is significant in the case of radioisotopes given their short half-lives.

The Commission is required to consider whether there are opportunity to expand the production of materials from radioactive substances and whether there might be associated opportunities in other sectors. To address that issue, the Commission will speak to those responsible for the operation of the cyclotron in South Australia and those concerned with related research and the range of potential applications and to those with an interest in the commercialisation and development of that research and technology. It will also speak to those at ANSTO to understand the market for radioisotopes and relevant opportunities.

Mr Prab Takhar is the director of the molecular imaging and therapy research unit at SAHMRI and has over 14 years of experience in medical research and development in both the private and public sectors. He has been involved in the start-up of global radiopharmaceutical facilities and has extensive knowledge in operating procedures for PET, SPECT, cyclotron and radiopharmaceuticals. Mr Takhar holds a Bachelor of Science with honours in physics, and Master of Philosophy in radiation and medical imaging, alongside a Master of Science and Medical Physics. He has been in South Australia for two years developing diagnosis and some treatment agents for the state and Australia.

Professor Eva Bezak is a professor in medical radiation in the School of Health Science at the University of South Australia. She holds a Master of Science

and Medical Physics and a PhD in nuclear physics. Professor Bezak is currently an affiliate associate professor at the University of Adelaide and was previously a chief physicist at the Royal Adelaide Hospital. She has also served as a member of the National Radiology Oncology Tripartite Committee to develop quality and performance standards for radiation oncology. Professor Bezak's research focuses on novel diagnostics and therapeutic radioisotopes and techniques involved in the treatment of cancer.

She is currently appointed a member of the South Australian Radiation Protection Committee and recently she was a member of the Expert Working Group under the Australian Academy of Sciences to prepare a report on the future of accelerates in Australia, including for medical purposes, and the Commission calls both Mr Prab Takhar and Professor Eva Bezak.

COMMISSIONER: Mr Takhar, I want to start with you. Can you briefly outline the capabilities of the Molecular Imaging and Therapy Research Unit at SAHMRI?

MR TAKHAR: Absolutely. So the MITRI, as it's abbreviated, is around 750 square metres and it was awarded a federal Therapeutics Goods Administration Licence at the end of 2014. What that means is that whatever materials we make in that area can be shipped not just to the state, but also outside the state to Australia itself as well as New Zealand. It means that also when you attain something like this, it means that anything we produce can be actually replicated across the world as well because we hold that licence. There are only five facilities currently in Australia which have this ability, and the cyclotron which sits inside is the highest commercially available cyclotron in the world, and what we've done with that ability is to expand out what we can actually make and what we're trying to do for the future.

So the capability of the cyclotron itself is not just to make the isotopes most people hear about when it comes to cyclotrons are short-lived, but also the longer-lived isotopes as well. Now, longer-lived in cyclotron speak is more than six hours. So you're talking about technetium; you're going all the way to three days. For us, three days is a long time on a cyclotron. Anything less than that is less than two hours. So cyclotrons have to exist to allow us to be able to make those pharmaceuticals to be able to inject them into patients and actually get a diagnostic result.

The difference and the complications occur when you're trying to make a pharmaceutical in the same level as a pharmaceutical that exists in any - say, whether it's a big global pharma company like Pfizer, you make the same kind of controls and the same kind of quality all the way through, but you make enough only for one day. Your shelf life for each of the pharmaceuticals that you make in its conduit form only last approximately 12 hours. So if you don't

have a cyclotron you're not allowed to really make those isotopes to be able to inject them safely into patients.

COMMISSIONER: What is the current capacity use of a cyclotron?

MR TAKHAR: It all depends on how hard you drive it at the end of the day, but currently what we're doing is only running the system for less than an hour a day to just deliver to our state. So with the capabilities that we have now we do over (indistinct) use the cyclotron right now even when it's one hour, and what it means is we should be able to compensate and any further work that we need to do we should be able to easily do on our system.

COMMISSIONER: So there's plenty of commercial opportunity.

MR TAKHAR: Absolutely.

COMMISSIONER: Thank you.

MR JACOBI: Can I just pick up on the technical capabilities of the cyclotron itself, and I'm interested to understand the extent to which it might be adaptable.

MR TAKHAR: Okay. So the cyclotron has ability to accelerate two particles at the moment. So one is normal protons, as we call it, and the other one is deuterons. Deuterons means that you can actually start making other types of isotopes. So some of the ones that we were discussing before previously are related to turning basically standard radium into actinium as an example, but it also means that - the proton beam that we have means that we can actually convert not just gases, liquids, but also solids. So when we start with metal solids, as long as you've got the perfect isotope you can then convert that into whatever you require. So this is where the therapy idea comes in, and also the capability of the system itself.

Those infrastructure placements have already occurred. So SAHMRI, in its wisdom, decided that the cyclotron should have all the abilities and that is possible of future expansion. So what the system was designed to do was actually to be expandable. So right now currently we have a very basic system even though it's the most advanced system that we've got, currently in the world, but it means that also we should be able to expand our future without huge infrastructure costs as well.

MR JACOBI: I'm interested to pick up on the comparability of the capabilities that the cyclotron in South Australia has compared to perhaps cyclotrons in other jurisdictions.

MR TAKHAR: Okay. So when you buy a cyclotron you have to - you either build one or you buy one yourself. So the way that we've done it is to buy a commercial system from GE Health Care. It's a high specification system but it actually has ability to be ramped up further and harder. The only other cyclotron in the world which is running harder than this - on this system itself is actually in Sydney. It's the only one in the world, but it's actually been given a special disposition from GE Health Care. Our system could also do the same thing and we're in negotiations at the moment with GE Health Care to allow our system to do this.

MR JACOBI: And so what's the expectation in terms of the outcome should those negotiations be successful?

MR TAKHAR: It means that we should be able to expand out production across Australia as well. So we should be able to generate enough of these isotopes not just for cancer, but also to other diagnostic requirements when it comes to cardiac disease as well as the neurological disease as well.

MR JACOBI: We've heard a little bit, and in our reading, in terms of cyclotrons having a fixed number of beam lines, and I'm interested to understand - and you might be able to pick up on this Professor Bezak - about the number of beam lines and the extent to adapt the cyclotron such that it might have multiple beam lines.

MR TAKHAR: So on our system itself, it has currently a beam line which is very similar to the one that you would fine in the large Hadron collider, it's just a very smaller version of it and what it means is that you can take the particles from the source, which would be the cyclotron, take it outside of that zone and then actually in a controlled manner know exactly where it's at all times and then be able to work externally, outside that. So what it means is that with one beamline you should be able to do a lot more work and do a bit more intensive work. What it also allows us to do is actually develop new concepts which are not currently available, or in the starting points and commercialise them. So once you commercialise a process, you can then actually own that right across the world as well and those abilities don't exist currently. So currently we have one beamline and that's probably enough for what we need. What you then need to do is convert the end point of that beamline in to more trial systems and that's where Eva comes in as well.

PROFESSOR BEZAK: The problem is that the current cyclotron is used clinically so we need to ensure the integrity and the cleanliness of the beamline so that the radioisotopes produced are safe for clinical use. So if for example, a research group wants to conduct experiments on that beamline, we might need to be forced to disassemble bits and pieces and put experimental targets at the end of the beamline for R&D purposes. And that takes time, that reduces

amount of time that the group can spend conducting the experiments and at the end of the day experiments, the cyclotron beamline needs to be put to its original state.

MR JACOBI: So the idea is that it would need to be assembled and reassembled each day - - -

PROFESSOR BEZAK: Yes.

MR JACOBI: - - - for the production?

MR TAKHAR: Actually in a way the beamline is actually not utilised as much as we'd hoped. I mean right now if Eva was doing an experiment, technically she could run for six hours on the system before I was ready to do my clinical work and then literally without – with a flick of a switch, as simple as that, you then go in to clinical mode and within an hour you've run your – what's recalled requirements for the state and then you switch it back, directly back to Eva's projects.

PROFESSOR BEZAK: Provided that you're only using your liquid targets.

MR TAKHAR: Yes.

PROFESSOR BEZAK: If you start using your solids targets that will be a bit more complex. So - - -

MR TAKHAR: Yes.

PROFESSOR BEZAK: - - - the idea what we've had is similar to – which is accommodated in larger accelerators in Australia, including synchrotron or the largest linear accelerator and you – that you basically have multiple beamlines where the end point is designed for different type of experiments. The multiple beamlines they used switching magnet and that we go exactly to what Prab is talking about, that with the flick of the switch you will direct the beam down a particular beamline to conduct the experiment of choice. And it could be either production of radio isotopes, it could be irradiation of cellular targets for radiobiological experiments, we are even talking about open beamline where the proton beam will actually exit the beamline and this could be used for pre-clinical studies with small animals which would - pre-clinical studies for protons therapy that we are hoping will come to Australia in near future.

MR JACOBI: I will come back to proton therapy in a minute.

PROFESSOR BEZAK: Yes.

MR JACOBI: But can I just pick up, in terms of what is currently being manufactured for the – perhaps for the local market, what is the main radioisotope that is being produced?

MR TAKHAR: F18, so it has 110 - - -

MR JACOBI: So that's fluorine.

MR TAKHAR: Fluorine, yes. So basically fluorine 18 is just – we convert oxygen, basically standardised water but it's a specialised water, we just call it enriched water, which is oxygen 18 which we convert in to fluorine 18. That lasts for around 110 minutes. The amount that we make is enough that we could conjugate it in to what's called radioactive sugar and then once we've got radioactive sugar, we then inject that in to patients, mostly cancer patients to work out planning, treatment, response, as well as long term, what's called reoccurrence as well.

MR JACOBI: So that is being used as a diagnostic – for diagnostic - - -

MR TAKHAR: Absolutely.

MR JACOBI: - - - purpose? And I am just interested, are you manufacturing anything else for commercial purposes using the cyclotron at the moment, or for health related purposes?

MR TAKHAR: Currently we are trying to develop a on – we have also got this solid beam target as well, solid target system which we're using cooper 64. So we've been making a bit of copper 64. Now there is (indistinct) that that would be able to be utilised because of course it's a longer half-life. So what it means for us is that you could actually ship it, so it's around 12 hours rather than the two hours. So because it's almost closer to 13 hours, you can ship it across Australia. What we're trying to do is build a consortium across Australia which will allow us to do this. So therefore we all combine our systems together because if everyone's got a small amount of access we can then all help each other out. We are now in the middle of developing zirconium 89. Zirconium 89 is designed for these antibodies, monoclonal antibodies where you can label them and utilise them for any types of disease. So this is the up and coming area. What that means is that pharma companies are very interested in this area. What they want to know is where their pharmaceuticals really go and the response that the body has, the best way to do this are to utilise the body to actually look at this but then you have got to do long term studies. Long term could be three days; this isotope is actually available and can be made for three days. We will have an upgrade of our system in February next year.

MR JACOBI: This is an upgrade, this isn't (indistinct) manufacture - - -

MR TAKHAR: Zirconium 89.

MR JACOBI: And I am just interested to get a bit of a handle in terms of what the commercial value of the market associated with radiopharmaceuticals is. Are you able to give me any idea about perhaps by reference to the fluorine, the sugar - - -

MR TAKHAR: Yes.

MR JACOBI: - - - that's ultimately being produced, what its value is and then – and perhaps a bit of perspective about where you think the value of this other products might go?

MR TAKHAR: So fluorine 18 is – with the (indistinct) that is being utilised at the moment, because it's on a Medicare rebatable system it's actually utilised and there is some kind of rebate that you get and from that, just from the costings that we're doing currently at this – in the state, it's around one million to 1.5 million and that's just running at close to 10 to 15 patients a day in 200 days working days, if you're asked to meet that. Now if you then expand that out to what is really required for a state this size, you're talking about 60 patients. Realistically 60 patients a day need to be scanned just to compensate for the number of cancer patients. If you then include other states, we would have to back up and other states that require it and as the cyclotron starts delivering to the other PET scanners you're talking about expansion. So that 1.25 million suddenly expands out to close to seven million and then goes on further. This is exactly what's happened in other states as well. Currently we only have two scanners in the whole of South Australia, other states if you just do the standard comparison, Sydney as an example has almost eight scanners and is about to have another two and then if you go across to Perth, they've got seven PET Ct scanners and only one cyclotron. So that one cyclotron is actually delivering to all those scanners.

MR JACOBI: Am I right in understanding from your answer before with respect to – you spoke of there being a consortium, is that a consortium between the cyclotrons in terms of offering backup supply to one another or?

MR TAKHAR: In a sense, yes. But they are mostly done from the research side of things, so Eva can probably talk a bit more about that but we have small groups, we want to just more than what is capable on a cyclotron. What it also means is that these new isotopes are being developed and also with the size of Australia you need to have longer lived isotopes which will actually allow us to utilise those compounds a bit longer.

MR JACOBI: I am just interested in terms of what the market conditions are in Australia for a supplier that is minded to develop new radioisotopes?

MR TAKHAR: Okay. So right now we – I mentioned there was five systems including ourselves which have a GMP licence. Most of the others that exist are actually – have only just got their licence within the last two years and the only one that's been existing longest is a commercial system. The problem is that once you have a commercial entity, all they want to do is generate revenue and everything else which there's nothing wrong with that but what it means is that the development of new isotopes that exist, has been really curtailed. So what it means is they can either charge whatever they require, and there's no real ownership that's needed for that. And what we then have is becoming part of samurai, the cyclotron then has the ability to develop these isotopes to a higher standard and that - Australia's seen before and also to compete with the rest of the world and then allows that isotope to be delivered elsewhere as well.

MR JACOBI: Now I think I will come back in a minute to the idea about how we might go about a process of exporting those sorts of ideas to the world and I am just interested, perhaps if we can start with you Mr Takhar about what the sort of opportunity you think – you've mentioned a number in terms of copper and zirconium and I am just interested to understand from you where you think the other prospective opportunities might be in manufacturing radioisotopes for radiopharmaceuticals in South Australia?

MR TAKHAR: So one of the other areas that has been looked at globally, and it's due to shortages of an isotope called technetium-99 and so technetium-99 at the moment will be generated and it can only be generated really on a nuclear facility like ANSTO. So what we're trying to do as well, is that not everyone has ability to have a nuclear reactor in their back garden, so the only way to do that is if you've got a cyclotron and you have the ability to actually commercialise technetium production on a cyclotron small scale, we're not talking about trying to compete but what we're trying to do is ensure that globally everyone has the opportunity to get this technetium scan.

So if you're in a remote facility - and Australia is great in that sense because we can actually trial it here. We can then examine whether technetium-99 could be manufactured to the levels that are needed for a small hospital or a hospital of the size that are currently being built in South Australia. So if we can actually develop that we can actually then make the cyclotron expand out the market in the big scheme.

The other isotope that's being really pushed right now in the last six months is gallium-68. Now, Gallium-68 is made on a small generator. What it means is, very similar to a nuclear system, you need to make a nuclear reactor. You then need to label it, ship it, send it over on a plane and deliver it to site. The site

problem that you've got with gallium is that we can't generate enough. So what it means is that a cyclotron therefore has the ability to generate a large amount in a short time. So what it means is that we should then be able to - if someone can commercialise this - should be able to allow any system to be able to generate this (indistinct) and then make the patients, which don't have the opportunity to have this, available. Gallium-68 has a very short half-life, just over an hour actually.

MR JACOBI: So there's no prospect of shipping it. It's going to have to be made locally.

MR TAKHAR: Yes, absolutely, but the thing is you can make more of it on a cyclotron compared to a generator. So if that could be commercialised - and there's lots of companies trying to get into this world where really, unless you've got the, what's called, skill set it's not going to happen.

MR JACOBI: Can I come to you Professor Bezak, and we mentioned proton therapy. Perhaps you can pick up and explain, first of all, what proton therapy is, and your view of the prospective opportunities for its use in the treatment of cancer.

PROFESSOR BEZAK: I might side track a tiny bit. Yesterday there was a meeting in Adelaide where the bust of Sir William Henry Bragg was uncovered on the North Terrace, and Professor Bragg did lots of his physics experiments here at the University of Adelaide and during the process of his experiment he discovered something that's called Bragg peak, and the Bragg peak is a way how protons and other heavy ions lose energy when they are passing through material, including human tissue, and they lose energy in such a way that at the initial start of their trajectory they use a small amount of energy, but they lose all of their energy towards the end of their track, and this peak spike in energy is called a Bragg peak.

And this is very advantageous from the point of therapies that would be using protons or carbon ions or oxygen for treatment of cancers, because what it means is that if you choose the right energy of the protons and the protons will stop in the cancer cells, in the tumour itself, the most amount of energy, up to 80 or 90% or their energy, will be released within the tumour itself while the surrounding healthy tissue is being spared, and this is much more advantageous compared to photon or x-ray therapy that we are using at the moment where photons are actually depositing their energy exponentially. So most of the energy is actually in the superficial regions rather than the tumour region.

We're getting around the problem these days that we irradiate the patients from multiple angles and all of the beams are meeting in the tumour so that we are building up the radiation dose within the tumour, and we're also sort of sharing

that unwanted dose to healthy tissues around a large volume of healthy tissues. So the photon physics is not really superb when it comes to irradiating the cancers, however, protons have absolutely ideal energy distribution in tissue. Not only that, but with the protons, when they come to a full stop all the energy has been spent; there is no exit dose, so the tissues beyond the Bragg peaks are not irradiated.

With photon radiotherapy there is always an exit dose. As a result, protons are ideal particles to treat particular-dose tumours that are sitting in a close proximity to critical structures: tumours at the base of the skull or on the spinal cord; eye tumours where you can literally spare the optic nerve and not only treat the cancer but (indistinct) preserve vision as well. Proton therapy has been a hot topic around the world for the last ten to 15 years, and as far as I know, most of the developed countries are building new facilities rapidly. The UK is building at least two to three facilities, both public and private. Japan has maybe one of the highest concentrations of (indistinct) facilities in the world. So I think it's just a matter of time when Australia will have to come onboard as well and set up some sort of proton hadron therapy in the country as well.

MR JACOBI: Could you explain the link between what you just described and the sort of techniques and technologies that are available at SAHMRI at the present time and how that might need to be developed?

PROFESSOR BEZAK: Yes. The cyclotron that's there only accelerates protons to smaller energies, so that cannot really be used for clinical patient treatments, however it can be used as a pre-clinical facility for research for the proton therapy to be established in Adelaide or in Australia. So what that facility can be used, for example - so some of the targets that we have been building together would allow us to put cell lines, cells, either in a medium or suspended in gels into the proton beam. We can irradiate those cell lines with proton beams and then use various molecular biology techniques and staining, look at the response of cells to irradiation.

Those cells can be also primed with other agents. For example, some of the research that the University of South Australia is doing is radiosensitisation of cells with gold nanoparticles, which seems to be also a very hot topic around the world. That means that if you can force the cancer cells to absorb gold nanoparticles and then irradiate them with a proton beam, the effect of the radiation, the detrimental effect, so that can be increased up to 20 per cent.

MR JACOBI: Can I just pick up on some of the other potential opportunities that you think might be linked to particularly the sort of work that might be associated with a cyclotron? I understand you've got a view about alpha therapy as well as with regard to using diagnostic tracers. Perhaps you might

offer us an insight into that.

PROFESSOR BEZAK: The proton therapy I was talking about until now would be something that would be delivered externally to the patient, which we call external beam radiotherapy. However, radioisotopes, as Prad mentioned, some of them, especially the ones that are a bit heavier that are produced through the decay of uranium isotopes - I think you mentioned (indistinct) radium, thorium and a few others - they usually decay by alpha decay, and alpha particles, similar to protons, are high ionisation particles. That means that they are causing very localised ionisation damage.

If we have these radioisotopes - and if I can use this picture here - the radioisotopes can be attached to special proteins that we call antibody, and they are glued together with another chemical that we call chelate, and all this compound is also known as radioimmunoconjugate, and this radioimmunoconjugate is inserted inside a patient, for example, by injection through the blood vessels. Depending on the type of the antibody, this antibody can be specifically seeking particular cells that have very specific receptors on their surface, and it is very well known that a number of cancer cells have surface receptors that are specific for those cancer cells.

There are different antigens, these receptors, for example, for melanoma, different for prostate, different for brain tumours, different for breast, and lots of work has been done in recent years actually identifying these tumour-specific receptors. So if you can find out or build a radioimmunoconjugate that is specifically tumour seeking, we can be able to attach this radioimmunoconjugate radioisotope on a particular tumour cell. Once the radioisotope is attached to the tumour cell it will undergo radioactive decay and that alpha particle will traverse through the cancer cells and also perhaps through a couple of other surrounding cancer cells and because, as you can see, indicated, the density of the ionisation track is very intense. All the energy is deposited locally so you are only affecting primarily the tumour tissue and sparing the healthy tissue. This is very important for what we call metastatic cancer disease. Linear accelerator in the hospitals or even proton therapy would be used for the treatment of the localised tumours within the first stage, within brain, within breast for example. But at the later stages of the disease as the cancer starts spreading out through the body, primarily we have to use systemic therapy, something like chemotherapy which is, a) quite costly and also quite toxic to the patients. So over the last maybe even 20 years, lots of effort throughout the world has been towards the targeted therapies that would actually differentiate the effect of any therapy, where you will be maximising your effect on the cancer cells while sparing healthy tissues.

So where the cycle of (indistinct) come up to this, it could help us with

production, some of those radioisotopes and it could also help us again, not only with the production of radioisotopes but in radiobiological experiments that we can label cells with radioisotopes and then give them external dose of proton therapy and see what the combined effort is.

MR JACOBI: I understand from the paper that you have published that you have expressed a view about what the – I guess the cost saving might be that might be associated with the development of this technology over the other sorts of alternatives that you have talked about. I am just wondering if you could express a view about that?

PROFESSOR BEZAK: The production of radioisotopes if the cyclotron is already in place and generating radio-immunoconjugate would be in my opinion much cheaper compared to other therapies especially compared to some of the chemotherapy drugs currently on the market. For example one of the latest drugs for melanoma, one of the single course costs about $100,000. Prab, you know speak more about the costs of radio-immunoconjugate.

MR TAKHAR: So I mean an example would be right now we are currently working on – so right now we have got an ability to look at neuroendocrine tumours, so using gallium base – the base of the immunoconjugate that we're talking about. And what that means is that we can look at exactly where those neuroendocrine tumour mastitis are. We can then replace – once we take a picture and we know exactly where the tumour is and everything else, all the micro calcifications – sorry, micro clusters that exist on the tumours, what we can then do is replace it with an alpha therapy, lutetium 177. Once we combine it with exactly the same monoclonal antibody that we're talking about, we can actually treat in two courses, probably about $10,000 two courses and then you scan again after. You know exactly whether the tumour has gone or not. And that means – that is without giving them chemotherapy, that's giving them exactly targeted therapy. Now you mentioned earlier iodine 131 and for us physicist, we used to sit there and think if only we could do that with everything and that's where the big push has been happening. Iodine goes exactly where it needs to go. It only goes to one place - - -

PROFESSOR BEZAK: Thyroid.

MR TAKHAR: And thyroid and that's it. So the whole thing is, if you could do exactly that and you can make it a compound which goes exactly where it needs to go, take a nice pretty picture then replace the metal that you've now taken a pretty picture with, with exactly something that will kill it and that's exactly what the hope is. We're now working on breast – sorry, not breast cancer, at the moment we're working on prostate cancer. So we're now getting - just about three weeks ago, we did our first prostate agent injected in to a human in the state. So we are now looking at directly in to the prostate, we can

see all the micro clusters of cells, they exist, which happen when you start getting rising PSA levels after you've done surgery, chemotherapy and everything else. So when all of a sudden our blood test shows there's a ramp up, we can actually see and look inside the – inside the body to look for those micro clusters. Once we can see them, the hope is that we can then replace them and actually with the gallium we can replace with lutetium and then we can do alpha therapy. So we can actually kill those cancers off. Now that's the hope that we want to do but it's not just those kinds of areas.

As Eva mentioned, there is melanoma as well as breast cancer, they're the two big hot topics that we are trying to do as well in concurrence.

PROFESSOR BEZAK: Also the target (indistinct) therapies are also used for the treatment of blood cancers, leukaemia, lymphoma and there has been quite a bit of research for (indistinct) blastoma (indistinct) which is the type of brain tumour for which we really do not have any treatment for the time being.

MR JACOBI: Can I just – just to change topics and you spoke before about the development of techniques for manufacturing technetium and indeed a range of other heavier elements and I am just interested, as I understand, it's not proposed that we would manufacture those here and export them to the rest of the world. I am just interested how the commercialisation of those techniques might work and what the vision is in terms of the commercialisation opportunities that might be associated with being able to manufacture something like technetium on a cyclotron?

MR TAKHAR: So an example is that you've got a cyclotron, you've kind of done a large amount of investment already. Then if you've got the ability to supply clinically to your own state, or to wherever your customer base is and then you've still got time on the cyclotron, it means that you can utilise that to actually commercialise the processes which don't exist at the moment. So if you've gone and spent a large amount of money on a cyclotron and you're not utilising it to its full capacity, you're basically not using your asset to its full capability. So what we will want to do is commercialise a method of making technetium on a cyclotron, as an example. Does it have to be technetium? There are many other isotopes that exist that are also required but what it means is that if you're a manufacturer of a cyclotron, doesn't matter which manufacturer you are, you've all of a sudden got a huge amount that you can – you've got the ability to sell a system which doesn't just make PET isotopes but also spectisotopes.

Now if you go to a nuclear medicine department, most of the scans that are carried out in nuclear medicine departments, probably 90 per cent of them are spect and then 10 per cent are about PET. So what it means is that all of a sudden you've got the ability to sell a cyclotron to a hospital which is in a

remote ability and that all of a sudden those patients that are in that area suddenly can get a diagnostic scan which they wouldn't have been able to before.

MR JACOBI: So is the hope to sell essentially a patented process to - - -

MR TAKHAR: Absolutely.

MR JACOBI: - - - a company such as GE, or other health care provider, such that it can increase the value of the products that it ultimately sells.

MR TAKHAR: Absolutely. And the other thing is that the process map itself has to reach the kind of levels that are needed with – like an example is we have a TG licence. What it means is that having a therapeutic goods administration licence means that we have to attain the highest quality which also means that we have to reach the levels that are globally set. Also means that anything that we trial, and if it needs to go in to humans or anything else, has had full validation from the starting point. So even though we're doing clinical research and designing a process, that commercial process will also have that backup of all the data and all the information that's required for it to get a licence change globally. And I think that's what a lot of sites have tried to do this, have just basically missed out because what they've done is they've gone to research facilities which don't have a licence. They've started processing things and then gone, well okay we've done a lot of research, we're kind of done there but not actually applied the commercialisation and from a starting point, applied these good manufacturing practices, actually trying to go for a full licensing ability. So what it means is that anything that we make here, or actually apply to the federal government for a change, it means that it's also able to be mutually recognised across the world, apart from the US, but the US is also trying to do something similar as well.

MR JACOBI: I understand the licence represents a real advantage. Is there anything else about doing these activities in South Australia that might represent an advantage?

MR TAKHAR: I think also because we've got such a close tie with the EPA, the Environmental Protection Agency is very close to ourselves as well because of course it happened because the cyclotron existed and we hadn't had a cyclotron before and we worked very closely with the EPA, which also means that we are in close discussions about research. Everything that we create and anything that we make, we also work closely with them to actually validate every single step that we do. Because the worse thing you would want to do, is actually generate something on the cyclotron which hasn't been seen before or anything else. So what we want to do is ensure that never happens. So the advantage that we've also done with some work with the University of

Adelaide is actually to simulate the cyclotron in virtual space. So what it means is that without even switching it on, just switching a computer on, you can actually run simulations. What we then do is use those simulations to go to the EPA, have a discussion and then we actually run experiments with them in what was called collaboration and we use their systems to actually see whether we made exactly what we think we made. So often what it means is that we've actually validated a computer virtual system and that wouldn't have been possible in any other state. An example would also be if you go for a proton therapy facility. Because we have such close ties with the EPA, it means that we could get a system up and running a lot quicker and a lot faster because we have that close tie.

MR JACOBI: We've spoken about a number of adaptions that might be necessary technically. Are there any other barriers in terms of being able to develop the sort of - I think you described them as a process map - and develop those sorts of processes in South Australia? Are there changes that might need to be made or are there investments that might need to be made to achieve those without - - -

MR TAKHAR: There would be. As I stipulated before, the large investment has already been carried out, but to be able to allow ourselves to do other external systems, as well as to validate and test in a controlled way without operators being in any kind of harm's way from the radiation, which we currently do - we have specialised systems to allow us to do that - those system cost a lot of money, not a huge amount in comparison to cyclotron, but they do cost. So the infrastructure costs are not significant in a sense, but what it means is that those designs and those prototypes that we design here would then be able to be rolled out and sold elsewhere as well. So that's the hope that we have and, step by step, that's what we're trying to achieve in South Australia. We're not retrospectively trying to change anything, and because of that reason, we could actually, in theory, only have to upgrade slightly in steps.

COMMISSIONER: What opportunities would be provided to you if we participated in the sorts of nuclear activities that we're contemplating at the moment?

MR TAKHAR: Well, the facility that we have isn't just a cyclotron facility. It's also a pharmaceutical manufacturing facility, and because of that reason, it means that anything that we do make, even the alpha therapy, if we could get hold of - right now there's currently a lack of these alpha emitters that we were talking about, lutetium and some of the other ones, which exist globally. Now, if we could actually access those, the big larger pharma companies - and we're talking about an example, as we were talking about, a melanoma compound which costs, for one shot for chemotherapy, $100,000.

If we could actually make alpha therapy where we're also at a lower cost, for one thing, but also means that the patient doesn't get sick, just to be able to get a full course we go exactly where we need to. Now, if we could get that infrastructure - now, most of the infrastructure that you've heard about for those kind of things are very similar to uranium enrichment. So you've got a centrifugal system which exists. If you could get one of those you could actually purify the alpha emitters in the first stage. So they're basically the same system.

Once you have a way of - whether it's enriching uranium, is actually the way you would enrich something else as well, like in alpha therapy. You can then purify it and then label it. Once you label it, you then verify it in a pharmaceutical facility which has the capabilities to do that. So this facility that we have, yes, we talked about the cyclotron, but we also have the ability to manufacture and combine these in a safe environment and also ship them. So once we can do that, we can then actually reduce the cost of making these targeted therapies, which means that in a sense, instead of a patient going through a huge amount of chemotherapy and hoping that something would happen at the end of it, we can actually image before, during and after to ensure that all of those stages that we've got where that alpha therapy occurs.

We can also do that from the pre-clinical side of things as well with zirconium-89 that I talked about labelling antibodies. Have we got an antibody that goes to like tumour? We can actually do that in animals or in what's called early humans if we wanted to, because our facility allows us to do that because we have the controls in place. So if we were able to get an enrichment system, whether it's for - it's very similar, like I said, to uranium, but what it means is that we could actually enrich any of those isotopes that exist. So if the state had an access to metals or some isotopes or alpha therapy kind of processes, we could actually make them to a level that we require and actually ship the globally, because these alpha therapies are longer-lived isotopes, which means that we could actually package them here in Australia and ship them anywhere around the world.

For that kind of infrastructure cost, we'd have to actually go back and work out whether it would be possible, but it's not impossible to do in a facility that we built, because currently in the 750 square metres we talked about, I've got three (indistinct) areas. Now, currently I'm only utilising one of those. So what we want to do is be able to expand all three if we could, but of course, we're doing a very slow, step-by-step method, because as the infrastructure money comes in we then go and apply it and then utilise it straightaway. So I think it's not impossible.

PROFESSOR BEZAK: In terms of the role of the Commission, I think if we are expanding production of radioisotopes there will be some waste. So have

some controlled facility for storage of radioactive waste would be very important as well.

MR JACOBI: In terms of skills, I'm interested to understand, perhaps from you, Professor Bezak, first, in terms of whether there is an existing cohort of people that would be interested in existing in South Australia and whether that might be able to be expanded associated with conducting this sort of research that you're talking about.

PROFESSOR BEZAK: Absolutely. Literally all universities in South Australia, including medical facilities, have been involved in cancer research, both in diagnosis, in therapy and in development of novel techniques. The University of South Australia has a very active cancer biology group. They are actually building a new cancer biology building in the new biomedical precinct at the west end. So there is a number of research groups there that would be looking at both radiobiological experiments, radiopharmaceutical experiments in combination with radiopharmaceuticals or external beam therapies. There will be groups at all three universities working with nanoparticle radiosensitisers that could be gold, bismuth oxide, cerium oxide, silver.

Nanotechnologies is the latest buzz word as well and nanoparticles is again something that can penetrate the cell and enhance the radiation damage from within. Within Flinders University there is Professor of Cancer Biology, Pamela Sykes, who does lots of work in terms of radioprotectors. Within cancer, we're looking at radiation to be causing radiation damage to cells, but in other areas, for example, for pilots, for astronauts or miners, other industries where the members of the public are working in a radiation environment, we would like to develop techniques that would protect them from harmful effects of radiation.

So Professor Sykes has been working with quite novel compounds that seem to, very interestingly, increase the radiation effect in cancer cells but increase repair in healthy cells. So again, this would be wonderful to test some of these novel compounds in a clinical environment like on the cyclotron, either on salines or on tumours grown in animals using open beam on a cyclotron. And the flow-on effect comes also to technology. So when we delivering any type of radiation therapy to a patient, we need to quantify, and to a degree pharmaceutical treatment for any disease is a bit easier, because you can physically measure the amount of antibiotics or painkiller that you deliver to patients.

It's quite a bit more complicated with radiation that’s coming from the outside. So you need medical physicists and radiation engineers to conduct quite complicated measurements of radiation to ensure that the right amount of radiation is coming to the right spot. So we already have projects both with the

University of Adelaide and the University of South Australia where we are developing specialised detectors that can measure the amount of proton beam being delivered to the material and cancerous tissues, and also that will scan the beam profile so that we know what the shape of the beam is, and these type of detectors - we are looking specifically at fibre optic type detectors -have then also a flow-on effect in commercialisation. So there are a number of companies that are potentially interested.

With the development of infrastructure, there are, I think, again further industrial flow-ons and development of know-how in South Australia, both science and engineering-wise.

MR TAKHAR: Yes. I mean, right now the skill set has reached a certain point where we now know that we can actually give back. So the whole thing is what we've been trying to do within SAHMRI as well, because we've got all the universities that Eva mentioned that were in the state in that building itself. So we get the coalface, in a sense, and what we've been doing with that is actually having students come through our facility, so upskilling our local students to ensure that they are getting all the best of the knowledge that we've brought in, whether it's from international experts and things like this. What we then do is try to apply that and then send them out there to actually understand that they can actually bring more skills to those centres that they go and work. So in a sense, it's actually upskilling people in South Australia.

So what we're trying to do within my little facility is actually try and utilise that and actually make it an APAC training centre. So to make a pharmaceutical facility to the level that we've done in South Australia is quite difficult. Like I mentioned before, two years ago there were only two facilities in Australia, New Zealand that would ever be able to reach that level. Now there's technically five. There's hope in the next two years there will be seven. And so because of that reason, it's a very slow growth. That's Australia, which is a western country.

If you then expand that to APAC region which is trying to catch up to the world and is accelerating like crazy in this area, this is where they want to actually join on, and so I think there's been a big push from the manufacturers to see whether we have the ability in South Australia, and because Adelaide is such a well location - it's location is phenomenal - to be able to actually connect all the different programs that we've got, as well as trying to get the skill set into those different regions of the world, and the APAC team within an example like GE Health Care has been really pushing quite hard to actually have a training centre.

But it's not just them. The other vendors that also exist within our little facility have also been coming forward saying, "The skills that we've got and the

things that we've developed already within the last two years just with procedures have been able to show that we can actually make a system which might not have been so robust into something that is robust," because we have to ensure that we can deliver what we promise, and the thing is that reason allows us to develop their systems better as well.

COMMISSIONER: Sharing intellectual property amongst those groups, I imagine, is not simple, but the system is robust enough, your relationships are robust enough, to be able to manage the sharing of intellectual property amongst groups, amongst universities, amongst commercial entities.

MR TAKHAR: Yes. I mean, I can only talk about the way SAHMRI is and I think Eva should probably expand about the University of South Australia, but because we developed in that sense and we got IP groups within - you know, there's lots of intellectual property within SAHMRI, and so there is development already into that area. With the universities, because they're partners within SAHMRI, it makes it a lot easier as well, and I think that's been an advantage. When it comes to larger groups, I think that's where we are developing that whole arm, because now all of a sudden, the pharma companies the different vendors that we have in our building are now realising what we could actually add to their profile.

PROFESSOR BEZAK: I think as the partnerships are being developed, you start slowly. If it then turns out to be promising, then you will put MOUs and intellectual property clauses in place. So we don’t necessarily start with an MOU because we just want to try out whether a particular idea will work or not, but I had a meeting with (indistinct) universities are obviously founding members of SAHMRI. So I think there is a very good attitude and interest to collaborate.

COMMISSIONER: Good.

PROFESSOR BEZAK: When we were talking about potential partners and everything, I only mentioned groups within South Australia, but if we increase capacity of cyclotron for radiobiological experiments, there will be number of groups nationally also interested in beam time, because all my colleagues that I know that want to do proton irradiation or carbon irradiation actually send their samples to Japan or Europe, which is then quite costly to send a team and samples across.

MR JACOBI: Can I just very quickly, Mr Takhar, just unpack a bit of your last answer? Is the model to sell a training service to a vendor so you can train people that they will be selling the product to, or what sort of model is thought about in terms of the training?

MR TAKHAR: There are various vendors and each vendor wants his own model. So what we've done is try to group them all together, in a sense, and sell it to the individual vendors or actually to individual groups. So an example would be you would go to Singapore, you would sell the whole process, "Come and train with us. Stay with us for about six weeks, two, three months, and by the end of it you'll be trained exactly on how to run a facility like what we've got in South Australia, which is the highest standard that you can actually have," and what it means is that because of that process, we would actually be selling a training service, in a sense.

MR JACOBI: And I'm interested in the other part. Am I right in understanding that it's a quality verification technique? You spoke of robustness of particular technologies. Is that a quality assessment, or are you able to demonstrate the particular technology works to a particular standard and that that's a marketable product?

MR TAKHAR: Correct. I mean, one of the things is if you've got a prototype system, just by looking at a system, if you've got the know-how and everything else, you should be able to then work out how to make that system more stable and how to make it also more commercially stable. So the two things go together: one is whether it's compound and stable for its full lifetime on the shelf. That's one important factor. The other thing is if it is stable, how is the rest of the equipment that goes along with it? An example is we work quite closely with the vendors to ensure that our systems reach the highest levels across the world. We don't just try to do it just for Australia or different regions.

What we're trying to do is say, "As long as we can hit all those high standards that exist in pharmaceuticals, in radiopharmaceuticals what we can then say is that your system is robust enough to do that," cause the controlled systems have to be done with robots and computers and everything else, and a lot of them are prototypes because a lot of people haven't made these things before. So what they're trying to do is turn a prototype into something commercial. So we have very close ties with these groups to ensure that they know what we're trying to achieve. We can then help them sell their systems more globally as well.

MR JACOBI: I think we touched on it a little bit at the start, but just to finish, what is the potential for an interrelationship with other producers of radiopharmaceuticals such as ANSTO?

MR TAKHAR: So an example is with ANSTO. ANSTO has shut down a couple of its cyclotrons. It had a cyclotron which was able to make iodine-123, as an example, and because it's lost that ability it needs to reintroduce that ability. Currently Australia is flying in iodine-123 and what we would like to

do is actually make our own cyclotron. So we think we have the ability and we know we have the ability to make it because we have the time. So if we've got the time and the ability, that means that scans which have actually reduced down and not had the ability to look inside certain disease types we can then actually reintroduce, and we're working quite closely with ANSTO to ensure there is synergy across what we're doing and what they're doing as well.

So we've been working with Life Sciences Group as well, with their new novel tracers that they make, because they've got some really good chemists. We've got some really good chemists in Australia. So we don't want to reinvent the wheel, but we do need to know that just because you're doing research you need to commercialise that to get its full potential, and this full potential is not just making money and profit and things like this, but it's also making a difference clinically and translating something from the basic, pre-clinical imaging all the way to translation into patients, because if you don't see a patient change or an outcome you've technically not done the whole process that you want to do. There is a commercial path for all these processes, but what we're trying to do, and we're working closely with ANSTO, is to convert the basic ideas that they've got into something commercial and real.

COMMISSIONER: Thank you very much for that physics lesson. It is very useful. We appreciate the work you put into preparing your evidence and the very clear way you delivered it this morning. We'll now adjourn until 1000, when we'll have Mr Marco Baccanti.

ADJOURNED **[8.59 am]**