REPORT ON PROCEEDINGS BEFORE

SELECT COMMITTEE ON OFF-PROTOCOL PRESCRIBING OF CHEMOTHERAPY IN NSW

At Macquarie Room, Parliament House, Sydney on Tuesday, 1 November 2016

The Committee met at 9:00 am

PRESENT

The Hon. P. Green (Chair)

Mr J. Buckingham
The Hon. C. Houssos
The Hon. T. Khan
The Hon. N. Maclaren-Jones
The Hon. W. Secord
The Hon. B. Taylor (Deputy Chair)

The CHAIR: Good morning ladies and gentlemen. Welcome to the second hearing of the Select Committee on Off-protocol Prescribing of Chemotherapy in New South Wales. I acknowledge the Gadigal people, who are the traditional custodians of this land, and I pay respect to the elders past and present of the Eora nation and extend that respect to other Aboriginal people present or those who may be joining us today on the internet. The inquiry is examining off-protocol dosing of chemotherapy in New South Wales and will consider the capacity of electronic prescribing systems to stop the limit of off-protocol prescribing, the process and systems around informed consent for medical interventions, the value of potential new patient information sheet on dose adjustment and the need for notifiable cancer patients to be overseen by a multidisciplinary cancer care team.

The inquiry will examine the capability of St Vincent's Hospital to comply with NSW Health policy directives and guidelines and mechanisms for staff to raise concerns about the practice of clinicians and breaches of the code of conduct at St Vincent's Hospital, and within NSW Health more broadly. Today is the second of four hearings we plan to hold for this inquiry. We will hear today from medical oncologist Dr John Grygiel, senior officers from South East Sydney Local Health District and academics from the University of Newcastle. I will make some brief comments about the procedures for today's hearing. Today's hearing is open to the public and is being broadcast live via the Parliament's website. A transcript of today's hearing will be placed on the Committee's website when it becomes available.

In accordance with the broadcast guidelines, I inform members of the media who are here or who may be joining us that while Committee members and witnesses may be filmed or recorded, people in the public gallery should not be the primary focus of any filming or photography. I also remind media representatives that they are not authorised to film outside the hearing room without permission and may not film witnesses entering or leaving the hearing room. Media representatives must take responsibility for what they publish about the Committee's proceedings. The guidelines for the broadcast of proceedings are available from the secretariat. Any questions may be directed to the secretariat.

There may be some questions that a witness can answer only if they had more time or with certain documents to hand. In those circumstances witnesses are advised that they can take a question on notice and provide an answer within 21 days. In terms of adverse mention and patient privacy, which is paramount to the inquiry, please be careful when using the names of individuals during the hearing in order to avoid unnecessary harm to the reputation of people. Please ensure your comments are relevant to the terms of reference. I also remind participants to respect the privacy of individual patients.

It is important to remember that parliamentary privilege does not apply to what witnesses may say outside the hearing about their evidence at the hearing. I urge witnesses to be careful about any comments they make to the media or to others after they complete their evidence. As such, they would not be protected by parliamentary privilege if another person decided to take an action for defamation. Specifically for this inquiry, some content of this hearing may be distressing, especially for patients and family members. If anyone in the audience feels distressed by the evidence that they hear today please approach the secretariat and they will arrange for someone to speak with you.

In terms of delivery of messages and documents tendered to the Committee, witnesses are advised that any messages should be delivered to the Committee members through the Committee staff. Finally, I ask everyone to please turn off their mobile phones or set them to silent for the duration of the hearing. Dr Grygiel, I note you have legal counsel. I note for the record that legal counsel is not to take questions. They can give you advice or help but they will not be taking questions from the Committee. There will be no opportunity for them to speak to the Committee throughout the proceedings. You are quite welcome to take advice.

JOHN JOSEPH GRYGIEL, medical oncologist, affirmed and examined

The CHAIR: Do you have an opening statement, Dr Grygiel?

Dr GRYGIEL: I do, sir. I am a medical oncologist and associate professor of medicine. I also have a doctorate in pharmacology. I have always had significant interest in pharmacology and oncology research, including running clinical trials in oncology. My involvement in the research process has maintained my interest and awareness of best practice and up-to-date advances in oncology. I have devoted my entire career to the ethical treatment of cancer patients. I very much regret the distress my patients have suffered as a result of the publicity surrounding this inquiry. I have always provided the best clinical management for each patient I have treated. I have always been open and honest in my discussion with my patients, their families and my colleagues concerning proposed treatment.

As time is of the essence I would like to make a number of points to conclude. First, the heart of my clinical practice has always been the best interest of each of my patients. Secondly, the most effective treatment is based on a combination of scientific evidence and clinical judgement. Thirdly, it is important to distinguish chemotherapy as a radiosensitiser and as a tumouricdal therapy. When treating head and neck patients it is intended as a radiosensitiser and not to kill cancer cells, which is the purpose of radiotherapy. Fourthly, the guidelines are important but the weight given to the guidelines depends on the level of scientific evidence behind them.

Fifthly, in the cases that have prompted this inquiry there is no evidence that the guideline dose would have led to a better outcome. Indeed, in many cases I believe it could have had a negative impact as it would have discouraged patients from continuing treatment. Cancer treatment is a complex process and there are numerous factors that need to be taken into account: the type of cancer and its stage; patient factors, including age, general state of health, and vital organ function; and co-morbidities. The purpose of treatment needs to be outlined as to whether it is curative in intent or palliative in intent. Lastly, the evidence of efficacy of treatment and the toxicity of treatment needs to be balanced. These factors are integrated to identify, if possible, the best choice in treatment before an ultimate agreement is reached between the patient and their family and the medical oncologists. Thank you.

The CHAIR: Yesterday the Committee heard that no evidence had been given to patients about this flat dosing issue. Do you have evidence that you can provide to the Committee explaining why you based your decision on that particular treatment?

Dr GRYGIEL: Are you asking me whether there is evidence—

The CHAIR: I am talking about the carboplatin flat dosing as it is known.

Dr GRYGIEL: To justify the practice?

The CHAIR: Yes.

Dr GRYGIEL: The evidence starts in 1985 with the publication in cancer treatment reviews of research by the scientist Evan Douple, which demonstrated that for carboplatin and cisplatin very low doses were all that was required to sensitise cancer cells to the cytotoxic effect of radiotherapy. That was the first issue. Then there are the dose finding studies of Maria Jacobs and Mario Eisenberger published in 1989 in the *International Journal of Radiation Oncology, Biology and Physics*, which demonstrated a series of doses of carboplatin from 60 milligrams per metre squared, which in the majority of Australian patients would be around 100 milligrams per week. They were tested and the level of dosing went up to 400 milligrams per metre squared. The conclusion of the study demonstrated that there was no difference in terms of efficacy between the doses. More recently, in 2012, a paper was published about the utility of flat dosing carboplatin using 150 milligrams per week with radiotherapy versus radiotherapy alone. It showed a clear benefit from the combination of chemo/radiotherapy over radiotherapy alone with fewer side effects than for more conventional doses of carboplatin.

The Hon. WALT SECORD: I am the Labor Party's health spokesperson. Dr Grygiel, we listened to your opening statement and you expressed regret. However, at no stage in that statement did you apologise to your former patients, your late patients, or their family members. Why have you not apologised to your patients and their families?

Dr GRYGIEL: I do not believe that there has been any demonstration that a dose of 100 milligrams of carboplatin per week with radiotherapy is in any way inferior to any other dose that has been published. Under those circumstances, I do not believe that any patient has not had the total benefit of the drug.

The Hon. WALT SECORD: Are you telling the Committee that of the hundreds of patients with whom you have been involved since 1989 there has been no adverse effect on their lives?

Dr GRYGIEL: No, I am not saying that. I am saying that there is no loss of efficacy in the use of a 100 milligram dose per week of carboplatin with daily radiotherapy compared with higher doses. In fact, the lesser degree of side effects associated with the 100 milligram dose gives those patients a benefit.

The Hon. WALT SECORD: Is there a reason that you are refusing to apologise? I notice that you used the word "regret". Why are you not apologising to your former patients and their families?

Dr GRYGIEL: I refer you to the Currow report, which made no finding of any harmful effect to any patient.

The Hon. WALT SECORD: Is there any point at which you questioned your clinical activity and dosing?

Dr GRYGIEL: In 2006 I had conversation with Dr Dalley, the Director of Medical Oncology at St Vincent's Hospital, who is a colleague. The discussion centred around the fact that he had been a member of the inaugural committee that set doses for carboplatin and head and neck cancer. He came back after a two- or three-day workshop and explained to me that the committee had inordinate difficulty in nominating an effective dose because there was no evidence of what that dose might be. There is evidence that a lot of doses work. As a consequence of that discussion, there was never any indication from my boss that I should adopt the guidelines that had just been promulgated. The basis of that was that there was an agreement that there was no correct dose and that my treatments had not been in any way demonstrated to be inferior to any other.

The Hon. WALT SECORD: So you decided to ignore the guidelines established in 2006, which are the guidelines to which everybody refers?

Dr GRYGIEL: No, I discussed them with Dr Dalley, who was my boss. It was a friendly discussion and it was largely pointing out the fact that the committee that set the doses set them on the basis that there was no strong evidence one way or another for any particular dose.

The Hon. WALT SECORD: Based on what you have just said, did St Vincent's Hospital or your immediate supervisor, Dr Dalley, know as early as 2006 that you were deviating from the guidelines and going off protocol?

Dr GRYGIEL: It is difficult to say that I was deviating when they were just agreed upon and not yet published. My practice until that time had been to use 100 milligrams of carboplatin weekly with daily radiotherapy. There was no other standard, and it was agreed by Dr Dalley and I as a result of that conversation that there was clearly no compelling evidence to make a change.

The Hon. WALT SECORD: How do you feel about the fact that you are the only person at St Vincent's Hospital who has lost their job since 2006?

Dr GRYGIEL: Losing my job is not the most important consideration. You must realise that maybe I am not the only person who uses those sorts of doses.

The Hon. WALT SECORD: Can you elaborate? Are there many other doctors who are doing what you were doing?

Dr GRYGIEL: Only in the sense that I have been making preparations for the Health Care Complaints Commission investigation and I was asked to review 84 patients from the St Vincent's Hospital cohort, and two of them were not mine.

The CHAIR: You said that there may be other doctors who use this dosing method for carboplatin. Are they in New South Wales, Australia or across the globe?

Dr GRYGIEL: They are from the St Vincent's Hospital cohort, so they are from New South Wales.

The Hon. WALT SECORD: So they are at St Vincent's Hospital? What has happened to those two patients? Are their cases before the Health Care Complaints Commission?

Dr GRYGIEL: I think so.

The Hon. WALT SECORD: Did you train other doctors to follow your treatment regime at St Vincent's Hospital?

Dr GRYGIEL: We had a rotational system where registrars would come through the system probably every three or six months. They would use the guidelines as their base point. I would encourage the registrars to use the guidelines to get an experience of what sort of toxicities come from using the higher dose that comes from using the area under the curve formula.

The Hon. WALT SECORD: Were there times when junior doctors, registrars or your colleagues said, "John, why are you doing this? This is different."? Were there times when they questioned your dosage decisions?

Dr GRYGIEL: Certainly.

The Hon. WALT SECORD: What did you respond to them?

Dr GRYGIEL: I explained to them the basis of the evidence that allowed a dose of 100 milligrams. They had their own personal experience of treating patients in the area under the curve formula and they had the option to use either.

The Hon. WALT SECORD: Were you surprised when Dr Richard Gallagher raised concerns with you but then continued to refer patients to you? What was your interpretation of that action?

Dr GRYGIEL: Was I surprised? I was certainly surprised because, in terms of any dissatisfaction with my practice, the only comments that were made by Dr Gallagher, on 31 August 2015, was at a meeting with Dr Brett Gardiner, Director of Clinical Governance, and Dr Gallagher, in his office, as my boss, where he told me that an internal investigation had been completed, that no patients had been harmed—

The Hon. WALT SECORD: Do you believe that no patients were harmed?

Dr GRYGIEL: I do.

The Hon. WALT SECORD: You believe that?

Dr GRYGIEL: Yes. I have been giving carboplatin 100 milligrams per week with radiotherapy since 2006 and before. In terms of the Head and Neck Clinic, the surveillance that recorded events of recurrence rates, and specifically locoregional recurrence rates referable to this group, had never changed. So there had not been more occurrence as a result of my dosing compared to the area under the curve.

The Hon. WALT SECORD: Why did St Vincent's take action against you if there is no adverse effect on patients? Why is the HCCC investigating if, using your words, there was no adverse effect on patients?

Dr GRYGIEL: That is what I was told at a meeting on 31 August.

The Hon. WALT SECORD: You were under-dosing from 2006 and on 31 August 2015 you had a meeting at St Vincent's with Richard Gallagher. What transpired at that meeting?

Dr GRYGIEL: What happened at the meeting was that the three of us met and Richard Gallagher explained the results of an internal investigation. The summary of those results was that I had been exonerated, I had no case to answer and no patients had been damaged or hurt by my treatment. They asked me at that stage, for the sake of any disgruntlement that may be held in the treatment team, would I mind adopting the area under the curve guideline. I said I had no problems with adopting the area under the curve guideline in the treatment of these patients provided I could retain the authority to down dose if side-effects determined that.

The Hon. WALT SECORD: Did you keep diary notes of that meeting? Because you used the word that you were "exonerated".

Dr GRYGIEL: I did not keep any diary notes at all.

The Hon. WALT SECORD: What do you say to patients in the State's Central West, particularly those in Orange and Bathurst, where you were their only source—the fly-in and fly-out doctor—between 1989 and 2012? Do you stand by your treatment to all those patients?

Dr GRYGIEL: I do.

The Hon. WALT SECORD: How many cases have been settled out of court involving patients from the Central West?

Dr GRYGIEL: There is only one, and that related to an entirely different matter.

The Hon. WALT SECORD: That was a cancer matter.

Dr GRYGIEL: That was a cancer matter but not a matter related to bowel cancer; it was a lymphoma case.

The Hon. WALT SECORD: So at no point did you question your activity, even after a meeting with Richard Gallagher and adverse media?

Dr GRYGIEL: There was no adverse media.

The Hon. WALT SECORD: There was no adverse media on your activity?

Dr GRYGIEL: Not in August of last year, but there was adverse media from 18 February this year.

The Hon. WALT SECORD: If, in your words, there was no adverse impact on patients—

Dr GRYGIEL: That is what I was told.

The Hon. WALT SECORD: Who told you that?

Dr GRYGIEL: Gallagher.

The Hon. WALT SECORD: Richard Gallagher. So why do you think you were removed?

Dr GRYGIEL: I cannot answer that.

The Hon. WALT SECORD: Did you tell your patients that you were giving them lower than recommended doses when you had discussions with them?

Dr GRYGIEL: They had options of using cisplatin where that was appropriate. The use of cisplatin as supposedly the most effective drug is limited to those people under 60. So people over 60 lose any advantage of cisplatin over carboplatin. Patients younger than 60 with comorbidities—

The Hon. WALT SECORD: I think you have misunderstood my question.

Dr GRYGIEL: Sorry.

The Hon. WALT SECORD: Did you tell cancer patients, people under your care, and their families that you were going to deviate from the accepted guidelines?

Dr GRYGIEL: I explained to them that there were guidelines and I explained to them that I use lower doses.

The Hon. WALT SECORD: In all cases?

Dr GRYGIEL: In all cases I explained why I use lower doses, yes.

The CHAIR: You would consider that that was informed consent?

Dr GRYGIEL: Yes, I would.

The Hon. WALT SECORD: Is there documentation to back this up or did you just have a discussion with someone?

Dr GRYGIEL: The way that the process is: you would take a history from the patient, you examine the patient, you look at all the investigational matters that had preceded you seeing the patient, order any investigations that were required and then, on the basis of all that, you would explain to the patient their options of treatment. In many cases those options of treatment were very restricted, and usually they were restricted to the use of carboplatin. I would explain to these people why that was—whether there was comorbidities or age and comorbidities—and proceed then to make a recommendation to these patients. Then I would clearly tell them that they were getting a low dose of carboplatin.

The Hon. WALT SECORD: Earlier you said that amongst the cohort that was sent to you, in the HCCC investigation there were two other patients. Are other oncologists deviating from the guideline like you?

Dr GRYGIEL: I do not know.

The Hon. COURTNEY HOUSSOS: Did you ever provide patients with the eviQ information sheets that are available?

Dr GRYGIEL: Pretty well all of them.

The Hon. COURTNEY HOUSSOS: When did you begin to provide them with the information sheets?

Dr GRYGIEL: When that program was instigated in 2009.

The Hon. COURTNEY HOUSSOS: Only from 2009 you provided them?

Dr GRYGIEL: I think that was when the program was adopted by St Vincent's. In 2006 I think the program, which was initiated by St Vincent's Hospital Medical Oncology, was called Ci-SCAT. It was taken over by the Cancer Institute and renamed and refashioned.

The Hon. COURTNEY HOUSSOS: So does your dosing, or what we would call under-dosing, of carboplatin appear anywhere in the eviQ guidelines?

Dr GRYGIEL: In the patient information that eviQ guidelines provide there is no clear-cut mention of dosing.

The Hon. COURTNEY HOUSSOS: Within the eviQ guidelines, which outline a potential range of treatments for a range of cancers, does the low, flat dosing of carboplatin appear anywhere within those guidelines?

Dr GRYGIEL: No.

The Hon. COURTNEY HOUSSOS: No?

Dr GRYGIEL: No.

The Hon. COURTNEY HOUSSOS: Not at all?

Dr GRYGIEL: It depends on what you call low dose carboplatin.

The Hon. COURTNEY HOUSSOS: 100 milligrams of carboplatin per week is what you told us is a low dose?

Dr GRYGIEL: That is right. That does not appear—

The Hon. COURTNEY HOUSSOS: It does not appear anywhere in the guidelines that are provided by the New South Wales Cancer Institute to the cancer providers in New South Wales; it does not appear anywhere?

Dr GRYGIEL: No.

The Hon. COURTNEY HOUSSOS: Did you ever seek to put that onto the eviQ guidelines?

Dr GRYGIEL: I was advised by Dr Dalley in 2013 on his retirement, when I took over the responsibility of the head and neck clinic, that it was an option to do so with the new program that was already in operation but not ready for electronic prescribing called MOSAIQ and there was an option for me to say, "Well, put in carboplatin 100 milligrams per week as a fall-back position."

The Hon. WALT SECORD: Most of the evidence relates to carboplatin. Did you flat or under dose your other patients at St Vincent's with other cancer drugs; for example, one of your patients that we are aware of who had a brain tumour? Did you also under dose those patients?

Dr GRYGIEL: I cannot say.

The Hon. WALT SECORD: You cannot say or you won't say?

Dr GRYGIEL: I cannot say because I do not know the specifics of the patient involved. I have not got the case record. I do not know who you are referring to.

Mr JEREMY BUCKINGHAM: When did you form the view that 100 milligrams of carboplatin was the most effective chemotherapeutic medication for patients with head and neck cancers?

Dr GRYGIEL: The evidence from Douple et al in 1985 refers to the fact that you can use very, very low doses of carboplatin to get maximum radiosensitisation.

Mr JEREMY BUCKINGHAM: And that is when you started adopting that methodology?

Dr GRYGIEL: Twelve years before guidelines, yes.

Mr JEREMY BUCKINGHAM: So 12 years before the guidelines. Is it not the case that you have just effectively continued to operate as you have since 1985 regardless of the guidelines and regardless of the lack of any scientific or clinical trials to back up that prescription?

Dr GRYGIEL: I think that you would be well advised to consider that there has been no evidence to define a better dose subsequent to 1987.

Mr JEREMY BUCKINGHAM: But the guidelines are based on clinical trials. The guidelines suggest that you should actually be prescribing cisplatin and you have said that once someone is older than 60 that cisplatin has no better outcome. On what basis do you make that assertion? Is there any scientific evidence to back up that when you turn 60 cisplatin is no better than carboplatin?

Dr GRYGIEL: Yes. The evidence comes from the meta-analysis data and there are two major papers that looked at huge numbers of patients, isolated patients who received single-agent platinums and came to the conclusion that single-agent platinums with radiotherapy were better than radiotherapy alone as a general statement but a very limited benefit of 5 to 8 per cent.

Mr JEREMY BUCKINGHAM: But a benefit though?

Dr GRYGIEL: A benefit absolutely. But also they made the comment that it would appear not by direct contrast, not by clinical trials that looked at cisplatin versus carboplatin, that they thought that cisplatin may be a more efficacious agent; it is a far more toxic agent and lastly they made the comment that any apparent benefit of the use of cisplatin was lost by the age of 60 and because cisplatin is such a toxic agent—

Mr JEREMY BUCKINGHAM: Are you prepared to table those reports?

Dr GRYGIEL: They are on the public record. They are referred to in the Currow report in detail.

Mr JEREMY BUCKINGHAM: And you think that they override the guidelines? You would ignore those?

Dr GRYGIEL: No, I think that they are consistent with the guidelines but they are not in a position, even though these are publications in 2010, they are not in a position to mandate dose.

Mr JEREMY BUCKINGHAM: You have indicated in your interview with Dr Currow that every patient in the western New South Wales LHD signed a consent form for chemotherapy?

Dr GRYGIEL: Yes.

Mr JEREMY BUCKINGHAM: Every single one?

Dr GRYGIEL: Yes.

Mr JEREMY BUCKINGHAM: But you were unable to provide any of those forms?

Dr GRYGIEL: The arrangement with medical records was that these consent forms were signed and they were kept in the oncology units both at Orange and Bathurst hospitals.

Mr JEREMY BUCKINGHAM: So they exist?

Dr GRYGIEL: They apparently exist.

Mr JEREMY BUCKINGHAM: And you do not have a copy of them anywhere?

Dr GRYGIEL: No.

Mr JEREMY BUCKINGHAM: It says that you handed them all over to Orange and Bathurst?

Dr GRYGIEL: That is where they belong, so yes.

Mr JEREMY BUCKINGHAM: And the patients do not have a record? They do not keep a record of that consent?

Dr GRYGIEL: I do not think so but if they wanted a copy there is no problem in them having a copy made.

Mr JEREMY BUCKINGHAM: Effectively you were the head of medical oncology in neck and head cancers at St Vincent's?

Dr GRYGIEL: Over a period of 2013 to 2016.

Mr JEREMY BUCKINGHAM: That is right so you were effectively the boss of that department then?

Dr GRYGIEL: Yes.

Mr JEREMY BUCKINGHAM: Did junior staff, either nurses, pharmacy or junior doctors ever raise with you the issue of the flat dosing of carboplatin outside the eviQ guidelines regardless of AUC guidelines?

Dr GRYGIEL: Yes, they did and I explained to them why I did it and they seemed to accept those explanations.

Mr JEREMY BUCKINGHAM: How many staff?

Dr GRYGIEL: Probably five or six?

Mr JEREMY BUCKINGHAM: So what was the process there? They came up and just said, "Dr Grygiel, why are you doing this?"

Dr GRYGIEL: "Could you explain why we are not following guidelines as opposed to using 100 milligram doses?" I said it depends on who you are talking to but if you were talking to the registrars I would encourage them to use the guidelines to experience what the toxicities were with that and then what they would realise is the down dosing of carboplatin that comes from using the guidelines gives you a dose ultimately in most patients that is about equivalent to 600 milligrams of carboplatin.

Mr JEREMY BUCKINGHAM: So effectively you knew best, you knew better?

Dr GRYGIEL: No, it is not a question of me knowing best. It is a question of them having the experience and me advising them in how to treat these patients' toxicities and how to get the best treatment.

Mr JEREMY BUCKINGHAM: But you had more experience; you had been doing this a very long time. Basically did you just bully them out of the way?

Dr GRYGIEL: No, not at all.

Mr JEREMY BUCKINGHAM: Did you ever think, "Well, maybe I should inform my peers of this"? Did you say, "Look, junior staff are coming to me." Did they ever go to Dr Gallagher or other oncologists in your area and raise those concerns and you have a discussion about it?

Dr GRYGIEL: If they went to anybody else I am not aware of it. Certainly there was no bullying going on. I explained in a friendly fashion why I did what I did. They were free as registrars to use the guidelines if they wanted and certainly I encouraged that.

Mr JEREMY BUCKINGHAM: Could you expand on the comment that was put in Dr Currow's report that at St Vincent's there were tensions, unresolved grievances and conflicts? What were those tensions, unresolved grievances and conflicts? It was a happy camp?

Dr GRYGIEL: I am not sure that you can say "a happy camp" in an oncology setting. I cannot expand any further on those comments. You should ask them whether they discovered tensions and whatever else.

Mr JEREMY BUCKINGHAM: Was this issue, the off-protocol dosing, ever raised at your multidisciplinary team [MDT] meetings?

Dr GRYGIEL: Not that I am aware of.

Mr JEREMY BUCKINGHAM: You cannot recall anyone ever saying, "Dr Grygiel, you have given this patient a flat dose. Why are you giving cisplatin and not carboplatin?"

Dr GRYGIEL: In an MTD meeting, no.

Mr JEREMY BUCKINGHAM: Was it ever raised with any of your other senior colleagues?

Dr GRYGIEL: Yes.

Mr JEREMY BUCKINGHAM: It was?

Dr GRYGIEL: Yes.

Mr JEREMY BUCKINGHAM: Who with and when?

Dr GRYGIEL: Dr Cooper and I would occasionally have discussions in which Dr Cooper would ask me to remind him why I used the dosage that I used, and I would explain to him. This started in the early 2000s.

Mr JEREMY BUCKINGHAM: He said yesterday that you never discussed dosage.

Dr GRYGIEL: I am afraid that is not correct.

Mr JEREMY BUCKINGHAM: Did you discuss it with anyone else, such as Dr Gallagher?

Dr GRYGIEL: Not with Dr Gallagher. We hardly ever spoke, and certainly not about dosing.

The CHAIR: Dr Grygiel, this is where I find systemic failure. You had multidisciplinary team meetings, with the optimal health of the patient as the outcome, and it seems that no senior clinician talked about dosage or treatment, whether radiotherapy, surgery, intravenous chemotherapy or oral chemotherapy. I find that amazing.

The Hon. TREVOR KHAN: I do not think that is the evidence.

The CHAIR: Dr Grygiel just said that he had a conversation with Dr Cooper about dosage. That is not the evidence that we had from Dr Cooper.

The Hon. TREVOR KHAN: I agree with that, but you are moving on from talking about dosage to talking about other things.

The Hon. WALT SECORD: Dr Grygiel—

The CHAIR: Order!

The Hon. WALT SECORD: You are using up our time for questions.

The CHAIR: It is the time for crossbench questions, thank you. We must remember the terms of reference. It is about process and systemic failure.

The Hon. TREVOR KHAN: I am not doubting that, but you are saying that the Committee has heard evidence that clinicians do not talk about options for surgery or the like. That is not the evidence.

The CHAIR: I did not say that.

Mr JEREMY BUCKINGHAM: Point of order—

The Hon. WALT SECORD: Dr Grygiel—

The CHAIR: Order! There is a point of order.

The Hon. WALT SECORD: Let us ask questions of Dr Grygiel.

The CHAIR: Order! This is the time for crossbench questions. Mr Jeremy Buckingham has a point of order.

Mr JEREMY BUCKINGHAM: My point of order is that the Chair is having a conversation with the Hon. Trevor Khan and taking up the time for questions.

The CHAIR: That is right. I return to my question. Dr Grygiel, is it usual practice that at an MDT meeting you would not talk about the dosage for every patient being managed by the team; you would talk only about the drugs used?

Dr GRYGIEL: Yes, it is.

Mr JEREMY BUCKINGHAM: Did you ever inform the management at St Vincent's Hospital that flat dosing of carboplatin was your practice? If so, when?

Dr GRYGIEL: In discussions with Dr Dalley in 2006 and again in discussions with Dr Dalley, my immediate superior, in 2013, on his retirement.

Mr JEREMY BUCKINGHAM: So from 2006 Dr Dalley knew.

Dr GRYGIEL: Yes.

Mr JEREMY BUCKINGHAM: Are you aware of when the executive became aware of this practice?

Dr GRYGIEL: No.

Mr JEREMY BUCKINGHAM: You do not know?

Dr GRYGIEL: I do not know.

Mr JEREMY BUCKINGHAM: So, to the best of your knowledge, it could have been when Dr Cooper raised it in June 2015.

Dr GRYGIEL: I do not know.

Mr JEREMY BUCKINGHAM: You do not know. It was never on the radar, never raised by anyone in the executive with you?

Dr GRYGIEL: That is right.

The Hon. WALT SECORD: Dr Grygiel—

The Hon. TREVOR KHAN: It is not your time for questions.

The Hon. WALT SECORD: I want to know—

The CHAIR: Order! This time has been allocated for crossbench questions.

Mr JEREMY BUCKINGHAM: Dr Grygiel, have you ever said to someone, "Do you want to die with your hair?"

Dr GRYGIEL: No.

Mr JEREMY BUCKINGHAM: You have never said that to anyone?

Dr GRYGIEL: No.

Mr JEREMY BUCKINGHAM: You do not recall saying that to my mother-in-law?

Dr GRYGIEL: No.

Mr JEREMY BUCKINGHAM: Do you think that you were acting like God?

Dr GRYGIEL: No.

Mr JEREMY BUCKINGHAM: Do you think that you were taking decisions out of patients' hands and deciding that flat dosing and low dosing was better for them in that it reduced toxicity, regardless of any evidence of whether it helped with the chemotherapy and radiation therapy?

Dr GRYGIEL: No.

The CHAIR: In your view, did the carboplatin flat dosing treatment have a benefit-to-risk ratio to the degree that you were happy to use that treatment?

Dr GRYGIEL: That is correct.

The CHAIR: You had three categories of treatment that you would use: cisplatin personalised levels, carboplatin personalised levels and carboplatin flat dose. When would you disregard the other two and choose a flat dose?

Dr GRYGIEL: The flat dose was, I suppose, a default. If you consider that the two choices of drugs are cisplatin and carboplatin, the evidence is—and it is a bias rather than strong evidence—that cisplatin is more effective than carboplatin. As I explained to Mr Buckingham, the meta-analysis made the comment that any apparent advantage of cisplatin over carboplatin in terms of efficacy is lost at the age of 60. So a patient who is 60 or older gets no benefit and gets all the additional toxicity with cisplatin. Cisplatin is given to those people who are under 60 and do not have comorbidities that prohibit its use. The distinction between the two levels of carboplatin is that if I felt a patient under 60 had significant comorbidities I would take them off the cisplatin dose, and the option was to have the area under the curve or a flat dose.

Often the general condition of these patients was such that there was no real option. One hundred milligrams was the dose that was most likely to enable these patients to get through combined chemotherapy and radiation treatment. It is very important to realise that in this treatment the dominant effect and the predominant benefit comes from radiotherapy. If you use carboplatin with radiotherapy in a dose of carboplatin that causes excessive toxicity, both treatments stop. If both treatments stop then the patient is at greater disadvantage. With the use of a flat dose, a 100-milligram dose, the toxicity coming from the chemotherapy is minimal and therefore the likelihood of completing six weeks and getting a full dose of radiotherapy is enhanced. If we look at the records at St Vincent's Hospital of the number of people who came off therapy because of toxicity, none of them came off because of chemotherapy toxicity.

The Hon. BRONNIE TAYLOR: I would like you to clarify what you said. Chemotherapy was used as a targeted combined therapy of chemotherapy and radiotherapy.

Dr GRYGIEL: That is correct.

The Hon. BRONNIE TAYLOR: The intent was to enhance the efficacy of the treatment, looking at the patient's comorbidities and their ability to complete the cycle of radiotherapy.

Dr GRYGIEL: That is right.

The Hon. BRONNIE TAYLOR: You had been using the modified dose with that intent since around 2006. I am not sure whether it was longer than that. It is now 2016. You made a comment earlier that at St Vincent's Hospital there were no alarming figures showing a recurrence in head and neck cancers. Has that been tested against the incidence of recurrence in head and neck cancer following treatment at other centres?

Dr GRYGIEL: I cannot say with absolute certainty because the data is kept by Dr Gallagher and, I think, by Dr Cooper. They keep a regular check on the patient's outcome. After a patient's treatment with chemotherapy we rarely, if ever, see them again. That is largely because we are very minor players, because we have the least to contribute to the benefit of the patients. People as skilled as Gallagher and Cooper keep a watchful eye on these people and document, in the longer term, their outcomes. The basis of assessing the effectiveness of treatment in this group of patients is the rate of locoregional recurrence. As far as I am aware, I have never had either of those doctors come to me and say, "We have a different rate of locoregional recurrence."

The Hon. BRONNIE TAYLOR: I would imagine that when you are dealing with head and neck patients—it is a more intensive treatment and you tend to diagnose later; correct me if I am wrong—if there were a glaring issue of recurrence out of a standard that that would have been evident.

Dr GRYGIEL: I agree.

The Hon. BRONNIE TAYLOR: In terms of the eviQ guidelines, my recollection is that it is clearly stated that they are guidelines and that they do not override the professional judgement of professionals in terms of their knowledge, expertise and experience. Would it be your knowledge that that is said very clearly within the guidelines of eviQ?

Dr GRYGIEL: I would agree, and specifically when referencing carboplatin use in head and neck patients, they acknowledge that there is very little data to back the recommendations that are made.

The Hon. TREVOR KHAN: Can I take you back to June of 2015. Is it the case that Dr Cooper came to you inquiring as to whether you were flat dosing?

Dr GRYGIEL: No.

The Hon. TREVOR KHAN: Are you aware of the evidence that he gave here yesterday?

Dr GRYGIEL: I am not.

The Hon. TREVOR KHAN: Did he not come to you in June of 2015, inquiring of you as to issues relating to dosage?

Dr GRYGIEL: As I have mentioned previously, we have had conversations over the past 10 years—

The Hon. TREVOR KHAN: I am asking about June, Dr Grygiel.

Dr GRYGIEL: —but June, no. The person who came to me to tell me that there had been an inquiry made about my dosing was Richard Gallagher, as my immediate boss.

The Hon. TREVOR KHAN: Having received the evidence of Dr Cooper and Professor Gallagher yesterday, your evidence is completely at odds with them on that issue. Do you understand that?

Dr GRYGIEL: I understand that.

The Hon. TREVOR KHAN: If we are to make a conclusion, we have to come to a conclusion as to who is telling the truth and who is not. Do you understand that?

Dr GRYGIEL: I understand that.

The Hon. TREVOR KHAN: We know that something occurred that initiated the concern of Professor Gallagher. He says that it was Dr Cooper. He says that he spoke to you about it.

Dr GRYGIEL: Dr Cooper?

The Hon. TREVOR KHAN: Dr Cooper. You still say no?

Dr GRYGIEL: No.

The Hon. TREVOR KHAN: After you were told that you were exonerated on 31 August 2015, what do you say you next found out from St Vincent's regarding their concerns with regards to your flat dosing?

Dr GRYGIEL: I had no other communication of any substance to do with it, because I was exonerated. I was completely blindsided to what happened on 18 February, when the issue was in the public media.

The Hon. TREVOR KHAN: Did you, at any stage during the period from 31 August 2015 to 18 February 2016, become alive to the fact that there was an external investigation being undertaken into your practices?

Dr GRYGIEL: Yes.

The Hon. TREVOR KHAN: So you did know that something else was going on.

Dr GRYGIEL: I was made aware by a phone call from Richard Gallagher made at Sydney airport—I cannot tell you immediately, but it will be on my phone—that he wanted to talk to me about whether I would take early retirement because it would avoid, in his words, "a shit storm" that may occur.

The Hon. TREVOR KHAN: He was certainly right about that, wasn't he? I ask you to reflect upon being blindsided. You did know that an external investigation was being undertaken.

Dr GRYGIEL: Excuse me. If you are referring to an external investigation related to Dr Brian Stein, I was aware that an external expert report was being commissioned. I had no inkling of that report until the day of the initial *7.30* report. That was shared with me by the new Head of Medical Oncology, Dr Joshua. But Dr Gallagher did ring me from the airport. He was heading off to London to some meeting. He said, "Think about this." He subsequently sent me, I think, an email—it may have been an SMS—that said, "How are you going? Are you considering what we discussed?" He said, "Don't worry, I will be back on Monday and we can discuss this further," but he never discussed it further with me.

The Hon. TREVOR KHAN: In the light of knowing that there was some form of external investigation or examination being undertaken, you never thought, "We've got a bit of a problem here"?

Dr GRYGIEL: I acknowledged that there was a bit of a problem but I did not see the solution as me taking early retirement and ducking for cover.

The Hon. TREVOR KHAN: I was not asking that. You recognised that they were undertaking an internal investigation, did you not, because St Vincent's had—self-evidently—serious concerns with regards to your practices?

Dr GRYGIEL: They never expressed those to me.

The Hon. TREVOR KHAN: Is that right!

Mr JEREMY BUCKINGHAM: Dr Grygiel—

The Hon. TREVOR KHAN: It is not your time.

Mr JEREMY BUCKINGHAM: The Chair has just said that we get one more question.

The CHAIR: Order! It is the Government's question time, and I think it is only fair to give them that time.

The Hon. NATASHA MACLAREN-JONES: I have been listening to the evidence that you have given today. It is clear that you believe that the dosing you were giving to patients was in their best interests, and you were causing no harm. If that is the case, why did you not challenge the guidelines with the Cancer Institute?

Dr GRYGIEL: Initially, because I was not really involved much in the treatment of head and neck patients in 2009. It did not seem to me, or to Dr Dalley, when we discussed it, an important issue to raise. I raised it with him. He was on the inaugural group of medical oncology consultants interested in head and neck, which came out with these guidelines. Even in our conversation at that stage—in 2006, I think—we agreed that my dosing was adequate.

The Hon. NATASHA MACLAREN-JONES: But you did not bother to raise it with the institute. You said "initially". Does that mean that at some stage you actually did go to them?

Dr GRYGIEL: In the year 2006 there was CiSCAT, which was St Vincent's program. In 2009 it had been adopted by the Cancer Institute. There was not any compelling reason, and I was not involved in a lot of—

The Hon. NATASHA MACLAREN-JONES: Surely, if you believed that your practice was the best practice you would have wanted that implemented elsewhere?

Dr GRYGIEL: I thought it was the least toxic, but equally efficacious practice.

The Hon. NATASHA MACLAREN-JONES: But surely you would want to conduct your own clinical trials?

Dr GRYGIEL: I think the issue is that the committee that set the doses said that the doses were manageable, and clinical experience had shown me that a cumulative dose that was ultimately reached was in the order of 600 milligrams over a six-week period. That, to me, meant that I could deliver that without the excessive toxicity.

The Hon. NATASHA MACLAREN-JONES: I just cannot understand why you would not have bothered to challenge it or call for proper trials.

Dr GRYGIEL: Why not do some trials?—because the benefit of the chemotherapy in essence is extremely small. So to show a difference between my dose and the AUC dose would probably require about 5,000 patients on each arm of treatment. It would require an internationally cooperative study to do it. What you would achieve, if I was correct, was the determination of bio-equivalence—an equivalent effect. Most people in oncology doing research would want to spend that time, money and effort in finding something much better. So, new drug development is where they would go. The idea of refining doses is not really in the ambit of most oncology research. Oncology research has a flaw in that it determines maximum tolerated dose. In lots and lots of trials of drugs, there is evidence that that maximum tolerated dose is not given to the patients during the trial, that the compliance is sometimes as low as 50 per cent, meaning that of the intended dose of a protocol in the trial, people getting that trial drug only get 50 per cent of the intended dose, yet there is still a benefit. That gives you the hint that the maximum tolerated dose is indeed what it sounds like, something that just does not kill the patient, to a dose which is much more moderate and gains the effect in respect of efficacy that promotes the drug into being a benefit to the patient.

The Hon. TREVOR KHAN: Doctor, I want to go back to your meeting of 31 August. You have said that you were told you were exonerated.

Dr GRYGIEL: Yes.

The Hon. TREVOR KHAN: Is that the word that was used?

Dr GRYGIEL: Yes.

The Hon. TREVOR KHAN: Who used the word "exonerated"?

Dr GRYGIEL: Richard Gallagher.

The Hon. TREVOR KHAN: Who was present apart from yourself when the word "exonerated" was used?

Dr GRYGIEL: Dr Brett Gardiner.

The Hon. TREVOR KHAN: If I go back to Professor Gallagher and perhaps go to Dr Gardiner, are they going to back you in that you were told you were exonerated on 31 August?

Dr GRYGIEL: Yes, I am confident, but I have proof that these statements were made in that in mounting a defence from the initial *7.30* report, I, with the help of my legal team, made a submission of what had actually happened, and had emailed it to Brett Gardiner and to David Faktor, telling them that we intended to release this information, and Brett Gardiner replied to the email that Dr Grygiel's version of the accounts of 31 August 2015 is the correct one.

The Hon. TREVOR KHAN: Would you like to provide us with a copy of your email and the response from Dr Gardiner?

Dr GRYGIEL: Certainly.

The CHAIR: Dr Grygiel, I know it is 10 o'clock, but if you would give us the grace to ask one more question each.

The Hon. WALT SECORD: Dr Grygiel, listening to your previous answer about toxicity and young registrars and your answer to the Hon. Natasha Maclaren-Jones's question, I put to you that you were running your own clinical trials at St Vincent's, without the knowledge of St Vincent's, or without the consent or permission of patients? You have talked about an intern seeing the impact of toxicity. I put to you that you were running your own clinical trials.

Dr GRYGIEL: That is incorrect.

The Hon. WALT SECORD: I put it to you it is not. You talk about the needs of 5,000 patients, but you seemed to be running your own clinical trials and decided what toxicity levels was best for patients?

Dr GRYGIEL: That is incorrect.

Mr JEREMY BUCKINGHAM: Dr Grygiel, you said that once people were of the age of 60, there was really no benefit in them going on cisplatin and that it was better for them to be on carboplatin.

Dr GRYGIEL: No, I did not say that. The meta analysis paper—

Mr JEREMY BUCKINGHAM: That is what you are basing your view on.

Dr GRYGIEL: Yes.

Mr JEREMY BUCKINGHAM: Half of the people you flat dosed were under 60.

Dr GRYGIEL: Yes.

Mr JEREMY BUCKINGHAM: How do you explain that when not all of them had comorbidities?

Dr GRYGIEL: Well, all of them did have comorbidities.

Mr JEREMY BUCKINGHAM: Not according to Dr Currow. Every single one under 50 had comorbidities. Are you saying that in every example of flat dosing, those people under the age of 60 had comorbidities?

Dr GRYGIEL: No. There was another group who selected the lowest dose as their preferred dose, because the patient is given a choice.

Mr JEREMY BUCKINGHAM: That was the choice that you gave to them?

Dr GRYGIEL: Of course.

Mr JEREMY BUCKINGHAM: That was on your advice?

Dr GRYGIEL: That was on my advice.

Mr JEREMY BUCKINGHAM: Have you not misled us?

Dr GRYGIEL: No.

Mr JEREMY BUCKINGHAM: That is a significant cohort of people.

Dr GRYGIEL: No, I have not misled you.

Mr JEREMY BUCKINGHAM: Why did you not offer them cisplatin?

Dr GRYGIEL: Why did I not offer them cisplatin?

Mr JEREMY BUCKINGHAM: If they did not have comorbidities and they were under 60, why did you not offer them the medicine that was most likely to cure them and help them defeat cancer?

Dr GRYGIEL: Because when they weighed up what was said about efficacy and what was said about toxicity, they made the decision.

Mr JEREMY BUCKINGHAM: On your advice?

Dr GRYGIEL: I gave them two or three options in that circumstance. The vast majority of these people had comorbidities that prohibited the use of cisplatin.

Mr JEREMY BUCKINGHAM: You just said some of them did not. Some of them did not. Some of them were under 60—

Dr GRYGIEL: We are talking—

Mr JEREMY BUCKINGHAM: —and you gave them the wrong medicine?

The CHAIR: Order! Let the doctor answer the question.

Dr GRYGIEL: We are talking about two or three patients who elected to have the lowest dose.

Mr JEREMY BUCKINGHAM: On your advice?

Dr GRYGIEL: That was an option I gave them, of course.

The CHAIR: Doctor, we took some evidence that this off-protocol carboplatin prescribing was associated with an unexpectedly high rate of recurrence in head and neck cancer patients at St Vincent's Hospital. What do you say to that?

Dr GRYGIEL: I am not aware of it, and I should have been made aware of it over the 10 years that I was practising.

The Hon. COURTNEY HOUSSOS: Dr Grygiel, you have said to us this morning you were at the cutting edge. You were providing treatment that you felt in your clinical experience was the best possible treatment for patients, but you only communicated this to junior doctors and interns who questioned your judgement. Did you ever seek to publish these findings? Did you ever seek to compare notes with similar level oncologists elsewhere in Australia or around the world?

Dr GRYGIEL: No.

The CHAIR: Thank you, Dr Grygiel. We need to conclude this session. Thank you for coming forward and giving evidence. It is very important to hear both sides of the story. It will be helpful to the inquiry's outcome. I thank your legal counsel for their participation. You have taken some questions on notice. You have 21 days to answer those questions. Given your evidence, some of the Committee members may choose to ask some further questions. The secretariat will be happy to help you in having those questions back in 21 days, which will assist us.

(The witness withdrew)

(Short adjournment)

MARGARET SAVAGE, Director of Professional Practice Unit, South Eastern Sydney Local Health District, sworn and examined

JO KARNAGHAN, District Director of Medical Services, South Eastern Sydney Local Health District, affirmed and examined

JAMES MACKIE, Medical Executive Director, South Eastern Sydney Local Health District, affirmed and examined

GERRY MARR, Chief Executive, South Eastern Sydney Local Health District, affirmed and examined

The CHAIR: I ask witnesses to be careful when using individual names during the hearing in order to avoid unnecessary harm to a person's reputation. Please ensure your comments are relevant to the terms of reference. I ask participants to respect the privacy of individual patients. It is important to remember that parliamentary privilege does not apply to what witnesses may say outside their evidence at the hearing. I urge witnesses to be careful about any comments they make to the media or to others after they complete their evidence, as such comments will not be protected by parliamentary privilege if another person decided to take action for defamation.

Mr MARR: Thank you for the opportunity to address the inquiry. Recent public matters raised in relation to off-protocol prescribing of chemotherapy are not the only aspect related to clinical practice in the South Eastern Sydney Local Health District [the district]. However, when general concerns were raised by a staff member in April 2016 regarding the clinical practice of a haematologist at Sutherland and St George hospitals the district took immediate action. Consistent with NSW Health policy related to the management of complaint or concern about a clinician the matter was immediately referred to the NSW Health Care Complaints Commission and an internal investigation was commenced.

As is required under that policy a review of patients was conducted as part of the internal investigation. The clinician was advised of the concerns and the relevant patients were contacted in advance of any matters being made public. The medical council subsequently placed conditions on the clinical practice of the clinician which are published on the Australian Health Practitioner Regulation Agency. As part of those public conditions the haematologist has to be supervised in his haematology and oncology practice, he is unable to accept new referrals for haematology patients and is to advise patients he intends to continue to treat.

Investigations are continuing and the district is cooperating with the Health Care Complaints Commission and their ongoing review. While these investigations continue it would be inappropriate for the district to make any comment on specifics of this matter as it relates to the clinician or to reveal information that is likely to be the subject to patient privacy considerations. The district is happy to support the inquiry in any way it can, noting the limitations described above, as the investigation is ongoing.

The Hon. WALT SECORD: I refer to the correspondence the Committee just received involving the censorship for staff members adhering to the code of conduct?

Mr MARR: Yes.

The Hon. WALT SECORD: How many of the submissions received by the Committee were examined by the South Eastern Sydney Local Health District [SESLHD] before they were submitted?

Mr MARR: None.

The Hon. WALT SECORD: Not a single one?

Mr MARR: None at all. A note went out from the general manager at St George reminding staff that they were entitled to make any submission as an individual, but drew their attention to the policy of NSW Health that if they identified themselves as a member of staff they are not able to speak on behalf of NSW Health.

The Hon. WALT SECORD: The submissions lodged as staff, were those vetted by the SESLHD?

Mr MARR: We did not vet any submissions from staff.

The Hon. WALT SECORD: I take you back to the matters that we are here about. The matters raised in April 2016 involving Dr Phadke's patients?

Mr MARR: Yes.

The Hon. WALT SECORD: What is the status of the current investigation and is that investigation still being conducted by the local health district?

Mr MARR: It is still being conducted by the local health district. I will hand over to Dr Karnaghan or Ms Savage to give you details.

The Hon. WALT SECORD: Can you take us through what is happening with those cases?

Ms SAVAGE: There are 27 cases being reviewed as part of the investigation. They are broken up into three tranches. The first tranche has seven cases in it. Those case reviews are completed and feedback is currently being given to those families. In tranche two there are 14 cases. That review process is perhaps two-thirds completed. There has been an initial review. Dr Phadke has had an opportunity to comment and his comments have gone back to the first reviewer to finalise the review.

The Hon. WALT SECORD: These 27 cases are at St George and Sutherland hospitals?

Ms SAVAGE: Yes.

The Hon. WALT SECORD: The first tranche was seven cases and the second 14 cases. What is the third tranche?

Ms SAVAGE: The third tranche is six cases, five haematology cases and one oncology case.

The Hon. WALT SECORD: What is the status of those six cases?

Ms SAVAGE: Four of those cases have had an initial review and been send to Dr Phadke to comment on and two more that are not completed.

The Hon. WALT SECORD: What Is Dr Phadke's employment status?

Ms SAVAGE: He has been suspended from duty and his clinical privileges have been suspended.

The Hon. WALT SECORD: Is he suspended with pay?

Ms SAVAGE: Yes.

The Hon. WALT SECORD: What is the status of the 27 cases? Have all family members and patients, if they are still alive, been notified?

Ms SAVAGE: Yes.

The Hon. WALT SECORD: All 27?

Ms SAVAGE: Yes.

The Hon. WALT SECORD: Are they all from the St George-Sutherland region?

Ms SAVAGE: Yes. Some of them have since moved on. We know that some families are now living in other States.

The Hon. WALT SECORD: What do you mean by "moved on"? Have they been relocated?

Ms SAVAGE: They have relocated to other States or have had their care transferred to other people.

The Hon. WALT SECORD: For clarity, do the 27 cases involve under and low off-protocol dosing?

Ms SAVAGE: That is not a huge feature of our inquiry. I can see there is potentially one case.

The Hon. WALT SECORD: What is the concern about the other 26 cases?

Ms SAVAGE: Generally speaking, the concerns are around clinical decision-making, clinical practice, and matters such as attendance at multidisciplinary team [MDT] meetings.

Mr MARR: Attendance at MDT meetings on treatment choice.

The Hon. TREVOR KHAN: Is that attendance or non-attendance?

Mr MARR: Non-attendance.

The Hon. WALT SECORD: What were the clinical practice concerns?

Ms SAVAGE: I am somewhat concerned about answering that question.

The Hon. WALT SECORD: Why?

The CHAIR: There may be a need to hear evidence in camera given that there is an ongoing investigation. I draw the member's attention to that. I ask members to keep that in mind and to request that evidence be heard in camera if required.

The Hon. WALT SECORD: I did not realise that I was stumbling into such an area.

The CHAIR: It is up to witnesses to say that they feel uncomfortable and that evidence is part of an ongoing inquiry and should be kept confidential.

The Hon. WALT SECORD: Of the 26 cases, without going into specific cases, what are the clinical practice concerns? I want to get a sense of what we are grappling with at St George and Sutherland.

Dr KARNAGHAN: As Ms Savage indicated, the specific concerns relate to clinical decision-making and clinical treatment choices. To go into further detail starts to stray potentially into the area of findings that have not been made. It would be pure speculation on our part to enter into any more detailed discussion.

The Hon. WALT SECORD: Mr Marr, earlier this year a patient called Ray Hadley's program on 2GB. Did you launch an investigation into that case? If so, what happened?

Mr MARR: That matter is now resolved. The patient was clearly very anxious when the matter became public. She thought she was in that first tranche of patients, who were notified via the nursing staff and about whom there may be serious concerns. She was very concerned about her treatment and her prognosis. We were able to reassure her that she was not in that tranche of patients—she was in the second tranche—and that we did not have significant concerns about her treatment. She was spoken to on the telephone and was then seen by her practising haematologist. She was reassured about her treatment and her future care pathway. We consider that the matter is now resolved.

The Hon. WALT SECORD: Does she consider the matter has been resolved?

Mr MARR: Yes, she is with her haematologist. She has made no further contact with me or the district to raise any material matters. I am satisfied that she has been treated appropriately.

The Hon. WALT SECORD: At any point did you consider that as a local health district the investigation of this matter should be external from NSW Health?

Mr MARR: There are two elements of the investigation. The first is the clinical review of the actual patients whose concerns were raised by the nurses and then subsequently by a five-year look back. They are effectively externally reviewed by a practising haematologist but they are in State, they are not out of New South Wales; I consider them to be independent practitioners—not part of St George and Sutherland. The second investigation is that I have ordered an investigation into the governance matters that surround this case. We have appointed an independent chair, a retired intensivist who worked for a considerable number of years in the Clinical Excellence Commission. I expect that report to be made available to me by the end of the calendar year. We need to learn the lessons of what may have gone wrong in our governance arrangements.

The Hon. COURTNEY HOUSSOS: What support has been provided for those patients who have concerns about their treatment?

Mr MARR: All of the patients who we considered needed review have been contacted by each of the medical directors of administration at St George and Sutherland. Each patient or the family—because some patients regrettably are deceased—were offered the opportunity to come into the hospital to discuss the matters that were of concern to us. In the second tranche of patients only two patients took up the offer of coming into the hospital for further information but in the first there were seven patients—one of the patients was actually in the hospital under treatment at the time—and we effected full disclosure of all the patients. So we have had nothing back from the patients. We also set up a helpline but I cannot remember the numbers. Perhaps Ms Savage could remind me of the numbers.

Ms SAVAGE: The numbers are published on our website as well as on the inquiry's website.

The Hon. COURTNEY HOUSSOS: We have heard that it has not been staffed appropriately.

Mr MARR: It is now a State helpline. Unfortunately, I can only describe it as administrative error, the phone was not manned for a period of about 10 days. But in the period of the whole of September no phone calls were made to that helpline at all.

The Hon. COURTNEY HOUSSOS: When was that 10 day period?

Mr MARR: Ms Savage, have you got the date? I will take that question on notice and give you confirmation of the date.

The Hon. COURTNEY HOUSSOS: So there was a 10 day period between the announcement and the—

Mr MARR: No, this was at the end of the period of phone calls. All of the phone calls happened from the establishment of the helpline and they tailed off very, very quickly during the months of August and September to the point where we were receiving no calls.

The Hon. COURTNEY HOUSSOS: Was a decision then made not to staff the phone line?

Mr MARR: There was meant to be a handover to another individual who would take the call diverts onto a mobile. Something broke down in that arrangement and then the State helpline came into play. But I do emphasise that there were no phone calls in that period of time, the phone calls had tailed off and by that time we had dealt with all of the patients and all of the families' concerns. Any patient or family who requested a review of a case automatically had that review undertaken.

The Hon. COURTNEY HOUSSOS: The Committee has received information that there were still patients out there, who perhaps were not affected but were seeking information, who were unable to seek the information through the 1800 number?

Mr MARR: I am not able to confirm that detail.

The Hon. COURTNEY HOUSSOS: I would be interested if you could provide those times.

Mr MARR: I will take that question on notice and advise you.

The Hon. COURTNEY HOUSSOS: You have obviously been contacting the patients directly. What is the rough time frame between the concerns being raised and when the patients were contacted?

Mr MARR: The first concerns were raised on 28 April and elevated to the district on the 29th—and that was one patient. The managers undertook to interview the nurses and what emerged was a further concern on five patients. At that time the current patients of Dr Phadke, 36 in total, were transferred immediately to the care of other haematologists. Dr Phadke was on leave and he agreed to extend his leave. Therefore from the time of the complaint being raised, Dr Phadke has not been practising haematology or oncology at St George and Sutherland. We then undertook a five-year look back at the haematology cases that were done, and this was done by the haematologists, and the head of cancer services took a five-year look back at oncology. What emerged from there was the second tranche of patients, the 14, and all of them have been contacted. That contact with them was completed by 27 July.

The Hon. COURTNEY HOUSSOS: Between April and July all of the patients concerned were contacted?

Mr MARR: Yes.

The Hon. COURTNEY HOUSSOS: There was obviously media attention before 27 July?

Mr MARR: I believe that the first time this came into the media was on 2 August?

The Hon. COURTNEY HOUSSOS: So all families were contacted prior to the information coming into the public domain?

Mr MARR: Yes.

The Hon. COURTNEY HOUSSOS: What ongoing support provisions are in place for those patients who had previously seen Dr Phadke but were not affected by this? Is it solely the 1800 number?

Mr MARR: It is now the helpline but if patients are in continued treatment then they have access to their doctor at Sutherland and St George. But we have not had any representations from any patients raising further concerns. We consider that those patients who had concerns, or indeed we had concerns about, is a complete list.

Mr JEREMY BUCKINGHAM: Can you step me through the policies, protocols and procedures when the South Eastern Sydney Local Health District [SESLHD] learnt of these incidents and how they were enacted? I am specifically interested in how you then engaged with government.

Mr MARR: Yes.

Mr JEREMY BUCKINGHAM: I understand that you have referred to the HCCC. Did this trigger a reportable incident brief [RIB] and also an incident management policy [IMP] in your organisation?

Mr MARR: The first report was immediately put onto to our incident management system [IIMS] and that RIB was generated. We initiated contact with the ministry—

Mr JEREMY BUCKINGHAM: Can you explain to the Committee who does the following: who makes the IMP in the local health district? Who does the RIB? Who contacts the ministry? How does the mechanism work?

Mr MARR: The system is administered through a Clinical Governance Unit [CGU], and I am happy for Dr Karnaghan to give you some further detail on that. The contact with the ministry rests with my office. The briefing and ongoing dialogue is my responsibility in relation to the Ministry. Perhaps Dr Karnaghan can give you a little more detail on the conduct of RIB and severity assessment code [SAC] 1s and 2s et cetera.

Dr KARNAGHAN: Normally we are either made aware of incidents via a staff member logging an incident in the system, which is the NSW Health system for incident reporting, or sometimes that concern can be raised with a manager or sometimes directly with the Clinical Governance Unit. Then the staff member can be advised to make an IIMS.

The Hon. TREVOR KHAN: I am sorry, to make a?

Dr KARNAGHAN: To make an entry in IIMS.

Mr JEREMY BUCKINGHAM: NSW Health Incident Information Management System.

Dr KARNAGHAN: The incident management system is referred to as an IIMS. In this particular case I am actually not sure, I believe it was a staff member who lodged the IIMS. That incident is then assessed by a member of the Clinical Governance Unit and on the basis of how significant they believe the matter is an RIB would be initiated. The RIB is normally initiated and drawn up by a senior member of staff within a clinical governance unit and is signed off by the director of clinical governance before going for approval to the chief executive and sent into the ministry.

The Hon. TREVOR KHAN: How many RIBs would be initiated in any 12-month period?

Mr MARR: I will just give you the actual details of that. In the period from September 2015 to September 2016 there was a total of 1,820 IIMS posted. That resulted in SAC1, which is the most severe rating of an incident.

Mr JEREMY BUCKINGHAM: What does SAC mean?

Mr MARR: It is an assessment of the severity.

Dr KARNAGHAN: It is severity assessment code.

Mr MARR: Then it follows a very precise procedure. In that period of time we have initiated 36 SAC1s in our district and for SAC2, which is the lesser category of concern, there were 228.

The Hon. TREVOR KHAN: And all of those go off to the ministry?

Mr MARR: Yes.

The Hon. TREVOR KHAN: Is that right?

Dr KARNAGHAN: Yes.

The Hon. TREVOR KHAN: So they are not like pearls before swine; just rare events?

Mr MARR: There is a committee called CRAG, which is a committee under privilege, which I happen to be a member of, that reviews all of the SAC1s or root cause analysis in the State to learn the lessons and to look out for trends.

Mr JEREMY BUCKINGHAM: So the staff and manager log it with IIMS and it is then referred to the clinical governance unit and they categorise it as a SAC1 or a SAC2. If it is a SAC1, then does that mean it has to be an RIB?

Dr KARNAGHAN: All SAC1s and SAC2s require an RIB to be initiated.

Mr JEREMY BUCKINGHAM: That is a requirement?

Mr MARR: Yes.

Dr KARNAGHAN: Yes.

Mr JEREMY BUCKINGHAM: And how is that required?

Dr KARNAGHAN: It is required under the incident management policy.

Mr JEREMY BUCKINGHAM: And that is signed off by all LHDs; it is a NSW Health policy?

Dr KARNAGHAN: It is a NSW Health policy directive.

Mr JEREMY BUCKINGHAM: What happens if you do not? Is it a complete failure if you fail to do it?

Dr KARNAGHAN: The failure would be, I suppose, on a couple of levels. One would be the failure to ascribe an appropriate severity code rating because the rating system goes from SAC1 being the most severe down to SAC4, but obviously, as we have discussed, only SAC1s and SAC2s require the initiation of an RIB to the ministry. Clinical governance units normally have very good processes within them to identify when an RIB is required to be initiated. I think for the purposes of this Committee the issue is whether the correct severity assessment code is actually ascribed to the incident.

Mr JEREMY BUCKINGHAM: Or one at all?

Dr KARNAGHAN: Well, one has to be ascribed. That is part of the review process. When a staff member initiates an HMS, they are asked to provide what is called an initial SAC rating, which is their understanding of how bad they think it is. All of those are then reviewed by a member of staff within the clinical governance unit who have the more specialised skills and knowledge to assess the incident. They will then ascribe a SAC rating, which would then determine the course of action for the management of that particular incident.

Mr JEREMY BUCKINGHAM: In doing that is there a set of precedents that you refer to? Is there a log of incidents that you refer to; do you say, "amputated wrong leg"?

Dr KARNAGHAN: There is a matrix, which is based on how severe the impact of the incident is and also how frequently it is likely to occur. Obviously things that are considered catastrophic are given a much higher SAC rating.

Mr JEREMY BUCKINGHAM: Anything that has potentially led to mortality?

Dr KARNAGHAN: Yes.

Mr JEREMY BUCKINGHAM: That is immediately a SAC1?

Dr KARNAGHAN: Yes, be a SAC1.

Mr MARR: Immediately.

Mr JEREMY BUCKINGHAM: Immediately.

Dr KARNAGHAN: There are also within the incident management policy certain things that are mandated as SAC1s, such as wrong site surgery, deaths of custodial patients and those types of matters.

Mr JEREMY BUCKINGHAM: Interesting.

The Hon. TREVOR KHAN: Well, look, the elephant in the room: a professor is advised by a senior oncologist that another oncologist may be grossly under dosing an unknown number of patients. Do you ascribe a SAC rating for that?

Mr MARR: When the first patient's concern was raised by a nurse that generated a posting onto an adverse management system which then immediately escalated to ourselves and that is why we initiated the investigation.

The Hon. TREVOR KHAN: I am not being critical of you in any way, from what we have heard. I am not being critical. Let us be frank: if you had been in the same position as St Vincent's what would you have done, and we will put it as at a date in June 2015?

Mr MARR: Just to put it into context, the first patient's case was escalated on 28 April. By 3 May we had completed interviews with the nurses through the managers and we were notified that the first tranche of patients were six. By 9 May I had already briefed the Minister for Health on this matter and we had initiated the investigation and had actually sent the first review to one of the haematologists and oncologists at Prince of Wales by 17 May.

The CHAIR: Can you tell us how you got in contact with the Minister for Health? Secondly, would it be unusual for you to make a call to the Health person, Dr Chant, for instance, and talk through these issues?

Mr MARR: There is no absolutely prescribed matter that you would follow but I, as the chief executive, have to take a judgement call on the severity of anything that I am advised of. If we were phoning on every incident across the whole of the State every day—

The CHAIR: No, that is not my point.

Mr MARR: I took the judgement that we had significant concerns about this particular sequence of events and I was also very conscious of the publicity that was surrounding the events at St Vincent's. I think there was an obligation on me to draw that to the Minister's attention because it was a reputational issue.

The CHAIR: That is not my question necessarily. What I am trying to get in this inquiry are the stories at different hospitals and how they operate. Would it be unusual to have a call to Dr Chant and say, "Hey look, I think this is coming on the radar. These are the sorts of actions I am thinking of" and take some mentoring on which way to go, which way to promote it or not to promote it?

The Hon. TREVOR KHAN: We do not know what that conversation was.

The CHAIR: I am not asking about that specific phone call. It is not unusual at your level to make a call to suggest there are some issues and that you are thinking of doing this, this and this, without promoting it to another level at that time?

Mr MARR: At that time and so my judgement was that it was of such severity and concern that I did a brief note to the ministry on 12 May.

The CHAIR: But I am not just talking about that; I am talking about any issue that may be a major issue for the hospital you might make a call and say, "Hey, got this on the radar; checking it out and just letting you know."

Mr MARR: Absolutely.

The CHAIR: Thank you.

Mr JEREMY BUCKINGHAM: Mr Marr, when you contact the ministry, do you always contact the Chief Health Officer?

Mr MARR: No.

Mr JEREMY BUCKINGHAM: How do you do it? Is it by email or phone call?

Mr MARR: An in-house brief is written. It goes through my executive services department, which administers all of these matters. It goes to the ministry, which then decides how it will be distributed and who will take carriage of it in the ministry. That is the procedure.

Mr JEREMY BUCKINGHAM: Have you ever done that with a matter that has not triggered a reportable incident brief [RIB]? Are they all RIBs?

Mr MARR: There may be administrative issues where we need advice, which are not about patient care.

Mr JEREMY BUCKINGHAM: I am talking about patient care.

Mr MARR: We go through our RIB procedure and notify the ministry.

The Hon. TREVOR KHAN: So a phone call is not a substitute?

Mr MARR: No. It is always in writing.

Mr JEREMY BUCKINGHAM: Is there a code of conduct at the local health district [LHD] that requires all staff to report through the incident management system [IIMS] matters that they think are of concern? How are staff directed to that, if at all? Is there training? Is there a code of conduct?

Mr MARR: Both. There is a code of conduct that governs staff responsibility in these matters, but there is also a great deal of training. I am encouraged when I see the figure of 1,820 notifications. I think that is evidence of staff feeling safe to report incidents and feeling encouraged to report incidents. That there are 1,800 notifications is not in any way an indication that there must be something wrong with a hospital. We are encouraged by that number of reports.

The CHAIR: There were probably 1,800 in the past that were never reported. You are right: it is an indication of good relationship building.

Mr MARR: Yes.

The Hon. BRONNIE TAYLOR: Do your medical and radiation oncologists have annual performance reviews?

Dr KARNAGHAN: We have a performance management system for all staff.

The Hon. BRONNIE TAYLOR: I am talking about a performance review.

Dr KARNAGHAN: Yes. There is a requirement for staff specialists to have an annual performance review. There is also ministry policy on performance reviews for visiting medical officers.

The Hon. BRONNIE TAYLOR: So do all your visiting and resident medical and radiation oncologists have annual performance reviews?

Dr KARNAGHAN: At the moment I cannot tell you that we are exactly 100 per cent compliant. I am happy to take that question on notice and provide you with a more detailed answer.

The Hon. BRONNIE TAYLOR: Do the other staff who work in the hospital—allied health staff and other staff—have annual performance reviews, and are they up to date?

Mr MARR: The policy is certainly—

The Hon. BRONNIE TAYLOR: I am aware of the policy, with all due respect.

Mr MARR: I can supply you with the figures on notice. We monitor compliance. We do not just put out the policy and not concern ourselves with compliance. I do not have that information with me.

The Hon. BRONNIE TAYLOR: You spoke about your IIMS. I take on board the fact that people feel they are able to report incidents. We are talking about medical oncology. What processes of clinical governance are in place to make sure that you deal with those issues before they are reported, before staff have to report against other staff? I would imagine that if I were going to make a report—

The Hon. TREVOR KHAN: It is getting long.

The Hon. BRONNIE TAYLOR: I like to ask long questions. My colleague's background is in law and mine is in health. He likes me to keep questions short, but I am struggling. Now it has become a lot longer. I have lost my train of thought.

Mr MARR: I understand the question.

Mr JEREMY BUCKINGHAM: Are you sure?

The CHAIR: Order!

The Hon. BRONNIE TAYLOR: If someone makes a report against someone in their clinical team, I would imagine that is at a fairly serious level. What is going on before that to prevent that?

Mr MARR: There is a considerable amount of activity on the review of quality and safety in our system. For example, the multidisciplinary team, which I know the Committee has been interested in over the past few days, is a check and balance on clinicians. It provides the opportunity to talk about current cases. It is a check and balance on whether their decisions on clinical care are accurate. We have mortality and morbidity reviews. We also have grand rounds, where everyone participates and reviews cases and the lessons learned. Within our clinical governance department we have systematic processes of measuring key performance indicators on areas of infection that may have occurred in the hospital, or other indicators of safety and quality. I believe there is a systematic approach to reviewing quality and safety. In the South East Sydney Local Health District we launched a patient safety program four months ago, in both mental health and adult acute. It is called Towards Zero Together and is aimed at reducing harm to the absolute minimum.

The Hon. BRONNIE TAYLOR: I can see that, but we are looking at medical governance issues specifically. If we are looking at medical governance issues but we are waiting until a series of medical incidents are reported that are then assigned SAC1 or SAC2, where is the governance before that to prevent it from getting to the point where you are looking at 27 in the three different sections that you mentioned over several years?

Dr MACKIE: We have been doing a lot of work in the past 12 to 18 months on how we engage our senior medical staff in all of these matters. For instance, we have been reviewing unwanted clinical variation. We have a large project reviewing that in every way that we can. We have engaged our senior staff in that. They are taking the challenge on and looking at our practices in many of those areas. That dovetails very nicely with the patient safety program that Mr Marr mentioned.

Mr MARR: It is really a question of building systems of prevention and mitigation. It would be wrong to say that that gives you a 100 per cent guarantee, but we are very systematic. We sometimes talk about the culture in hospitals. We are now working with the Cognitive Institute on a program called Speaking Up for Safety. It is specifically for doctors, to give them the skills to engage with their colleagues when they have concerns, long before any adverse events occur.

The Hon. BRONNIE TAYLOR: You mentioned that the MDT is an opportunity for people to question clinical practice. Do you not think that, existing within those MDTs, there is an evident hierarchical structure amongst the health professionals? Do you think that forum is open and conducive to questions from any health professional?

The CHAIR: That question could be for any of the witnesses.

Mr MARR: There is no straightforward answer to that question.

The Hon. BRONNIE TAYLOR: A yes or no answer is fine.

Mr MARR: My background is in nursing. I was an acute nurse. I have participated in some very effective MDTs in my career. We know that there is a variation. That is why we have engaged the Cognitive Institute. We want to improve the culture and the opportunity for clinicians to feel safe in their workplace to raise matters of concern about clinical practice. That is the entire strategy that we are developing in our district.

The CHAIR: We have talked about MDTs. Given the topic of this inquiry, would it be unusual that, in an MDT that is working on a particular client's case, the senior clinicians in the MDT would not know the dosage of medication—in order to understand the outcomes for that patient?

Mr MARR: That is one of the core discussions in the MDT.

The CHAIR: You would think so, would you not?

Mr MARR: Yes. Dr Mackie may like to talk about looking at prescriptions and dosage post an MDT meeting. Would you like to make a comment on that?

Dr MACKIE: Sure. Often the MDT will decide the appropriate course and order of treatment but will not prescribe the drug protocols to be used. That would be left up to the specialist oncologist. In what I would consider to be the ideal environment, that would be done electronically. There would be a write-up session where all team members would be present. They would look at the condition, look at the eviQ guidelines and write up the appropriate chemotherapy. As those cycles go on, those write-up sessions happen each time. There should be an opportunity at each of those write-up sessions to challenge the procedure. For instance, if some of the information is missing in the electronic entry about why a clinician wants to drop a dosage, where we have an electronic system in place nurses and pharmacists will not proceed with the treatment until they have a satisfactory reason for that to occur. I think that is where we get to a great combination of clinical responsibility and the good use of an electronic environment.

The CHAIR: So, in the MDTs do you include the patient and family or next of kin to be part of that discussion, given the fact that they are part of the holistic approach to the person's outcomes?

Dr MACKIE: I believe some MDTs have patients present, but I would not say that they are always present.

The CHAIR: Normally the patient knows best about what is happening with their body when it has toxic drugs in it—and their outcomes—so one would think that that was important information to have in a discussion.

Dr MACKIE: With respect to their views—for instance around chemotherapy—they may have already had a conversation with their oncologist or haematologist about that, who would then represent their views at that discussion.

The CHAIR: That is my point. You nailed it. The fact is that an oncologist may not talk about that. He may talk about carboplatin, but the patient may say, "I am on 100 milligrams", for instance, or might give you some other input so that the other senior clinicians go, "Whoops, I have to take this into consideration because I am just about to do this or this." A senior clinician may say, "I notice a patient outcome is deteriorating. That might be because of that." That would be a reasonable thing, would it not? A patient or relative might have that key information for that MDT.

Dr MACKIE: Yes. Also, the patient information sheets that the eviQ database provides gives them a lot of that information, so they are aware of that treatment protocol and where things might go, and possible complications.

The CHAIR: Good point. So at an MDT you have a patient information sheet that would tell you that a patient may be on 100 milligrams of carboplatin a week.

Dr MACKIE: Yes, the protocols would be there.

The CHAIR: The dosage?

Dr MACKIE: The actual dosage might not be at the MDT, no.

The CHAIR: That is where the issue lies.

The Hon. TREVOR KHAN: But the dosage may vary consistently over time.

The CHAIR: It may. That is exactly my point. It might not be the same every time.

Dr MACKIE: Absolutely. The protocols allow for variation for a large range of potential, well-understood complications, and there are recommendations within those guidelines about when to drop the dose and by how much.

The Hon. TREVOR KHAN: Consistent with that, the dosage may be varied a number of times during the treatment of that patient.

Dr MACKIE: Absolutely. Sometimes it may go outside those guidelines.

The Hon. TREVOR KHAN: For quite legitimate reasons.

Dr MACKIE: Absolutely, and there would be consensus among the team that that is a sensible thing to do . That would be decided usually, rather than at the MDT, at the write-up session. That is my understanding.

The Hon. BRONNIE TAYLOR: EviQ clearly states that it is a tool and that it does not override the knowledge of the team.

Dr MACKIE: Yes.

The Hon. TREVOR KHAN: Mr Marr, you talked about why you initiated, in a sense, the formal notification procedure. That was based partly on the publicity that had developed from February on in regards to Dr Grygiel in particular. What is your evidence with regard to what you would have done, say, in January 2016 if the events that had occurred in your health district had occurred? What would you have done without that publicity having taken place?

Mr MARR: We would have initiated exactly the same investigatory process immediately.

The Hon. TREVOR KHAN: Are you sure about that?

Mr MARR: Absolutely.

The Hon. TREVOR KHAN: You did not become gun shy because of the publicity?

Mr MARR: Absolutely not. I have a very personal standard in following procedure as it relates to this. This is about patients. This is about people being harmed. This is about families being distressed. I have an absolute obligation to instigate these proceedings as quickly as possible once the evidence is put before me. As I said, we actually had instigated the first review within less than a month of the thing being notified to us that was affecting patients in that particular unit. I think that should be standard practice. Disclosure, as well, to patients and families is absolutely vital. They deserve to have disclosure. They deserve to be told and they deserve to have informed consent on the treatment that they are having or the treatment that has been changed. This is an absolute obligation on the part of the organisation. As the chief executive I have to carry that responsibility.

The Hon. TREVOR KHAN: Have you got any examples of events that occurred, let us say, before the middle of February 2006, where you initiated a course of conduct like you are describing?

Mr MARR: No. Nothing comes to mind.

The CHAIR: We are going to conclude this part of the questioning now. I ask everyone to remove themselves from the public gallery; we are going to go in camera because we want an update on a confidential investigation that is ongoing.

JENNIFER MARTIN, Chair of Clinical Pharmacology, University of Newcastle, and

STEPHEN ACKLAND, Director Hunter Cancer Research Alliance, University of Newcastle, affirmed and examined

The CHAIR: Thank for appearing before the Committee today and for being part of this inquiry. As previously stated, witnesses should be mindful that people's reputations should not be compromised, and that their comments are relevant to the terms of reference. We should be particularly respectful of the privacy of individual patients. I point out that witnesses are subject to parliamentary privilege in this room, but will not be protected once they leave it. They should be mindful of what they say to the media because they could be caught up in defamation proceedings. Do you wish to make an opening statement?

Professor MARTIN: I thank the Committee for the opportunity to speak today about what is a very important area for patients, their carers and their care. It also has implications for health services, health, and particularly pharmaceutical budgets and support services. We note the terms of reference and have three additional points that we feel are directly relevant to this inquiry. The first is that good quality, evidence-based guidelines are not generally available for tailored dosing of cancer medicines in today's complex patients. I put emphasis on the word "evidence", because there are many guidelines but many are not evidence-based, such as how we dose in the case of obesity, which is relevant for more than 50 per cent of women presenting with breast cancer. Tailored dosing is also emphasised because it is difficult for us to measure whether or not someone is getting enough of the drug, and complex because today's patients are older, frailer and co-morbid—which means they have multiple medical problems and are on many medications. That is not the same for drug trial patients.

Secondly, calculating the dose of a cancer drug is a challenging and very complicated process. No amount of guidelines will ever enable best practice for an individual patient. Thirdly, additional factors must also be considered that affect how much of the cancer drug gets to the tumour. Some of these factors are genetic, and some are related to age or other medical problems, such as whether your kidneys are operating at 100 per cent, 50 per cent or only 25 per cent, which can hinder chemotherapy. Once we accept that the pharmacology is difficult and that it may be difficult to predict, we are then left with four questions: how do we know when someone is acting appropriately outside the guidelines; how do we provide research, ethics and governance around inappropriate use outside of the guidelines; how do we get better evidence for how to individualise a dose for a patient, particularly those who fall outside the trials; and how do we implement current individualised evidence into eviQ and our current guidelines, and in particular where evidence already exists but which is changing as we get more data? I am happy to discuss aspects of clinical pharmacology and general dosing and prescribing principles, but Professor Ackland is the expert in cancer, cancer care and the dosing of cancer patients.

The Hon. COURTNEY HOUSSOS: Thank you for your time and your informative submission. I was going to start by raising the point you made in your opening statement about the lack of good quality, evidence-based guidelines available for tailored cancer dosing. That is probably the essence of what we are trying to establish. There is a very fine line between tailoring and providing standardised guidelines for patients that will give them confidence.

Professor MARTIN: Yes.

The Hon. COURTNEY HOUSSOS: In your experience as the Chair of Clinical Pharmacology, is it normal for a particular hospital or a particular department in a hospital to have an operating procedure that is outside the eviQ guidelines?

Professor MARTIN: I will let Professor Ackland talk about cancer specifically. I am a general physician and from an infectious diseases perspective we have Australian guidelines telling us how much antibiotic we should use in a standard person. However, we use that information based on the known pharmacology of that patient. We might double or halve the dose even though guidance tells us to use a specific dose. We determine whether we have it right by measuring other outcomes. We might see that the infection is getting better or we might measure the level of the antibiotic in the blood because we know that if the blood level is enough then the patient is getting enough exposure. It is like a double check and you can tailor the dose once you have made a best estimate. That is the procedure for infectious diseases, not cancer. Professor Ackland can talk about cancer.

Professor ACKLAND: It is a good question. The Committee has probably heard the answer already from the experts yesterday and perhaps this morning. There are several issues with cancer therapy that we need to bear in mind when we are dosing. The first is a thing called the "therapeutic index", which is the window of opportunity between toxicity to normal tissue on the one hand and the benefit of anti-cancer effect on the other. With most anti-cancer drugs the therapeutic window is actually quite small—that is, the first point. Secondly, medical oncologists have developed their profession incrementally since about 1964 by generally incorporating science into drug delivery, let us say that, through clinical trials. We have been very ardent in our pursuit of clinical trials and establishing a good evidence base for drug treatment of cancer, and our trainees are taught that. I would say that in general across the board, internationally as well as in Australia, medical oncologists deliver chemotherapy according to a mixture of evidence that is available in the literature, which can vary from level four to level one if you are familiar with the levels of evidence—that is, low quality versus good quality—and guidelines, which are generally based on evidence with some variation according to professional expertise consensus—and the eviQ guidelines are that way—then trying to take into account certain individual factors in an individual patient, which might lead to variability in that patient's perceived individual requirements for treatment. Does that answer your question?

The Hon. COURTNEY HOUSSOS: Is it normal practice for hospitals to build up what is considered perhaps to be an area of expertise—for example, a particular dosing system or a particular way of treating patients—that is common across a range of patients, irrespective of comorbidity?

Professor ACKLAND: In medical oncology I would say yes. It is not just common hospital practice but through a variety of meetings, conferences and things medical oncologists tend to do the same or similar things as their colleagues in other institutions would do.

The Hon. COURTNEY HOUSSOS: So if one hospital was doing something as a broad practice it would then share it through conferences, meetings or other forms of collaboration at a senior medical oncologist level or perhaps at a head of department level?

Professor ACKLAND: By and large, yes, but not in any systematic way.

The Hon. COURTNEY HOUSSOS: It is logical that if you feel you have a good way of treating patients you would then want to share that news with your colleagues, it is not?

Professor ACKLAND: Particularly if it were different to some other protocol or something else that was already in the literature.

The Hon. TREVOR KHAN: Like flat dosing?

Professor ACKLAND: I would have expected so, yes.

The CHAIR: Dr Grygiel mentioned the evidence he had on which he was basing some of his decisions. You have talked about levels of evidence one and four. Can you unwrap that a little more? For example, what would give an oncologist a tipping point to say, "That evidence gives me confidence so that I can step out a little bit further than the protocols and the eviQ system. I am going to step right out there because I have seen enough evidence to warrant a treatment that basically no-one is doing."

Professor ACKLAND: Level I evidence is what is called meta-analysis; it is an analysis of a number of randomised control trials. Level two evidence is generally randomised control trials. Either of those appearing in the peer review literature would be satisfactory evidence to follow the recommendations of those studies generally speaking. Levels three and four—level four is pretty much anecdotes and level three I cannot remember the terminology, but it is lesser levels of clinical studies that are not randomised and controlled well. In those circumstances there may be occasions, like rare things where level one or two evidence does not exist, where you could exercise judgement and step outside of—well, there may not be a standard practice. I would expect that mostly in those circumstances where those levels of evidence prevailed there would not be a standard practice.

The CHAIR: So to step outside a spectrum of reasonable bounds of care?

Professor ACKLAND: No, I do not think a physician—

The CHAIR: Should step outside that?

Professor MARTIN: Would.

The CHAIR: Would?

Professor ACKLAND: No.

The Hon. BRONNIE TAYLOR: I join the Hon. Courtney Houssos in thanking you for your submission. I draw your attention to the last section in your submission about what is not needed. What you have said there is really pertinent. I am concerned that we have had a lot of discussion about this issue, and there are obviously serious concerns, but I would like you to elaborate further on the crux of what you are saying in that part of your submission. You talk about eviQ, but if you were faced with a situation outside that normal protocol and if we had more research to demonstrate that efficacy then it is justifiable.

Professor MARTIN: It is difficult, is it not? There is the issue of evidence and then there is the issue of standard practice. I think the issue with guidelines is that they usually reflect current practice but it is the expert opinion of the people who are on the committees. Now we have had examples in Australia, for example, how we prevent deep vein thrombosis, where a pharmaceutical company has been involved in the writing of some of those guidelines. There are issues around guidelines. We have to be cognisant of who writes the guidelines. Who badges them? Who supports them? If we just take chemotherapy—I am interested in obesity and how we dose in obesity—at various hospitals around Australia the cut-off for where we cap the dose with obesity changes. The body surface area of a normal man is approximately 1.73 metres squared, based on 1980s data. Most men are now not 72 kilograms, they are probably 90 or 100 kilograms, and many men, and even women, are well over 100 kilograms. There is a question when you get over 160 kilograms, for example, which is twice the average body size, do we just double the dose for those people? Some hospitals cap the dose at a body surface area of 1.8 metres squared, which means as soon as your body's surface area is over 1.8 you do not get any more dose for that extra amount of weight. Some hospitals cap it at two metres squared, some cap it at 2.2 metres. These are guidelines that hospitals have. There are American Society of Clinical Oncology Guidelines that also give recommendations about how to dose but they are not based on evidence.

So it is the issue of evidence and then the issue of what the guidelines are, and they are very different things. But the issue with guidelines that we have is that it depends, I guess, on whether they are based on evidence, who writes them, how often they are updated; or if they are in eviQ, does it come with dosing support software that is updated by the local oncologist or the pharmacologist or pharmacist in the team? It is not just that we have a problem with guidelines per se, it is all these other issues around guidelines that need to be taken into account. The final thing about guidelines is, we have a lot of guidelines for a lot of things all the time and one of the issues is that people stop thinking. An area of reflection may well be the emergency department [ED] where we have rules about patients having to leave by four hours, or that is the incentive of when they should really go and if they should have this test and that test to make sure they have not had a heart attack. There are all these guidelines that people have to read for every single patient and it stops us sometimes thinking about, "Hang on, this patient has come with something different. They are actually quite different. They do need to sit in the ED for these number of hours." So guidelines can actually start to take away the uniqueness of somebody actually talking to a patient and understanding that they are an individual with specific health needs and a specific framework. They are our concerns around guidelines, not necessarily a blanket statement that we do not think guidelines are good.

The Hon. BRONNIE TAYLOR: Professor Ackland, do you want to add anything in particular about eviQ and cancer treatment?

Professor ACKLAND: In relation to that particular issue, no. I think in the section "What is not needed?" the thing that I was particularly passionate about is what I think is needed—that is, better quality evidence that will allow us to be more precise about the way we dose anti-cancer drugs, both the old ones and the new ones.

The real question is how do we go about gaining that better quality evidence? In the last five to 10 years the approach has been science around genetics and genomics to try to understand genetic differences between people that might be contributing to different drug behaviour. Now people are thinking about proteomics, which is the study of all the proteins in your circulating blood or whatever to do the same thing—rather expensive, possibly limited capacity to improve the predictability of the effect of drugs but I still think that we need to do something in the way we think about delivering drugs in order to understand the variability between individuals better.

One thing we can do relatively simply with existing technology is give a dose of drug and then measure how much is actually in the body, in the bloodstream; measure how quickly the patient is metabolising or eliminating that drug from their system and if it is slow then that might explain why they have more side effects than someone else and then you might be able to attach that bit of information with some other information about the patient that leads you to be able to predict the effect of the drug. What I am just describing is not predicting but explaining about the effect of the drug. Do you follow me?

The CHAIR: That would be incredibly difficult because if you have liver impairment, renal impairment or a system breakdown, that is individual.

Professor ACKLAND: Absolutely, so what I am suggesting is one way to improve the precision of what we do and understand the variability between individuals is to actually measure something in the bloodstream rather than just the side effects of the drug and in the paper from 1996 that I think we suggested by Howard Gurney, a Sydney-based medical oncologist, he explains all this in a really good, heavily cited review paper about the variability between individuals with dosing. You would know already as health professionals that you can measure liver function in the blood but it does not tell you with a great deal of precision how to dose Warfarin or Docetaxel or Gentamicin.

You are still better off to actually measure the level of the drug in the blood. In the case of Gentamicin, an antibiotic, that is done commonly. In the case of Warfarin we measure its effect; the effect that we are trying to achieve—thinning the blood. In the case of Docetaxel, an anti-cancer drug, we just do not measure it. So that leads to a lack of understanding of whether the dose that we have given of an anti-cancer drug to a patient is the right dose or not. We know what the average dose should be. That is what is in the eviQ protocol, which is based on good quality, scientific, clinical trial evidence but we do not know for that particular patient whether it is the best dose we could possibly provide, so we do not know whether 30 per cent less or 30 per cent more might be better for that patient.

The Hon. COURTNEY HOUSSOS: One of the solutions to this question of flat dosing that has been given to us is about pre-loading electronic prescribing software with the eviQ guidelines. Can you tell me whether that is appropriate or not?

Professor ACKLAND: I think it is absolutely appropriate and I think it is already being done in New South Wales, both in the public system and in the private system. At the public hospital I work at we use the ARIA database, which is supported by the Department of Health and the Cancer Institute, thank you very much, and it has been a boon for us in terms of the speed at which we can prescribe, as a repository for having the data that helps us make some treatment decisions, even though I say that there is a lot of variability around that. In the private system we are about to institute a database called MOSAIQ, which I think is in St Vincent's, which also will have the eviQ protocols loaded into it.

There is not yet a direct integration between the eviQ system and these databases but I can tell you that the people who have developed MOSAIQ are writing the connecting program so that when a change is made in eviQ it automatically goes into the prescribing databases. We would either need many more resources of other types, including human, to deliver the number of chemotherapy doses, units, whatever, to the number of patients we do in New South Wales if we did not have those sorts of electronic prescribing systems already.

The Hon. TREVOR KHAN: I have a non-medical background but I take it that the evidence from Dr Grygiel is that he was not dosing some of his patients for the purposes of chemotherapy but, rather, as a sensitiser?

Professor MARTIN: Yes.

The CHAIR: That is right, yes, radiation, a potentiation drug.

The Hon. TREVOR KHAN: So I am left with this question: if he is not using it for chemotherapy purposes but rather as a sensitiser—it is a question for both of you—what expectation would you have that he would communicate the use of that drug to the radiation oncologist? Do you just do this in a complete vacuum?

Professor MARTIN: I am not very excited about getting involved in the politics of it but the idea of using it in that way is to make the radiation more effective.

The Hon. TREVOR KHAN: I get that.

Professor MARTIN: You are interested more in looking at the overall health outcomes.

The Hon. NATASHA MACLAREN-JONES: What would your process be?

The CHAIR: As a multidisciplinary team, [MDT] would it be something you have some discussions about? As a pharmacologist, would you think there would be some interest for him to know what level you were dosing at?

Professor MARTIN: I am not sure I can really speak on that. As a pharmacologist and general physician I often get asked to give comments on other people's patients and their management. I go there and explain the way the drug should be used or this is the way I think the evidence supports it and sometimes the doctor treating that patient decides to ignore that or to do something else, usually based on their own evidence or

because there is some other factor that they think I might not have considered. I do not go to the cancer MDT meetings that in general meet and it is not uncommon for me to explain to a team that, for example, their antiepileptic or their antimicrobial drug might be used in a more appropriate way and that evidence is not always taken on board.

The Hon. TREVOR KHAN: My thought process is this: If you are using the drug as a sensitiser—again I use that terminology—you are using it essentially as a supplement or as an adjunct—

Professor MARTIN: An enhancer.

The Hon. TREVOR KHAN: —to the primary mechanism, which is the radiotherapy; if that is the case, my mind ticks over, as a poor, dumb lawyer, and says: Well, would you not have a discussion with the radiotherapist saying, "I am doing this essentially because I want to assist your outcome in the treatment of the patient"?

Professor MARTIN: I would personally but I cannot speak for somebody else.

The Hon. TREVOR KHAN: Professor Ackland?

Professor ACKLAND: I think the answer is yes. One of the principles behind multidisciplinary care is that each of the care providers communicates with each other and each of them is operating in the best interests of the patient and that is particularly the case when the care is being delivered concurrently, so I would expect my radiation oncology colleagues to pull me up if I was doing something to enhance their treatment and there was concern about the appropriateness of that. Speaking personally, in my practice there are many drugs where I believe I understand the adverse effects of combining them with radiotherapy, where I am comfortable administering the drug, but the radiation oncologist is not. In that case we usually have a discussion and most of the time I withdraw. I have never personally got into a discussion about dose in that circumstance.

The Hon. TREVOR KHAN: I understand that. It seems that if I accept what Dr Grygiel has said—and I am happy to accept in that respect what he said—then I am left with the feeling that there is something profoundly dysfunctional in not joining with your colleague in a team to say, "We can achieve the best outcome for this patient if we do X." I invite your comment on that. The very failure to communicate that is worrisome.

Professor MARTIN: It may be an individual thing or a cultural thing or an age thing.

The Hon. TREVOR KHAN: It clearly is.

Professor MARTIN: I teach and train medical students. The way that doctors communicate with each other today is quite different from the way they used to communicate. I graduated in 1993, which was 23 years ago.

The Hon. TREVOR KHAN: It is not as long ago as I graduated.

Professor MARTIN: The way we interact with our colleagues, accept feedback and challenge, take advice and work with a multidisciplinary team and with others on the board who might give us information about our patients is completely different from the way things worked in a hospital many years ago. I cannot comment on this particular case.

The Hon. TREVOR KHAN: I am 59 and I live in a world that is different from when I started practice as a lawyer, but that does not mean I am incapable of living in this world and interacting with people in a way that is reasonably expected. I understand the difference in ages—

Professor MARTIN: I agree with you, but I cannot explain what has happened there. Certainly graduating doctors of today would be expected to communicate. Issues would be raised by their supervisors and other people in the hospital if that communication was not happening.

The Hon. TREVOR KHAN: Professor Ackland, do you have anything to add?

Professor ACKLAND: I do not think I can add any comments of substance on that matter.

The Hon. TREVOR KHAN: I am left scratching my head as to why this happened.

Professor ACKLAND: There needs to be good communication between people who should be working together. It is important for them to work together well.

The CHAIR: That is right.

Professor ACKLAND: One of the real advantages of multidisciplinary team meetings is the capacity to question each other's views and reach a consensus on the best way to deliver multidisciplinary care.

The Hon. TREVOR KHAN: We have spent a lot of time talking about dosage rates. If what Dr Grygiel was doing really had a different intent—that is, to use it as a sensitiser—then a lot of this discussion falls away. We seem to be confronting a different issue from whether it was a sufficient dosage for chemotherapy purposes.

Professor ACKLAND: Absolutely.

Professor MARTIN: Yes. There may be a communication or cultural issue. I cannot answer that for him. In fairness, people may not communicate something that they think another consultant or physician may not need to know. For example, it is sometimes the case with physicians and surgeons that the communication is better between the registrars because the senior surgeon may not think that the physician needs to know about a specific issue. The surgeon has done the operation and the patient is fine, so they may think that other things do not need to be communicated unless they are asked about them. As I said, it may be a personality or a cultural issue, but it is not something that we are seeing in the younger generation of doctors.

The CHAIR: There are studies that followed that, showing that experts are shocking at giving lesser details because they just do not operate at that level anymore.

Professor MARTIN: That is correct.

The Hon. NATASHA MACLAREN-JONES: Hypothetically, in the event that a medication was not being used for its registered purpose, if you came across that situation and felt the medication would be better used for X, Y and Z, what process would you go through? Rather than writing a prescription and saying, "I will just use it," is there a process that you could or should follow?

Professor MARTIN: In a hospital, yes.

The Hon. NATASHA MACLAREN-JONES: What would that be?

Professor MARTIN: It depends on which area you are talking about.

The Hon. NATASHA MACLAREN-JONES: Oncology.

Professor ACKLAND: It depends upon the existing science behind that individual's thinking and whether that individual has identified that there is a gap in the science that needs to be filled. In other words, there may be a scientific hypothesis for doing something that is outside of convention. In that circumstance there are two ways to go. Professor Martin can comment on this because she has worked in this area for a while. If it is an individual patient experiment then you have to go through a series of regulatory processes to obtain appropriate ethical approval for that individual patient—N=1—trial to be undertaken in your hospital, under appropriate supervision. If you think it is a bigger issue and you have a scientific hypothesis for a clinical trial then you have to write a protocol, submit it to a research ethics committee and make it a proper research study in a statistically justified cohort of 25, 30, 200 or 5,000 patients.

The Hon. NATASHA MACLAREN-JONES: Before doing that, is it reasonable to expect that you would speak to colleagues and say, "I am thinking this"?

Professor MARTIN: Yes.

Professor ACKLAND: There would need to be a degree of peer review to make sure that the individual physician's thinking was sound and evidence-based enough to proceed. Then there would need to be some sort of regulatory oversight.

The Hon. NATASHA MACLAREN-JONES: Is it reasonable to say that anyone working in a hospital would know to follow those protocols or would be able to speak to someone in the hospital about following those protocols?

Professor MARTIN: Yes. During the training process there are a huge number of regulatory and supervisory arrangements in place for interns, residents, junior doctors and registrars. There is a lot of monitoring and oversight of the behaviour of junior staff and what they do every day. Amongst the consultant staff there are processes in each hospital. I have worked in a number of hospitals. Each hospital has its own way of dealing with and managing these sorts of issues. Certainly, the culture is changing and people are feeling much more comfortable about talking about mistakes, issues and concerns that they have on the ward and following them up. At my level I go straight to the consultant involved and deal with it. There has certainly been a cultural shift in the past 20 years in how we notice adverse events that are about to happen and set in place processes to fix those problems. That may be hospital specific.

Professor ACKLAND: May I add to that something I was thinking after the Hon. Courtney Houssos's earlier question. In the old days medical oncologists practised alone. There might have been two or, at most,

three in a hospital. Medical superintendents did not have a lot of understanding of what a medical oncologist did in the course of their day or why. It was too complicated and too specialised. There are drugs that have been on the Pharmaceutical Benefits Scheme since the year dot that are available for certain indications but have been consistently and conventionally used beyond those indications. Cisplatin and carboplatin are good examples. The only indication for carboplatin is small cell lung cancer, if I remember correctly, yet it is used for ovarian, head and neck, oesophagus, stomach and a number of other cancers. That is all outside of indication, according to our regulatory system. Medical oncologists routinely use those drugs, according to the available evidence in the peer-reviewed literature, outside the current registered indication for those drugs, with the approval of the hospital.

The CHAIR: They would go to conferences and just deliver their latest outcomes. Back in the early nineties and late eighties they were cutting edge in Australia, because cancer care has come so far just over this time. So, they were taking some risks for the betterment of people's care.

Professor MARTIN: Yes.

The Hon. BRONNIE TAYLOR: I presume you operate out of John Hunter Hospital. You also talked about a private facility.

Professor ACKLAND: Me?

The Hon. BRONNIE TAYLOR: Yes. I think you said that at John Hunter you were using MOSAIQ but at the private facility they were choosing to use ARIA.

Professor ACKLAND: No, in the public system it is ARIA; in the private system it is soon to be MOSAIQ.

The Hon. BRONNIE TAYLOR: Across the State there are multiple different systems, including CHARM and others.

Professor ACKLAND: Yes.

The Hon. BRONNIE TAYLOR: What is your professional opinion? Do you think it would aid in this if everyone was using the same system? Take your example in Newcastle. You have two facilities using two different software programs to prescribe.

Professor MARTIN: I know.

Professor ACKLAND: It is like Holdens and Fords, isn't it? It is like Microsoft and Apple. There are benefits in having diversity.

The CHAIR: There is no comparison; Apple is far better.

Professor ACKLAND: There are benefits in having some competition in the marketplace for things like that—you get things done quicker and so on—but on the other hand it is more difficult to integrate systems, yes.

The Hon. BRONNIE TAYLOR: That is the point I am trying to make. It is also relevant in the sharing of information when you have patients going from one facility to the next.

Professor ACKLAND: Yes; agreed. Good quality communication is required.

The CHAIR: I would like to draw your attention to an article in the *Journal of Clinical Oncology*, on 20 December 2008. Way back then they were talking about self-reported practices. A survey was done on the attitudes of US oncologists regarding off-protocol therapy. There were 146 out of 471 oncologists who responded to that. The end report virtually suggests that the attitudes and practices may vary substantially. That is certainly what we are hearing. But the feedback from that survey was that they are particularly against the idea of off-protocol treatment but many of them still agreed—I think 60 per cent agreed—that it still should be an option if the patient dared to go there, because of their treatment. So an oncologist should be able to choose to use that methodology, while many of them still disagreed with the process. Do you have a comment on how you would translate that to practice?

Professor ACKLAND: I am not familiar with that paper.

The CHAIR: I know you are not, but I would like a general thought. Should off-protocol chemotherapy be an option for patients?

Professor ACKLAND: I think it depends upon your definition of off protocol. Somewhere in the middle there is a grey zone.

The CHAIR: That is right.

Professor ACKLAND: Guidelines are established by convention and by consensus, and are based on science and a degree of experience and expertise, which is vague and hard to quantify. I argue that we should be trying to quantify that better. There should be, in a system, capacity to diverge from consensus and observe the effects of that divergence in the interests of the subject. As we are discussing generally, that should be done with discussion amongst colleagues, approval by whoever is in charge and everybody else in the team, and close observation of the effects of that change—if you can observe it.

The Hon. COURTNEY HOUSSOS: When you say "discussion among colleagues" do you mean across sub-specialities that were working together?

Professor ACKLAND: Do you mean sub-specialities like medical oncology, radiation oncology and surgical oncology?

The Hon. COURTNEY HOUSSOS: Yes.

Professor ACKLAND: Yes, but if the sub-specialties had an interest in the particular question that was being addressed. But also nurses, pharmacists and, obviously, the patient, should be involved in that discussion.

Professor MARTIN: I agree with what you say but I have an additional point. Maybe it is a cultural point for me, being involved in clinical trials, but I think that research governance and ethics should be applied too. The issue for me is knowing where it is off protocol but within evidence or current practice versus off protocol without evidence and without support. But at some point in there, as Professor Ackland has said, there is some grey. That is where I think there is a role for research and ethics committees, and in the work that we do. Often we are changing the way we dose—for example, in infectious diseases or something else. I err on the side of always giving research to the research ethics committee to have a look at our protocols. I think this is also a new development over the last 10 or 15 years; we have realised that a lot of the stuff needs to be set up properly so that we have enough patients that we are studying and that we are doing it properly so that we can get an answer at the end of it. To do that it really needs to go through a research ethics and governance process so that we can write it up and publish it at the end so that everyone else can understand what we have done and how much better or worse it is than the current protocol.

The question for me is knowing when it is really off-protocol and a research question versus its being off protocol but with reasonable hypothetical evidence to support it and the colleagues in the department supporting it. That is the grey.

The Hon. TREVOR KHAN: Can you assist me with this? We were provided with a paper yesterday entitled " Eligibility of patients with advanced non-small cell lung cancer for phase III chemotherapy trials". The results were in part that 199 patients with advanced non-small cell lung cancer were registered during the 14-month period. Characteristics of 100 patients were defined respectively. It says:

> Common reasons for ineligibility were: co-morbidities 75(40%); ECOG Performance Status ≥2 72(39%); symptomatic brain metastasis 15(8%); and previous cancers 21(11%).

Essentially, it found:

> Only 35% met trial eligibility for E1594 and 28% for SWOG9509 and TAX326.

Professor MARTIN: Yes.

The Hon. TREVOR KHAN: Is what you take from that, that something like two-thirds plus of patients are outside the guidelines?

Professor MARTIN: That is correct. That is why you are not really sure whether it is just in the grey or whether this is something that should go through ethics, because most of our patients are over 80, most are obese and a lot are not in the ethnic group that was studied. So the actual trial data that we have—from which guidelines are usually taken—do not actually apply to the individual patient in front of us.

There is a whole issue because something is outside the evidence but within it, versus giving a completely different dosing regime. Because they are older we are only going to give them half the dose, or we will give it every six weeks rather than every three. It is knowing whether it is off protocol or whether it is a research trial of a new way of using this drug in an older population group. That is the grey zone. Where you are in the culture or the organisational development of research committees depends on how close you think this is to being a new research agenda.

The Hon. TREVOR KHAN: I accept all that, but if you start from what I think was the Chair's point—that really you should not depart from the guideline or from the protocol—if you have two-thirds plus of patients who do not fit within the eligibility criteria you cannot start from a position of not departing from the protocol. It is almost as if you have to start with the guideline or protocol and then work to where you are going to end up.

Professor MARTIN: That is right. You use your pharmacological principles to understand that this is likely to be overdosing for this particular patient. I think what Professor Ackland was saying, was that we need to do what we do in infectious diseases—we measure a level of the drug and we say, "Yes, it is within the range of what we know we need to get a benefit from this drug." We do not routinely do that in New South Wales or, in fact, anywhere in Australia apart from for methotrexate, Busulfan and one or two others. We do not routinely do it for all the other drugs that we use every day, even though we know that most of the patients that we give the doses to will not get a level that is either going to give the outcome that we expect, or is without side effect.

The Hon. TREVOR KHAN: Do I take it you are capable of testing for the presence of these levels in a patient's bloods?

Professor MARTIN: We are at the stage in New South Wales that we have the capability to set this up as a statewide service.

Professor ACKLAND: But not the resources.

Professor MARTIN: Not the resources, so there are a few steps.

The Hon. TREVOR KHAN: I understand why you are here.

Professor ACKLAND: We are here to help you.

The Hon. TREVOR KHAN: Of course.

Professor MARTIN: Knowing that people have been trying to do statewide therapeutic drug monitoring for 20 and 30 years, it has been difficult for a whole lot of reasons. We realise that it is difficult. Knowing that we currently do not do that, how else can we guide dosing? What is a new research project and what is outside the guidelines but within the understanding of what should be reasonable?

The CHAIR: Guidelines are only as good as you define the key terms of why you are producing them. So there is a limitation in them.

Professor MARTIN: That is right.

The CHAIR: If you do not get that right, you are pretty well stuffed.

Professor MARTIN: Yes.

The CHAIR: That is from your education, Professor. When we are dealing with people with terminal cancer, it is devastating and they try to grab on to anything. They proceed through treatments and when nothing is working they try to grab at anything. Do you think at any point that a person should be able to work with an oncologist, in particular, to work outside the spectrum of reasonable bounds of care to achieve that small percentage that could turn their situation around?

Professor MARTIN: My thoughts are that that should be offered, but it should be in a research framework, so we are actually collecting the data and the person knows that they are in a study, for which there is not good evidence that the treatment will help them. My feeling is that it should be under a research framework.

The CHAIR: I think everyone would rather go that way, but resourcing research frameworks—

Professor MARTIN: That is exactly the problem.

The CHAIR: —which is the issue about the paper in the United States. Everyone is chasing to do the trial because they are paid by big drug companies or they are sponsored by someone, so they want the money to come into their institution, but we do not have that situation necessarily in Australia. So if you want to move outside the protocols—I think the Hon. Walt Secord was suggesting that perhaps Dr Grygiel was trying to get the evidence-based information, but within his own treatments.

Professor MARTIN: I think that is a fair thing. I was going to talk on cannabis. My other area of research is cannabis. That is a big issue for us in New South Wales at the moment. There are people who do not have other options and cannabis is a potential option for them. We know that the cannabis that is currently grown is full of fungus and heavy metals. It is not standardised; there are a heap of different compounds in it.

We do not know how much to give. We do not have a registered good, but the patient community pressure for doctors to prescribe something is huge. Doctors are saying, "I cannot give you this because there is no evidence", which is essentially what we do because we cannot give someone a drug that might make them sick. It is a real conflict for doctors in this situation.

The CHAIR: This is a key point. Having worked in palliative care, many of the patients are going to die anyway. Is this treatment going to kill them quicker or will it give them longevity?

Professor MARTIN: Yes.

The CHAIR: That is only something that a patient can take on once informed whether it is a trial, not a trial, or if we are guinea pigs, so to speak. It should be up to the person after that informed consent to allow the doctor to move outside the spectrum of reasonable bounds of care.

Professor MARTIN: Yes, although there is a regulatory framework and there are costs in that. There are costs to the health service, costs to the hospital for an expensive drug for which there is no evidence that there will be a benefit. There are other ethical issues as well. Also, the major issue is that the drug may hasten the patient's demise or make them very unwell, so there are other issues tied up in that.

Professor ACKLAND: I was going to say that this is the environment in which medical oncology and modern haematology has grown up in. In my lifetime, doctors were blamed and shamed for treating little kids with acute leukaemia with nitrogen mustard and methotrexate and amethopterin, and now we cure 90 per cent of them. It is through good quality clinical trials that patients, and in the case of children their parents, have agreed to participate in that has allowed us to get to where we are today in modern medicine. I guess what we are proposing here is that there are more things that we could do to improve the precision of delivery of drugs above and beyond what is currently available.

The CHAIR: Hear, hear! On that positive note, if there are no further questions, I thank you for participating today. It has been very helpful. You may have taken some questions on notice and you may have brought some information forward so that some Committee members may want to ask further questions. You have 21 days to answer those questions. The secretariat will be more than happy to help you. Thank you for travelling down from Newcastle. Enjoy your trip back. We wish you the best in your future endeavours and studies with the university.

Professor MARTIN: Thank you, chair, for the invitation.

(The witnesses withdrew)

The CHAIR: For the sake of people in the public gallery, the next session is in camera and I ask you to vacate the public gallery. We will re-establish the public inquiry at 9 o'clock tomorrow in Orange.