AFL ANTI-DOPING TRIBUNAL

WEDNESDAY, 21 JANUARY 2015

DAY NINE

(TRANSCRIPT-IN-CONFIDENCE)

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CHAIRMAN:	MR DAVID JONES
	MR JOHN NIXON
	MR WAYNE HENWOOD
COUNSEL ASSISTING:	MR JUSTIN HOOPER

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MR J. GLEESON QC with MS R. ENBOM appeared on behalf of AFL.

MR M. HOLMES QC with MR P. KNOWLES appeared on behalf of the CEO of ASADA.

MR D. GRACE QC with MR B. IHLE appeared on behalf of 32 players.

MR N. CLELLAND QC with MR D. HALLOWES appeared on behalf of [redacted] and Mr [redacted]

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CHAIRMAN: Are we ready to proceed as proposed with the expert witnesses?
MR HOLMES: Yes. I recall Professor Handelsman.
CHAIRMAN: Professor, would you like to go into the witness box for us; thank you.
MR HOLMES: I understand they want to keep cross-examining him.
CHAIRMAN: Yes.
MR HOLMES: I'm not sure about the Tribunal's convenience this afternoon.
CHAIRMAN: What we thought we would do, if it was convenient to everyone, was perhaps we go through to 1 and take a lunch break at 1 until 2, and then proceed from there.
MR HOLMES: Professor Handelsman has to go back to Sydney tonight.
CHAIRMAN: We will just burn the midnight oil. You're used to doing that.
MR HOLMES: Except that he must catch the plane tonight.
CHAIRMAN: He'll catch the plane, don't worry. All right. Mr Grace, would you like to continue?
MR HOLMES: I think Mr Ihle was cross-examining. Mr Grace had finished his turn.
MR GRACE: Could I just introduce to the Tribunal Dr John Vine, who is present. He will remain during the course of Professor Handelsman's cross-examination. Then he will be of course involved in this hot tub exercise.
CHAIRMAN: Okay. Sorry, Mr Ihle, to do you out of your role.
MR IHLE: No, not at all. I'm more than happy to hand over to my learned leader, if he wants to take it.
<DAVID JOSHUA HANDELSMAN, recalled:
<CROSS-EXAMINED BY MR IHLE, continued:
MR IHLE: Professor, thank you for coming back. I only have a

limited number of questions to ask you, and hopefully it won't take too long. Just before I do launch into those questions, there was a journal article that was forwarded through to the solicitors of ASADA that was requested that you familiarise yourself with. Have you had a chance to read that and digest it?

A. I read it this morning, yes.

Q. You feel familiar enough with the contents to answer a limited number of questions about it?

A. Yes. I mean it depends on the depth of the questioning, but I have had limited time to look at it but, yes, I'm happy to have a go.

Q. Before we go into questions on that article can I ask you in all of your expansive research on this topic, Thymosin Beta-4, Thymosin alpha, Thymomodulin, et cetera, et cetera, had you seen that article before?

A. Yes.

Q. You had?

A. Yes.

Q. So, prior to you being provided that by the lawyers for ASADA, you had seen that article and read it?

A. About some months ago, and it was sort of one of - you read it and it didn't stick in my memory particularly, but I have seen it and it was actually referred to in my report.

Q. That article is referred to?

A. I believe so. I'm not 100 per cent certain, but I have certainly seen it before. But I hadn't really absorbed it in the way that I would be prepared to sort of have such a discussion.

Q. I understand. Just put that aside for the moment. I just

want to ask you about some of the other articles you have cited in your report. One of those articles, and I think it is cited as the only human study of intravenous administration of Thymosin Beta-4 that you have cited, it is cited at reference No. 99.

A. Yes.

Q. And it's from the annals of New York Academy of Sciences by Ruff and others.

A. Yes.

MR HOLMES: Can I just refer to report No. 102.

CHAIRMAN: Can you just remind us, Mr Holmes, where the professor's - - -

MR HOLMES: The professor's report is in AS-4. At page 64 the report starts. He's being cross-examined about the references to that report, and his attention was drawn to 99, but 102 is the reference to the report that Mr Ihle was asking about where the professor thought that he had included a reference to it.

MR IHLE: Yes. I accept that. 102 is a reference to the article that's been provided to you.

MR HOLMES: That's at page 88.

A. Yes, as I recall.

MR IHLE: Now, as I indicated, if you could put that to the side for the moment and if we could look at the one cited at 99.

A. Yes.

Q. That's an article that's titled in relation to a study, "A randomised placebo controlled single and multiple dose study of intravenous Thymosin Beta-4 in healthy volunteers"?

A. Yes.

Q. Just so we have all got that, I circulate copies of that down the Bar table and I can hand some up to the Tribunal. Do you have a copy of that article there?
A. Not in front of me.
Q. There should be 10 copies.
CHAIRMAN: Mr Ihle, this is not already in; is that right?
MR IHLE: It's not an exhibit.
CHAIRMAN: Do you want to make it an exhibit?
MR IHLE: I will be seeking to tender it.
CHAIRMAN: We might as well do that now.
#EXHIBIT PG-12 - Article of the New York Academy of Sciences "A randomised placebo controlled single and multiple dose study of intravenous Thymosin Beta-4 in healthy volunteers".
MR IHLE: With the exception of a human trial which was abandoned because the Thymosin Beta-4 used in that human trial was not from a GMP-certified source, this is the only article you have been able to find about the administration of intravenous Thymosin Beta-4 to humans?
A. That's correct.
Q. And the focus of the study that's reported in this article was looking at adverse effects of doses of Thymosin Beta-4 on humans, was it not?
A. It's a typical phase 1 study where you are only looking to make sure the dose is safe. It's got no efficacy outcomes of any interest usually.
Q. They are not looking for benefits?
A. That's correct.
Q. They are looking for any negative - - -
A. They are looking for safety. It's a safety focus, yes.
Q. Would you agree with this classification: insofar as this

article is concerned, there was no significant adverse consequences for the administration of Thymosin Beta-4 on the subjects sampled?

A. In this study, yes.

Q. If we look at that study - - -

MR HOLMES: Can I just object to the relevance as to whether or not significant adverse consequences.

MR IHLE: One of the things that will need to be proved by ASADA is the three criteria for the addition of a substance to the prohibited list; that is, that it has performance-enhancing benefits, that it's contrary to the spirit of sport or that it's damaging to the athlete.

CHAIRMAN: Okay.

MR IHLE: This deals with the third of those.

CHAIRMAN: Okay.

MR IHLE: We see in this study that the dosages that were administered to the subjects of the study were administered over a course of 14 days?

A. Yes.

Q. And those dosages ranged from 42 milligrams?

A. Yes.

Q. To 140 milligrams?

A. Yes.

Q. 420 milligrams?

A. Yes, yes.

Q. To 1,260 milligrams?

A. Yes.

Q. So the highest dosage in relation to the subjects of that study was 1.26 grams a day?

A. That's correct.

Q. And no adverse consequences were noted?

A. In a very limited study. It is very typical that a phase 1 study is kind of like a veto system. If it is not safe in that you can't proceed. But safety of regular usage is not determined in this way. It requires phase 2 and 3, much more extensive and more detailed studies.
Q. At page 229 of that article, immediately above the heading "Acknowledgments", the conclusory sentence is, "These initial results should allow further development of a planned efficacy trial in acute myocardial infarction"?
A. Yes, that is very standard.
Q. And you would agree with that?
A. I would agree with that, yes.
Q. Thank you. So that has been tendered. I want to ask you about your 11 December report now. This is the one that responds to five specific questions that were asked of you.
A. Yes.
CHAIRMAN: Do you have that there, Professor?
A. I have it here somewhere. Yes, I have it here.
MR IHLE: In relation to the first question Mr Grace took you the other day to the reference to China, and I think you have clarified your intention in relation to that, or at least to some degree you shouldn't have said China, you should have talked about - - -
A. Yes, look, it should have been broader without reference to China. But, having said that, most of the commercially available peptides do come from China. But the comments were broader than that.
Q. And you exclude Thymomodulin as being one of the things discussed in that email for a number of reasons. One, you say it has no known performance enhancing benefit, and you

assume a performance enhancing context of that communication?

A. Correct.

Q. And you also say that Thymomodulin is obsolete and not produced anywhere in the world commercially?

A. To the best of my knowledge, the original acid lysate Thymomodulin I don't think would be produced in any Western environment, yes.

Q. That's not what the report says. It says it's not produced commercially anywhere in the world, doesn't it?

A. I think that's correct.

Q. You think that's a correct statement?

A. I do think that's a correct statement.

Q. Did you do any even preliminary searches online to see the availability of Thymomodulin?

A. I can say that if you do put that word into a search engine products will appear from disreputable sites, and I don't believe that it's likely that those represent the same material. They are just a name that's used for an unknown substance.

Q. But, if someone was to go to those disreputable sites, they could order something they believe is Thymomodulin because that's what it is advertised as?

A. That's possible, yes.

Q. Are you aware that ASADA requested a testing laboratory in Cologne to purchase Thymomodulin and have it tested?

A. No, I wasn't aware of that.

Q. I want to hand you some documents that we have been provided by ASADA.

MR HOLMES: Before it is handed up can I just have a moment to get some instructions?

CHAIRMAN: Yes, certainly, Mr Holmes.
MR HOLMES: No objection.
MR IHLE: I just want to hand to you - there are two stapled documents there. One is an email chain which commences ASADA marked document ASA-2.0068.2434 through to 2440, and then ASA-2.0068.2442 through to 2444. I will hand those and I'll hand copies up to the Tribunal.
MR HOLMES: 2440?
MR IHLE: Yes.
CHAIRMAN: It is headed "Thymomodulin - a question." So we can use that for the purposes of identifying it, Mr Ihle.
MR IHLE: It is an email chain between Dr Stephen Watt from ASADA and Hans Geyer between the date of 20 November 2014, stretching back to 12 February 2014.
CHAIRMAN: Okay. I have noted the email chain, 20/11/14 to 12/2/14.
MR IHLE: Professor, this is the first time you have seen these documents?
A. That's correct.
Q. Through your consultations with the lawyers for ASADA, Dr Watt, counsel for ASADA, no-one made you aware of the fact that at ASADA's request a testing laboratory in Cologne purchased TFX Thymomodulin and had it analysed?
A. No, I was not aware of that. I haven't been so informed, no.
Q. Does that surprise you in light of the definitive nature in which you have stated that no-one produces it commercially in the world?
A. I think that that comment still applies in the sense that it's as an acid lysate I think at least maybe in the Western world, I should say, but I don't believe that that

product is produced, at least I have not been able to find other evidence that it's produced. The fact that a product has the name "TFX Thymomodulin", it may or may not have any relationship to what I was referring to as the original thymus extract.

Q. When you now qualify the statement that it's in your report about not being commercially available in the Western world - - -

MR HOLMES: Gentlemen, this chain of correspondence, it's been suggested to the witness that that is a reference to Thymomodulin simpliciter, but TFX Thymomodulin is a totally different substance. So the assumption upon which the question is based is misleading, on my instructions. So I would ask Mr - - -

CHAIRMAN: Perhaps the professor could be asked about that in terms of TFX Thymomodulin.

MR GRACE: Where is the evidence of that?

MR HOLMES: The professor has a computer. If my friend wants to challenge this, he can look up TFX Thymomodulin and will find it's a mixture of peptides. It is a different substance.

MR IHLE: Thymomodulin itself is a mixture of peptides, is it not? I think you described it - - -

A. Yes, it is a soup. Yes, it is a soup of probably hundreds and thousands of peptides, yes.

Q. I just observe that my learned friend will of course have a right of re-examination. This document says what this document says.

CHAIRMAN: No, you continue, Mr Ihle.

MR IHLE: I tender both the email chain and the analysis report of the Deutsche sports school from Cologne in relation to

the purported analysis of TFX Thymomodulin dated December 1, 2014 from Professor Mario Thevis, PhD.

CHAIRMAN: Both those documents are PG-13.

#EXHIBIT PG-13 - Email chain between Dr Stephen Watt and Hans Geyer dated 20/11/14 to 12/2/14, and an analysis report from Deutsche Sporthochschule Koln.

MR IHLE: Just in relation to that, Professor, you will see that in the analysis report itself the reference under the description to what was tested refers to Eagle Pharmaceuticals Limited?

A. Yes.

Q. Are you familiar with Eagle Pharmaceuticals?

A. No.

Q. You have heard no reference to Eagle Pharmaceuticals in the course of your preparation for this case?

A. No.

Q. I also want to ask you about - sorry, before I do, when you - and I will refer to the question that I asked - now say in relation to Thymomodulin being produced commercially anywhere in the Western world - - -

A. That was a tentative qualification. I don't believe it's being produced in the way in which it was originally described as an acid lysate of thymus. What this material is, I have no idea.

Q. It appears to be represented as TFX Thymomodulin?

A. By God knows who and with what sense of responsibility, I don't know.

Q. At least on the face of it it would tend to suggest Eagle Pharmaceuticals; do you agree with that?

A. It appears to be. They could be just simply a post office box buying products from somewhere else and sending them

out. I don't really know.
Q. Are you aware of a company called Thymus Therapy?
A. No.
Q. When you put the tentative qualifier on "not produced commercially in the world" and include the word "Western", would you include China to be part of the Western world?
A. Look, I can't comment in any depth about where products called Thymomodulin may now be produced. I'm pretty confident that they are not produced by the standard methods that were used 100 years ago. I think that's very unlikely. I think that the commercial production plants in China are very focused on modern technology. They make peptides. They sell them sometimes with bodgie labels, but they don't usually, as far as I'm aware, extract biological material with unknown potential virus or other contaminations and so on. I don't believe that even in China that's done much.
Q. So you don't believe that there would be substances commercially produced in China that are marketed as Thymomodulin?
A. They would be marketed as Thymomodulin, but they are probably a mixture of peptides they make on a peptide synthesiser. I don't believe that they are a lysate of the thymus as originally described before Thymosin and so on were identified properly, that's going backwards 100 years, which I think in China they don't do.
Q. So, coming back to the answer to question 1 of your 11 December report, when you exclude Thymomodulin should that be read as "Thymomodulin being the lysate extracted from the thymus gland"?
A. Yes.

Q. It shouldn't be read more generally as "Thymomodulin that might be marketed as Thymomodulin"?
A. Well, no, I agree with your comment that it referred to Thymomodulin as in my original report described as an lysate of the thymus. If others choose to use misleading names, I can't account for that.
Q. I just want to show you this document. This has already been tendered. This is part of - I just want to show my learned friend because I have some markings on it and I want to be comfortable that he's happy for me to show the witness. For ease of reference I have extracted parts of Mr Mullaly's affidavit so I can ask the professor about it.
MR HOLMES: No objection.
CHAIRMAN: That's AS-16, the affidavit. So this is actually in the affidavit?
MR IHLE: This is in the affidavit. I'm not going to tender this. It has already been tendered. It is just for ease of reference. Professor, this is an affidavit that's been deposed by Mr Mullaly, a lawyer at ASADA who you know and have conferred with on a number of occasions; is that right?
A. I have met him. I have met him, yes.
Q. You see at paragraph 94 and into 95 what he says is that on 4 December last year he performed a Wayback Machine search. I don't know if you are familiar with the Wayback Machine?
A. No, I'm not actually. It sounds like a bit of science fiction.
Q. Sounds like it. He indicated that using the Wayback Machine a website from a company called Thymus Therapy

listed a product called TFX Thymomodulin for sale, and that that was for sale on their web page as of about 18 February 2012. You will see attached to that document I have given you the very next page, which is 214 - sorry, those pages might be - 213 and 214 are the extracts of that page.

A. I don't actually have page numbers like that. I have two copies of page 11 - 214, yes, okay.

MR HOLMES: I think it starts at 213.

MR IHLE: 213. See he says - - -

A. I don't have a 213. I have two copies of page 11 and then 214.

MR HOLMES: I think it starts on 213.

MR IHLE: It does, and I apologise for the photocopying error. I will hand that up. 213 is the start of exhibit DM-23.

A. Okay.

MR HOLMES: Perhaps the professor can be given the opportunity to read 213 to 215.

MR IHLE: I'm just asking him whether he has seen this and pointing to him the evidence that's already been given.

A. No, I haven't seen it, but I do note a very important point in composition. It says it's "a family of six peptides biotechnologically derived", which means it is synthesised. It is not purified by an acid thymus extract.

Q. And that's the distinction that you want to make clear today as opposed to the bald statement in your report of 11 December?

A. I'm elaborating on what I said.

Q. Clarifying?

A. Clarifying that the Thymomodulin that I referred to is

originally the acid lysate of thymus. I don't believe that's produced any more, and I think what they say here is probably a little bit ambiguous, but when they say biotechnologically derived six peptides, that can only be produced by a synthesis machine, not by a lysate. So it is not Thymomodulin by its generally accepted definition. They are just using the name.

Q. When you say "its generally accepted definition" - - -

MR HOLMES: Perhaps he could be allowed to finish.

A. The term "Thymomodulin" has a significant place in the history of the development of thymus peptides. Allen Goldstein and others have been involved in the purification. It has a very firm place. It has a specific meaning, and it means an acid lysate of calf thymus. In that sense what this represents is an attempt to hijack that name for people who perhaps have not caught up with what's happened in the last 50 years, and remember that calf thymus has got some youth promoting properties and so on. So I think this is mostly hocus-pocus, but there's enough information there to say that it is six peptides, which means it is made on a peptide synthesis machine, not by an acid extract.

MR IHLE: Okay. That is a distinction which you are able to make given your knowledge of the history of Thymomodulin and the studies that have been done by Goldstein and others?

A. From reading them, yes.

Q. And we have no knowledge or you have no knowledge as to whether the people that were party to that communication - - -

A. Which communication?

Q. -- which is the answer to question 1 of your 11 December report - - -
A. Yes.
Q. -- are so familiar with that background either?
A. I answered the question which was which is the most likely of those in the context of that message. I wasn't reflecting terribly much on the people who sent the message, other than that there is a sports scientist and a high performance manager. So their focus is on performance enhancement. That's what I took. Beyond that I wouldn't infer anything about how they think.
Q. If you go on, paragraphs 96 and 97 on page 11 of the affidavit refer to the Thymus Therapy web page as it appears on 9 January 2015, taking that on face value?
A. Sorry, can you just point me again to where you are looking?
Q. Paragraph 96.
A. Yes.
Q. On 9 January.
A. Yes, yes, got it.
Q. Mr Mullaly deposes that he performed a direct search of TFX Thymomodulin on the Thymus Therapy web page?
A. Yes.
Q. And he produces a screen dump of that at DM-33, which hopefully you will have, at page 216 and 217.
A. I have page 15 and 17, no 16.
CHAIRMAN: Yes, we are the same.
MR IHLE: I will have a word to my instructor later.
A. It is probably two-sided photocopying going wrong.
Q. Paragraph 98 - I want to read to you from Mr Mullaly's affidavit: "On 5 December I performed an internet search

on a web site called Alibaba.com for Thymomodulin powder." He says that he's "aware that the Alibaba website was a giant Chinese E-retail site that had floated on the New York Stock Exchange", et cetera, et cetera, and he refers to a Mirror newspaper article at DM-34. That's not there. He then at DM-35 produces a true copy of the search results for Thymomodulin powder on the Alibaba.com website. So, reading those things together, would you understand that to be a giant Chinese E-retailer?

A. Mm-hm.

Q. A search has been done in relation to their website and he has produced the results of that search at DM-35?

A. I'm quite familiar with Alibaba. It is well described as a giant retail site, but it's also well known that it will advertise anything that's not nailed down and there's no guaranteeing what's on there is actually available or is as it is described. It's a huge unregulated market.

Q. Do you have pages 221, 222, 223 and 224?

A. Yes, I do.

Q. Do you see the screen dump that constitutes DM-35?

A. Yes, that's it, yes.

Q. And you will see that starting on 222, the third entry there, Thymomodulin powder?

A. Mm-hm.

Q. "China, mainland. One kilogram minimum order"; yes?

A. Yes.

Q. Do you see the very next one, "Thymomodulin powder, GMP approval"? Would you have an expectation that a GMP-approved laboratory or supplier would advertise something as Thymomodulin powder without making that distinction that you have made?

A. I don't believe for a minute that a GMP-approved place would be selling Thymomodulin powder because the current status of GMP certification is such that they wouldn't meet it if they make it as an acid lysate of thymus. If they make it out of peptides just thrown together, they may or may not, but I wouldn't even take the statement that that's GMP approved without further investigation.
Q. You would have to look behind the assertion "GMP approval"?
A. Yes.
Q. Especially if it is coming from someone who themselves purport to be GMP approved?
A. Correct.
Q. It goes on "thymus extract powder" under the same heading?
A. Yes.
Q. Over the page, "GMP supplier, Thymomodulin powder. Thymomodulin. Thymomodulin powder"?
A. Yes.
Q. You see that this stuff is available by the truckload, whatever it is, they call it Thymomodulin?
A. Yes.
Q. And you can buy tonnes of it?
A. So it appears.
Q. Page - - -
A. Many of these - in fact, the last page, all of them are the same thing just repeated. They all come from Hangzhou something Pharmaceutical Company. In fact, I think all of them come from that. All of the second and third pages come from that. So it's really just one ad in various slightly modified headings.
Q. You would agree, would you not, then, that it appears that an entity purporting to be from China advertises for sale

something it calls Thymomodulin on a commercial basis?
A. It appears so.
Q. I don't need to tender those documents.
CHAIRMAN: It's already in.
MR IHLE: Going to that document which you have cited at 102, reference No. 102.
A. That is a paper, the one that you just - the one by Pierluigi, the first author?
Q. Yes, "Thymosin Alpha-1: The regulator of regulators".
CHAIRMAN: What page is this on?
MR IHLE: You don't have it. It is something that has been referred to by the professor in his report, and I'm providing copies now. He has one.
MR GRACE: 101, I think.
CHAIRMAN: At 101, is it?
MR IHLE: Or 102. First of all, that's a paper that you have referred to in the body of your report?
A. Yes.
Q. And it is a paper that you have relied on in forming the opinions of which you have advised this Tribunal?
A. Yes, in the sense that it was used in various immune stimulating settings, yes. It's one of a series that have reported that.
Q. I tender the report, the article.
#EXHIBIT PG-14 - Article entitled "Thymosin Alpha-1: The regulator of regulators".
MR IHLE: Professor, this article, does it not, focuses on, amongst other things, the effect of Thymosin Alpha-1 on endogenous T regulator cells.
A. It does.
Q. Endogenous T regulator cells, can you tell the Tribunal

what they are?

A. They are an important component of the adaptive immune system. The immune system has an innate form which is really more related to inflammation and an adaptive one, which is the sort of thing that produces antibodies and responses to viruses or bacteria and so on. So it relates to the adaptive immune response; that is, it adapts to the external environment, whether it is chemicals or infectious agents and so on.

Q. Tell me if I'm wrong about this. The T regulator cell has an integral role in regulating the immune system to outside influences, whether they be bacteria, viruses, chemicals, whatever?

A. Yes.

Q. And this article focuses on the effect of Thymosin Alpha-1 on the T regulator cells?

A. It's a study of mainly mechanisms, how those things come about, yes.

Q. And that's why it poses the question: "Is Thymosin Alpha-1 the regulator of regulators?"

A. Yes, that's a fairly flamboyant description I don't think anybody would accept in the field. It's just a vivid title that catches attention.

Q. Catchy?

A. Yes, catchy.

Q. When you say "in the field", you mean in the medical field?

A. Well, I meant specifically in immunology, but I think more broadly in medical research. This would be just regarded as a somewhat flamboyant description. This whole issue of the Annals of the New York Academy of Science, I think it was chaired by Allen Goldstein, it was a bit of a tribute

to him, so a lot of groups who worked in that area published things more or less paying tributes to him. This is a little bit like that. So it's a little bit tricked up. It's not a peer reviewed article in the same sense that most journals are.

Q. But, notwithstanding this Annals of the New York Academy of Sciences, this is at least the second one we have referred to today that you have relied upon in forming your opinions?

A. It contributed to it, yes.

Q. Notwithstanding what you have just said about it being a tribute to Mr Goldstein, under the heading "Conflict of interest" there is no conflict of interest declared; page 4?

A. Yes. I didn't mean as a conflict of interest.

Q. I want to take you now to another article that you have referred to. Do you have your report there?

A. Yes, I do.

Q. Can you just help me out for a second. What is the article at 65? Is the author Davison?

A. Davison and Brown, yes.

Q. I want to refer to that one briefly. Do you have a copy of that with you?

A. No, I don't.

Q. I will hand up a copy to you and some to the Tribunal. Again, this is an article that you have had some recourse to - - -

A. Yes.

Q. -- in preparing your opinions in this case?

A. It's an editorial that summarises viewpoints. It's not primary data, but it's thought out.

Q. You don't doubt the veracity of it?
A. It's not a question of veracity. An editorial is an opinion piece. So you can agree or disagree to some degree with the opinions in it. But it's not an unreasonable editorial.
Q. You don't disagree with the opinions expressed in that article?
A. Not in any substantial way, no. I think it's speculative, but that's the purpose of an editorial.
MR IHLE: I tender that.
#EXHIBIT PG-15 - Journal of Sports Science article "The potential use and abuse of Thymosin Beta 4 in sports and exercise science."
MR IHLE: I just want to come back a second to what we were talking about about Thymomodulin being advertised. As you pointed out in the document annexed at DM-35 to Mr Mullaly's affidavit on I think it was the second and third or the third and fourth page you say the same company is effectively advertising the same - - -
A. Two-thirds of it is one company, yes.
Q. And that's Huajin pharmacy or something?
A. It is Hangzhou Huajin Pharmaceutical something.
Q. I don't have this but we will produce it because it has just been looked up on the i-phone. But the Huajin Pharmaceutical Company advertises that Thymomodulin - it says, "Thymopeptide (Thymomodulin powder) extracted from healthy cattle thymus organ." That's the representation they make as to how this is made. We can't assume that's true, first of all.
A. Yes.
Q. But for the purposes of this question assume that it is

true.
A. Mm-hm.
Q. Does that place doubts on the opinion expressed in response to question 1 in your report?
A. Only to the extent that I make that conditional statement of belief which I really doubt. Despite what's written there, I am doubtful that that's genuine. I find it difficult to accept that assumption to make any further interpretation.
Q. It's the case, isn't it, that there are in relation to this industry incredibly unscrupulous operators who make representations which are very difficult for someone in your position and of your esteem to accept.
A. To evaluate, yes. I think that that is true. I don't know how scrupulous or unscrupulous they are. I think as I mentioned last time where somebody caused harm in milk substitution the heads of those pharmaceutical companies were executed. So it's not a totally unregulated, free environment. So I would say with some caution as to whether anything's possible or anything goes in China. I don't know that that's true.
Q. You would be very surprised, would you not, if a company that was GMP approved produced Thymomodulin powder from extractions from calf thymus?
A. I would find that hard to imagine, yes.
Q. If that company represents (a) that it's GMP approved and (b) that that's how it produces Thymomodulin you would say at least one of those two things has to be wrong?
A. I think that's more than likely, and I think it's a question of caveat emptor. If anyone goes to those sites they really should take some effort to make sure that both

of those facts, if that's what they are, are correct.
Q. You would hope so.
A. You would hope so.
Q. You were asked by ASADA to answer those five specific questions that resulted in your report of 11 December.
A. Yes.
Q. You were taken to specific parts of the evidence upon which they rely, including, for example, consent forms; you were taken to evidence of an SMS in relation to question 1; you were taken to peptide manuals and things like that.
A. Mm-hm.
Q. At any stage of your consideration of the evidence in this case and your communications with ASADA has it ever been brought to your attention that in 2011 there were communications involving the same types of people that you have been asked to comment on where the terms "Thymosin" and "Thymosin Beta-4" were used exclusively to describe two different things?
A. That was not drawn to my attention or I'm not aware of that.
Q. If that were to be brought to your attention - - -
MR HOLMES: Perhaps if my friend can be more specific. I don't know what "that" is.
CHAIRMAN: He's going to.
MR IHLE: What this Tribunal has been taken to, albeit subject to objection at this stage, is what is said to be a note of a discussion between someone who claims to be a biochemist or words to that effect and a sports scientist. At AS-3, page 114 - the Tribunal was taken to this yesterday by Mr Grace in relation to the types of questions that might be asked of Mr Charter - there's a

reference to what's been described as the shopping list. One of the items is Thymosin Beta-4 and other one is described as Thy. So that's the first piece of evidence I wanted to draw your attention to.

CHAIRMAN: What's the page, Mr Ihle?

MR IHLE: Page 114 of AS-3.

CHAIRMAN: Yes, I have it.

MR IHLE: The bottom box with the word "Ed" in the left-hand column, "Thymosin Beta-4" and then under that "Thy". So that's not something that was brought to your attention?

A. No, and I'm still not aware of it. So if you want me to comment on it I would prefer to see it.

Q. If anyone objects to what I have suggested to you is represented on the page then we will hear the objection. But assuming that to be the case - - -

MR GLEESON: I'm prepared to object. If what is happening here is that the witness is asking to see a page he's being cross-examined about and that's being resisted, then I would submit that's unfair. He should be allowed to see it.

CHAIRMAN: He should be allowed to see it.

MR IHLE: I'm happy if he sees it.

CHAIRMAN: It is probably best if the professor sees it. This is the document that Mr Ihle is referring to. It is a diary note.

MR IHLE: We are just trying to establish whether he has seen it or not; that's all.

CHAIRMAN: I don't think so.

MR IHLE: There's that document. Is that something you have seen before?

A. No, I don't believe so. I did get a bundle of documents,

but I have trouble even reading this, and I don't - no.
Q. Can you hand that back. I now want to take you to in AS-3 page 214.
A. Yes.
Q. This is again an email that the Tribunal has been taken to that bears the date of 16 December 2011.
A. Mm-hm.
Q. You will see in that table that there is both Thymosin mentioned.
A. Mm-hm.
Q. And Thymosin Beta-4.
A. Yes.
Q. Ostensibly as different items.
A. It appears so, yes.
Q. Hand that back, please. Again, is that a document you had seen before today?
A. No, I don't believe so.
Q. You draw some conclusions in your 11 December report based on a number of things that you have identified. Does the fact that Thymosin and Thymosin Beta-4 were used interchangeably around this time by people who were involved in any way influence your conclusion in relation to answer 1, keeping in mind two things: what we have now said about Thymomodulin and what we have seen in relation to what is advertised as far as Thymomodulin is concerned?
A. The document you just showed me said "Thymosin". It didn't say "Thymomodulin". So I would exclude Thymomodulin from the further comments. If there is Thymosin unspecified and Thymosin Beta-4 it is possible the unspecified form is either Alhpa-1 or Beta-4. That is a possibility, and I think that's just logical.

But, nevertheless, I come back to the point that there is no known, suspected or even rumoured performance enhancing effects of Thymosin Alpha-1. So in the setting like that I don't know why it is listed there twice. There are many reasons why that might happen. But I would still assume that it's more than likely that it is Thymosin Beta-4. But where it is not directly specified it may come in a bottle with just "Thymosin" written on it.

Q. With your experience as an endocrinologist and someone who has proffered expert evidence in a number of doping related cases and things like that - - -

A. A very limited number.

Q. Would you be aware, given your understanding of the immune system, that training at a high level of intensity and sustained training at a high level of intensity can have an immuno compromising effect on the body?

A. Not in the sense of a real immuno deficiency or serious immuno competence. I don't believe that that's true. The athletes essentially are healthy - elite healthy individuals. I don't believe they have immune deficits. Despite the fact that that's talked about, I think that that's mostly hot air, frankly.

Q. More susceptible to colds?

A. No, I don't believe so.

Q. You don't believe so?

A. No.

Q. There is no impact on the immune system?

A. I don't believe exercise has a deleterious, adverse or some other type of effect on the immune system. Athletes are not inherently immune to getting colds and flu, like

everyone else. But I don't think there is any evidence that I have ever seen that they are more likely to get it than others.

Q. You would say even if people are training at high levels of intensity for sustained periods of time that there is no compromise to that person's immune system.

A. I don't believe there is any evidence to support that. It is something you will read about in the vast echo chamber of the internet, but I don't think it has any evidence to support it. It is one of those folklores that people have. So when an athlete gets a flu they say, "It must be due to their exercise program." In reality it is not clear that that is any more common than anybody else getting the flu. Their training will be interrupted by it, so it draws attention. But I don't believe that the frequency or the severity of upper respiratory tract infections, for example, is any more in athletes than any others.

Q. What I want to ask you to do is, if you can, distinguish between that which you have read and that which you believe as an expert. Do you understand that distinction?

A. There isn't a distinction in this question.

Q. You said that there is a lot of information out there about immuno - - -

A. Yes. I don't believe it, yes.

Q. And you don't accept that?

A. No.

Q. As a professor of endocrinology you don't accept that?

A. I don't think that the evidence is there. As a career medical researcher I'm used to looking at claims as to whether they are supported by reliable evidence, and

I don't believe that that is supported by reliable evidence.

Q. You know that there has been a number of studies and attempts to boost immunity for athletes because of this alleged compromise of their immune system, don't you?

A. Look, there may be such studies. The medical research is open to all - it's a real democracy. It is open to any sort of ideas that can be tested. It doesn't mean that they have even a priori credibility to start with.

Q. If someone has a cold or a flu and they are training at strenuous levels what will that insult to their body, being the cold or flu, do by way of affecting their ability to recover from the activities they are engaged in?

A. When a person has an infection like that they need to rest a little bit, depending on how severe it is. If they overexert themselves they will feel unwell and their athletic performance may deteriorate. But I don't believe that amounts to immune deficiency or anything that needs immune boosting. That's just hype built on the fact that people who are athletes get colds and flu as well as anyone else.

Q. The same type of hype or hype that fits in the same category as giving athletes Tribulus?

A. More or less, yes. There is plenty of it around, hype that is.

Q. Don't believe the hype is what you are saying?

A. Yes, look, as a career researcher again my task is to distinguish as much as you can fact from fantasy, and there's a great deal of fantasy that needs a lot of filtering.

Q. And there's a lot of suckers out there too?
A. One born every minute, I think it was said.
MR IHLE: I don't have any further questions at this stage.
CHAIRMAN: Mr Hallowes, you are going to ask some questions?
MR HALLOWES: Yes, hopefully about 15 minutes or so.
CHAIRMAN: All right. We'll complete your questioning, if we can do it in that timeframe.
<CROSS-EXAMINED BY MR HALLOWES:
MR HALLOWES: Professor, I want to actually take you back to some questions you were asked last week about certificates of analysis.
A. Yes.
Q. Although, as I understand from your evidence, you wouldn't suggest you have seen every certificate of analysis from every manufacturer, you obviously have some familiarity with them?
A. Yes, some.
Q. I'm wanting to first of all take you to a certificate of analysis that was referred to last week, which is at page 224 of AS-3.
A. Is that the one Mr Grace called the dodgy certificate?
Q. No, it's not the one he called the dodgy certificate. It's at page 224. It is the GL Biochem certificate or what appears to be the GL Biochem certificate.
CHAIRMAN: Do you have that, Professor?
A. Yes, I have, thanks very much.
MR HALLOWES: One of the things you referred to last week was that in these sorts of certificates you will have what you might call boilerplate information.
A. Yes.
Q. That you would expect to see in essence for every

certificate of analysis that came from GL Biochem, there would be certain information that would be replicated every time.

A. Usually, yes.

Q. Putting aside the fact that we have the heading "GL Biochem" and the address down the bottom, which presumably you would expect to see every time, you have also got the warranty which says "GL Biochem warrants".

A. Yes.

Q. I take it you would expect that if a certificate of analysis came from GL Biochem on every occasion that you would see "GL Biochem warrants".

A. I would expect so, yes.

Q. Similarly, this certificate of analysis has information showing that it was prepared and checked by someone?

A. Yes.

Q. And that's what you would expect if it appears on the certificate of analysis from GL Biochem, you would expect that's what they would have every time?

A. I agree with you in general. But it is possible that a company may be so large or so disorganised that it doesn't always happen the way you expect. But in principle and in general I think you are right, yes.

Q. If it was a well-run, well-organised company you would expect to see those sorts of things repeated every time.

A. Yes, certainly.

CHAIRMAN: It's a document of some importance, Professor, isn't it?

A. Yes, very much.

CHAIRMAN: And the purpose of it is the manufacturer is saying - - -

A. This is what's in the product, yes.
CHAIRMAN: "We are supplying this product."
A. Yes.
CHAIRMAN: "And we have undertaken the process whereby we certify that this is what's in the product."
A. Yes. I agree it's very important; that's correct.
MR HALLOWES: It also clearly has a stamp on the bottom right indicating GL Biochem (Shanghai) Limited.
A. Correct.
Q. And again you would expect to see that stamp on every occasion?
A. Yes.
Q. There is some information which is clearly the actual testing results.
A. Yes.
Q. Am I right that that information is within that box that you see there which has the headings "Tests. Specifications. Results"?
A. Correct.
Q. And that's, as I understand it, indicating the actual testing that was done and the results in relation to the analysis?
A. Yes, I believe so.
Q. Then there is other information above that which would appear to be particular to the actual product that's been manufactured and it's purporting to be; have I got that right?
A. Yes, I believe so, yes.
Q. In relation to this one it is for the product MGF, Mechano Growth Factor.
A. Correct.

Q. In terms of the information we see above the box, am I right that that's not information suggesting that that is the result of the testing they have done but that is information about the product itself, its name, what its sequence should be?
A. Yes.
Q. What its molecular weight should be?
A. Yes.
Q. And what its molecular formula is?
A. Yes, it's an intention. It spells out what they intended to provide and manufacture and supply.
Q. If we just take MGF, Mechano Growth Factor, as an example, if the manufacturer has that as one of the products that they sell and they make, would it be the case that this information might not be entered by the particular operator every single time; that might actually come up every time simply - - -
A. Yes, it might be a template that they type in the catalogue number and they get the template out; yes, very likely.
Q. As you say, it is very likely. It is unlikely that every single time, if it is something that is being sold and manufactured, that the operator has to look up the sequence or type in the sequence?
A. Yes.
Q. It is likely that that information would simply be there in essence allied to the catalogue number?
A. Yes, I agree. Agree.
Q. One of the things that comes up is the molecular formula, and you would expect again that that would most likely come up. If the person typed in the catalogue number who was preparing this document the molecular formula of MGF,

Mechano Growth Factor, as it is set out there, would likely come up rather than have to be entered by the operator?

A. Yes, very likely, barring any sort of computer failure or circumstances which mean that their system isn't working and that these templates may not be available for some reason. But, yes.

Q. In terms of that molecular formula, you were taken last week to the way it's written there with the numbers in the lower type.

A. Yes.

Q. Is it fair to say that that's something that if you do year 10 science you are probably taught that's the way that you will represent any chemical formula?

A. That's a convention, yes.

Q. But it's a convention that you don't have to be a professor of endocrinology to know about?

A. No.

Q. You'd get taught that in secondary school?

A. It's a very standard convention, yes.

Q. Is it fair to say that in terms of those sorts of things therefore any time that GL Biochem were providing a certificate of analysis in relation to MGF, Mechano Growth Factor, or indeed any other substance, apart from the boilerplate, the warranty, and apart from the other matters that I have taken you to, you would expect that they would be getting the molecular formula in that same sort of notation?

A. Yes. Yes, indeed.

Q. I just want to take you now to the one which, as you indicate, Mr Grace has referred to as the dodgy - 280.

A. I have a copy.
Q. You have a copy. That's the one that's simply headed "Certificate of analysis". You have that, page 280?
A. I have it.
CHAIRMAN: Yes, we have it.
A. I have it from last time.
MR HALLOWES: What it doesn't have compared to the one at page 224, it doesn't have the heading "GL Biochem", it doesn't have GL Biochem's address, it doesn't have "GL Biochem warrants", it doesn't have anyone preparing and checking it, it doesn't have the stamp. It has the molecular formula written in a different fashion.
A. Yes. Yes, it does.
Q. Given all of those things you would say, "Well, that's highly unlikely that it would have come from GL Biochem"?
A. Look, it certainly casts doubt on it. If I knew that the company was using these boilerplate certificates of analysis consistently then this would really stick out. But there are circumstances in a laboratory, say, for example, the computers are down or somebody bought the product from GL and then decided to add some mark-up and then sell it on themselves, you know, you can imagine scenarios where this would happen. But this isn't the same as the GL Biochem's certificate of analysis.
Q. There are numerous differences?
A. Yes, sure.
Q. Including one that hasn't been raised. On page 224 there is in fact a lot number given. If you look at the certificate of analysis at page 224 for Mechano Growth Factor it says "Lot No.".
A. There is a lot number, yes.

Q. Which would suggest, would it not, that GL Biochem, apart from having the catalogue identifying the particular substance, for each certificate of analysis there is a lot number that is being analysed?
A. Yes, and you would expect to see something like that.
Q. The catalogue number itself, do I take it that that's not some chemical term?
A. No, that's an arbitrary number that a company will have in their own catalogue.
Q. That's just simply that company has a catalogue and for each item they are selling it has a number?
A. Correct.
Q. You see interestingly in relation to that - and I will take you first of all to another document which is at page 693 of AS-3 which you might not have. I will hand up a copy if you don't. Do you see at page 693 what would appear to be something that's been downloaded from the internet from GL Biochem's website?
A. Yes.
Q. And do you see that in relation to the products this would appear to be products where under the letter T you have the second one being the Thymosin Alpha-1 acetate?
A. Yes.
Q. Then you have the Thymosin Beta-4 acetate?
A. Yes. For some reason the Thymosin Alpha-1 acetate doesn't have a catalogue number.
Q. Putting that to one side for a moment, do you see the catalogue number at least for Thymosin Beta-4 is 55820?
A. Yes.
Q. And you see on the certificate of analysis, which has been called into question at page 280, they have the same

catalogue number?
A. Correct.
Q. So, despite all those other differences, whoever has produced this certificate at page 280 has, it would appear, put in the same catalogue number that in fact belongs to GL Biochem?
A. Yes.
Q. And I think you said in relation to the certificate of analysis last week at page 280 that you would describe it, certainly if an Australian company had produced it, as being substandard?
A. I believe so, yes.
Q. And that was for a number of factors including that for whatever reason it's the wrong molecular weight that's put there?
A. Yes, although - - -
Q. You have given the explanation that it might be transposed. But, however that's occurred - - -
A. But it is certainly not right.
Q. If it was the fact that whatever company had a standard when you put in the catalogue number that all the information such as molecular weight came up, somehow that hasn't happened for this one; they have the molecular weight wrong?
A. Look, I think it's very likely this is not the same sort of template that the other certificate was produced by.
Q. And the other problems you mentioned is the product name, it doesn't properly identify it; it simply says "Thymosin" without identifying what it is actually talking about?
A. Yes.
Q. And the molecular formula is written there in a way that

you wouldn't expect?
A. That's correct.
Q. They are the questions I wanted to ask about the certificate of analysis. There is just one other topic that will take about five minutes, Mr Chair.
CHAIRMAN: Go ahead, Mr Hallowes.
MR HALLOWES: This is touching on a matter you raised in the report that you prepared on 11 December 2014. In that report you referred to an email that you had been provided with from a Mr Charter to Mr Alavi and Mr Dank. In relation to answers 4 and 5 you referred to an email that had been sent on 12 January.
A. Okay. Yes.
Q. That appears at page 227 of AS-3, Mr Chairman. That's the email that I'm referring to. Just before I ask you any questions, do you see there that you have referred to that email of 12 January from Charter to Alavi and Dank?
A. Yes.
Q. Do you have a copy of that, or I can hand you up a copy if necessary?
A. If there's more than just what was in the question, yes, I would need to look at it.
Q. I will just hand that up in any event.
A. Okay.
Q. You can see that the email was sent, it would appear, at 6.42 am that morning?
A. Yes.
Q. In terms of the recommended concentration of TB500 (Thymosin Beta-4) do you see that the recommended concentration in that email talks about 10 milligrams per 2 millilitres?

A. Mm-hm.
Q. Do you see that?
A. Yes.
Q. Can I ask whether you were provided with any text messages which were sent later that day, being 12 January 2012, between these people, Mr Charter, Mr Alavi and Mr Dank?
A. Not that I can recall directly. No, I don't believe so. But maybe you could refresh my memory. There was a sequence of text messages we looked at last time which - - -
Q. I'm not sure if they were there. I will hand up two documents in relation to that to you.
A. Yes, I think we saw some of it, but I'm not sure exactly which one.
Q. If you see in relation to the text messages exchanged between Shane Charter and Steve Dank - Mr Chairman, these appear in AS-4 at page 34 of the text messages.
CHAIRMAN: Thank you.
MR HALLOWES: Do you see on page 34 text messages exchanged between Shane Charter and Steve Dank? If you go down to the third line, 56, after there's been some exchanges about, "Which peptide do you need next," at 56 it says, "Thymosin 20 by five millilitre vial"?
A. Yes.
Q. And then if you go to the other text messages, this is at page 12 of the text messages between Charter and Alavi, at 224 you will see, "Hi, mate. Thymosin 20 by five millilitre vial".
A. Mm-hm.
Q. Do you see that one sent at 10.19? If you go across it has a date and a time?

A. Yes.
Q. 12 January at 10.19.
A. Got it.
Q. If you go back to the other one, Dank to Charter, that was at 10.14 am on 12 January?
A. Yes.
Q. Just some simple mathematics. 20 by a five millilitre vial, that would be 100 millilitres?
A. It depends if the 5 ml refers to the fluid in it or just simply the size of the vial. So it's not completely clear that it refers to 5 mls as a vial, which may have less than 5 mls of fluid in it or whether that's the fluid volume.
Q. Let's take it that at least for the purposes of this mathematics that that's referring to 100 millilitres of Thymosin.
A. Okay.
Q. You would agree that at the concentration referred to in the article on 12 January you would need 500 milligrams of Thymosin, whether it be Thymosin Beta-4 or otherwise, to make up 100 millilitres; correct?
A. Yes.
MR HALLOWES: Thank you. I have no further questions.
MR IHLE: Sorry, Mr Chairman. There is one very brief - - -
CHAIRMAN: Okay.
<FURTHER CROSS-EXAMINED BY MR IHLE:
MR IHLE: Professor, you were asked some questions the other day about your familiarity with compounding, and I understand that you don't have a great deal of familiarity; but, notwithstanding, as an endocrinologist you would have dealt with solutions and substances that

had been compounded; is that fair?
A. Yes, I know about them, a little bit.
Q. You are also familiar with the name Charter? You have been taken to a number of SMSs and things like that?
A. Yes.
Q. One of the things that Charter has represented in an interview to ASADA which is subject to objection at the moment is that one of his roles in relation to this enterprise was to work out what preservatives these things should be compounded in.
A. Well, if you say so.
Q. I want to ask you about a representation that he made to ASADA. It may well be hypothetical, we don't know, because Mr Charter is not coming along to be cross-examined. But at AS-7, page 49 of his interview, he talks about a sodium chloride solution at 35 per cent.
A. At 35 per cent?
Q. Yes. What would you say about someone who talks about compounding a substance at 35 per cent sodium chloride?
A. I would say they don't know what they are talking about.
Q. It would be sludge?
A. Yes. If you take it literally as to what that's usually meant to mean to a competent biochemist, yes, it would be. It wouldn't be soluble, probably. It would be sludge, as you say.
Q. Someone who talks about that doesn't know what they are talking about, I think was - - -
A. I would say that that's a reasonable conclusion, yes.
MR IHLE: No further questions.
CHAIRMAN: All right. We will adjourn until 2.15. There may be some re-examination of the professor, Mr Holmes, before

we move to the hot tub.

<(THE WITNESS WITHDREW)

LUNCHEON ADJOURNMENT

UPON RESUMING AT 2.15 PM:

CHAIRMAN: Mr Holmes, do you want to re-examine the professor before we move to the - - -

MR HOLMES: No, I don't. Mr Gleeson would like to ask a question.

CHAIRMAN: Okay. Professor, just for a moment, in that location, and then we will relocate you.

<DAVID JOSHUA HANDELSMAN, recalled:

<FURTHER CROSS-EXAMINED BY MY GLEESON:

Q. Professor, I just wanted to ask you a question about your report of 11 December. Do you have that handy?

A. Yes, I do.

Q. Could you turn, please, to paragraph 10 of that report?

A. Yes.

Q. Which is your answer to question 4?

A. Yes.

Q. It's the part of your report where you express the view in the final sentence of the first paragraph of paragraph 10, "These dosage recommendations correspond precisely to those in the consent form for Thymosin, suggesting that the substance was actually TB500 rather than Thymosin Beta-4." Now, you refer earlier in that paragraph to the email of 12 January, which attaches the article headed "How to use TB500 (Thymosin Beta-4)"?

A. Yes.

Q. I just wanted to clarify with you is it the case that the sole reason that you tend towards TB500 and tend away from Thymosin Beta-4 as expressed there the fact that that article refers first to TB500 and then in brackets Thymosin Beta-4?

A. Yes, it does, and I have to say that's a fairly weak

inference but it was sort of on balance going towards TB500. But it may not be correct.

Q. You did say in your evidence that it was a fairly weak inference?

A. Yes.

Q. The article in question refers in a sort of compendious fashion to TB500 and Thymosin Beta-4, and do you agree that the article doesn't purport to distinguish between a dosage regime for one as distinct from the other?

A. Yes, that's correct.

Q. So, if what the article is purporting to do is to refer to them as being synonymous or indeed not synonymous but similar, either way the dosage specified is the same for both products?

A. Yes. I mean, essentially neither of those products has well established clinical dosage, so it's very likely these are just more or less somebody's conjecture and they could well be the same or equivalent or similar.

It's - I don't think it's a ground for distinguishing them based on any real evidence one way or the other.

Q. Just to be 100 per cent clear, you are not aware of any dosage regime for Thymosin Beta-4 that's separate and distinct from that which is specified in this article?

A. I don't believe there is any dosage regimen for either of them in any substantial form. For Thymosin Beta-4 there is, as we discussed before, a single study which allows further research to go on, but that doesn't mean it's safe. It just means it's safe enough to go on. So there is no established dosage from that, nor for TB500.

MR GLEESON: Thanks, Professor.

<(THE WITNESS WITHDREW)

CHAIRMAN: Professor, if you and Dr Vine wouldn't mind going to the Bar table, be seated in the middle there. Going into the lion's den, if I could describe it. I'm sure it won't be a lion's den. We will take your evidence from there. Perhaps you start, Mr Holmes.

MR HOLMES: Dr Vine, you realise these are proceedings before the AFL disciplinary tribunal?

DR VINE: Yes.

CHAIRMAN: We are not swearing witnesses in, Dr Vine, but you understand the importance of telling the truth and expressing your opinions truthfully?

DR VINE: Yes, I do.

MR IHLE: Sorry, Mr Chair, may I suggest at the outset, notwithstanding that Mr Holmes is going to start, as I understand it, cross-examining Dr Vine as well as asking Professor Handelsman the questions, if it hasn't already been marked - - -

CHAIRMAN: I think the report is in. Dr Vine's report is in.

MR IHLE: At least as an introductory range of questions he should be asked whether he adopts the report.

CHAIRMAN: Yes, I follow that. I'm pretty sure it is PG-7. You or Mr Grace could do that. But there's no reason why Mr Holmes can't do it.

MR HOLMES: I'm happy to do it.

CHAIRMAN: You do it, Mr Holmes, I think, and then lead into your questioning and we will move on from there.

MR HOLMES: Dr Vine, you prepared a report dated 19 January?

DR VINE: Yes, that's right.

Mr HOLMES: PG-7. Do you have it in front of you?

DR VINE: Yes, I do.

MR HOLMES: Paragraphs 1 to 25 respond to some specific

questions that were posed to you by the solicitors' firm Tony Hargreaves & Partners, and the letter is there at JV-2; correct?

DR VINE: That's correct.

MR HOLMES: Then you have given some comments in 26 and 27, which have been objected to. I want to ask you just a couple of questions, and I think Professor Handelsman deals with this in the report that you responded to. Professor Handelsman, do you have your report dated 10 January?

PROF. HANDELSMAN: Yes, I do.

MR HOLMES: Just going to you firstly, Dr Vine, your figure 1 in JV-4, it's got a long name at the top. "Vania" is there, and somebody has put in "Thy A-5"; do you see that?

DR VINE: I'm just turning to my figures, sorry.

MR HOLMES: JV-4, page 1. It is figure 1, upper and lower. The lower one is a zoom of the top one.

DR VINE: I'm just trying to find my copy, sorry. I have them attached as a separate document. Yes.

MR HOLMES: You have those two?

DR VINE: Yes, I have.

MR GRACE: We just want to clarify it is the same page we are - - -

MR HOLMES: JV-4, page 1, figure 1, the upper figure and the lower figure.

MR GRACE: Yes.

MR HOLMES: Dr Vine, the lower figure is a zoom of the upper figure; correct?

DR VINE: That's correct, yes.

MR HOLMES: And in the upper figure, in the lower part, in about the centre there's a very small peak for 4971.429?

DR VINE: Yes.
MR HOLMES: And that's been zoomed to create the lower figure?
DR VINE: That's correct.
MR HOLMES: That is the result of an analysis conducted at Bio21 in May 2012?
DR VINE: I believe so, yes.
MR HOLMES: Then if you go over the page, figure 2, figure 3, figure 4, figure 5, they all relate to some testing in 2013?
DR VINE: Yes, that's correct. They were in a separate folder in the set of files that I was given, yes.
MR HOLMES: If we go to paragraph 3 of your report, you had some documents provided under cover of the letter. You had a USB memory stick, a copy of the software, and you used that software to view the files from Bio21?
DR VINE: Yes, I did. In the time I had available I used that software as best as I was able, it being a software platform that I'm not familiar with. But I was able to use it sufficiently to extract some data.
MR HOLMES: Okay. I think in paragraph 16 you came to the conclusion, "All of these materials have peaks in roughly the right range for Thymosin Beta-4. In my opinion, none of them can claim to prove the presence of Thymosin Beta-4 to any recognised standard"?
DR VINE: That's correct, yes.
MR HOLMES: So on all those occasions in figures 1 through to figure 5 there are a rough - I just want to use your words - there are results "with peaks in roughly the right range for Thymosin Beta-4"?
DR VINE: Yes.
MR HOLMES: If we go to Professor Handelsman's report, at

paragraph 6 he's got test 1 on 9 May 2012. There's a peak indicating a substance with a molecular mass of 4971; correct?

DR VINE: Yes.

MR HOLMES: And for tests 2, 3, 4 and 5 they are all the tests that you refer to in 2013; correct?

DR VINE: Yes.

MR HOLMES: Just so that I have it correct, in paragraph 13 you refer to Professor Handelsman's tests in 2 to 6?

DR VINE: Yes.

MR HOLMES: I take it that's a mistake and it should be 2 to 5?

DR VINE: Yes, that's correct, yes.

MR HOLMES: Coming back to your paragraph 16, you have looked at the 2012 analysis, that's JV-4, paragraph 1 - paragraph 18. The molecular mass of Thymosin Beta-4 is 4971, on your review of that analysis; correct?

MR IHLE: I object to the question, Your Honour. It begs the answer - - -

MR HOLMES: I will rephrase the question. Dr Vine, the molecular mass of Thymosin Beta-4 is what?

DR VINE: Well, it really depends what you are talking about molecular mass, if you are talking about the average molecular weight, or whether you are talking about the monoisotopic mass that you would see in a mass spectrometer, which would be just one mass of a range of masses that you would expect to see.

MR HOLMES: What would you expect to see for Thymosin Beta-4 on the test conducted that appears in JV-4, figure 1?

DR VINE: I don't know what you would expect to see because the mass spectrometer is not properly calibrated at that range and it doesn't have the resolution to show the mass

spectrum of Thymosin Beta-4 properly.

MR HOLMES: It it was properly calibrated, what would you expect?

DR VINE: It would depend on what the resolution of the instrument is, and I don't know what the resolution of the instrument is other than it appears to produce peaks 10 mass units wide or 10 daltons wide. So I think perhaps I could sum up and I could say I would expect to see a kind of a blob, something similar to what is shown in the zoom trace, and that blob would probably be centred somewhere about 4964 or 4965. But unfortunately the way the mass spectrometer has been set up, or should I say the lack of the way it has been set up, doesn't really engender any confidence in its mass calibration or its resolution. So this is all a little bit vague, I'm afraid.

MR HOLMES: All right. But you mention that you would have expected to see 4963; correct?

DR VINE: I would have expected to have seen something like you can see in that lower figure in figure 1. So a blob like that about 10 mass units wide unresolved, and the centre of that mass I really would expect to be, if it was Thymosin Beta-4, about 4964, possibly 4965. You can't say exactly where it would be because of the nature of the data that's coming out of the mass spectrometer.

MR HOLMES: If you were testing for Thymosin Alpha-1 what would you expect to see for the blob when you zoom as you have done on the lower figure?

DR VINE: You would expect a peak in the range of about 3,000, somewhere close to 3,000, I think, from memory.

MR HOLMES: It's clear then, if you had two substances, one you

suspected was Thymosin Beta-4 and one you suspected was Thymosin Alpha, and this was the result of your test, would you agree that that clearly shows of the two alternatives it's clearly Thymosin Beta-4?

DR VINE: Well, that makes the assumption that one of them is Thymosin Beta-4 and the other one is Thymosin 1 Alpha. If that was the case, if you were certain that one of them was Thymosin Beta-4 and one of them was Thymosin Alpha-1 and you were presented with that data, you could say, well, the one with the mass up in the 4000s is Thymosin Beta-4 clearly, the one with the mass in the 3000s is Thymosin Alpha-1 clearly. My thesis is that you cannot on the data that's presented in these mass spectra be certain to any requisite standard that the peak with the mass 4971, or in fact 4974, as I later refer to it, as a result of the zoomed data, you cannot be certain or even comfortably confident that that is Thymosin Beta-4. It's simply too far out.

MR HOLMES: Did you want to say comfortably satisfied?

DR VINE: I'm struggling to find a word that expresses exactly what I want to say.

CHAIRMAN: You use your language, Dr Vine.

DR VINE: As a mass spectrometerist, you would reject that that peak is Thymosin Beta-4 on those data.

CHAIRMAN: Without other information?

DR VINE: Yes. There's a fundamental reason for rejecting it anyway, and that is that a single peak in a mass spectrometer can never constitute an identification, not with any degree of certainty. It's an indication, but it doesn't provide a degree of certainty. That's just a fundamental property of mass spectrometry. One ion is

never enough.

MR HOLMES: Your paragraph 18 says the difference is too great for whatever is present in the material to be Thymosin - designated as Thymosin Alpha-1; correct?

DR VINE: No, I said the difference is too great for you to - sorry, which paragraph are you referring to?

MR HOLMES: 18.

CHAIRMAN: 18 of your report, Dr Vine.

DR VINE: No, I say in there that the difference between the two is such that that difference between 4970-something and 3,100, I believe, that difference is too great for those molecules to be confused. You couldn't tell them apart or fail to tell them apart on that basis. But that, as I say, is based on the assumption that they are both what they are supposed to be, and I don't think there is any evidence for that, or not convincing evidence anyway.

MR HOLMES: All right. But if you were to be asked whether the result is either Thymosin - either Alpha or Beta-4 it would suggest that that one is Thymosin Beta-4, on a rough and ready basis?

DR VINE: Well, I don't accept that it does suggest that it's Thymosin Beta-4. As I said, the data doesn't really support it to a degree that would allow you to make that conclusion.

MR HOLMES: Even if it was one or the other?

DR VINE: If you knew with certainty that it was Thymosin Beta-4 and you knew the other one with certainty was Thymosin Alpha-1, then those data together would enable you to distinguish between them, clearly. What I'm saying is we don't know with certainty that either one is what it seems to be.

CHAIRMAN: Can I ask you this, Dr Vine: taking those two calculations, would it be correct to say that the lower calculation, that's the 3,000, is not consistent with it being Thymosin Beta-4?

DR VINE: Certainly not, no.

CHAIRMAN: And, similarly, the upper calculation is not consistent with it being Thymosin Alpha?

DR VINE: No, not on the face of the data.

CHAIRMAN: It doesn't tell you which one it is?

DR VINE: No.

CHAIRMAN: But it's not consistent with those substances in those circumstances?

DR VINE: That's correct, yes.

MR HOLMES: Could I ask Professor Handelsman to respond to the same question?

CHAIRMAN: Yes; that's why we are doing it this way.

PROF. HANDELSMAN: I would agree with Dr Vine that if you were to take a - what I'm going to say is that the context is very important here. If you were to take a vial with no label, no marking on it whatsoever, and put it into a mass spectrometer and get a peak like that, identification of any particular named substance, that is not sufficient. If you know it's a protein, you would have to have the amino acid sequence. But this is not the context in which I believe these data arose. These data arose from a compounding chemist who ordered what I think he would have ordered as Thymosin - Thymosin maybe with or without an additional qualification, but it was Thymosin. It probably came in a vial which had written on it Thymosin. In my report I said that I thought that there was incomplete information for a really well-done forensic

analysis, and that sort of information on what the sample looked like when it came, what was written on it would have helped a lot. But I think in this context they got something, they ordered something that was probably Thymosin, and what they are doing in here is a rough and ready way of saying, just making sure that it's - of the two alternatives, which one it is. So in that sense it's not a perfect identification as if it arose in a vacuum. But it is a way of identifying which of two alternative thymosins that they would have possibly ordered from the external supplier - which it is, and it is clear that the molecular weights are so different that you can't confuse them, even if the machine is a little bit out of calibration. This is not intended to be a perfect identification from scratch, but it is an attempt to distinguish between the two. That's how I would read it. That's why in my report I said if the question underlying the analysis - and every analysis has an underlying question that has to be answered, but if the question underlying the analysis was which of these two it was, within the error of the methodology and software, it gave one or other answer in all of those analyses.

MR HOLMES: All right. Dr Vine, you have said in paragraph 11 there's a lack of a reliable calibration and resolution in the first sentence?

DR VINE: Yes.

MR HOLMES: So you have taken the figure of 4974?

DR VINE: Yes.

MR HOLMES: And you have said that the calibration error was approximately 10 daltons?

DR VINE: Yes.

MR HOLMES: That's 4974 plus or minus 10?
DR VINE: Well, it appears to be - if the material really was Thymosin Beta-4, then the calibration error would be plus 10 on that basis.
MR HOLMES: Plus 10?
DR VINE: Yes. Approximately.
MR HOLMES: Then you have in paragraph 12, "The data indicated the presence of a substance with a molecular weight of perhaps", and then you have a figure of 4955?
DR VINE: Yes.
MR HOLMES: 4985?
DR VINE: Yes.
MR HOLMES: And if you look at that it's 4974 plus or minus - it is plus 11, and just help me with the maths there, Doctor.
DR VINE: The difference between - it's really just a 30-dalton range of a 4955 to - so it's about 10 daltons from 4955 to 4965, and then another 10 daltons from 4974 to 4985, 11 daltons. So I have taken a bit of a range there because, quite frankly, looking at the data I can't be certain what the true mass is. It's impossible to tell from the data. So I have applied a range of about plus or minus 15 daltons, so I'm encompassing a 30-dalton range, which I don't think on my reading of the data is unreasonable, given the operation of the instrument.
MR HOLMES: All right. Your briefing letter at JV-2 from Tony Hargreaves & Partners, 13 January 2015, asked for a report setting out a number of bullet points there?
DR VINE: Yes.
MR HOLMES: You have been asked whether or not in the second last bullet point on that page, "Could it be a substance

other than Thymosin Beta-4 but with a similar molecular weight, for example, Thymosin Beta-10 and Thymosin Beta-15"?

DR VINE: I don't see that. Where is that?

MR HOLMES: Sorry, page 2.

CHAIRMAN: Page 2 of the letter of 13 January.

DR VINE: I see, yes.

MR HOLMES: You don't mention Thymosin Beta-10 or Thymosin Beta-15 in your report, do you?

DR VINE: No, but I do say that it could be a - well, in fact it's very likely to be a substance other than Thymosin Beta-4.

MR HOLMES: Can I just show you a document. Can I provide them to the Tribunal.

CHAIRMAN: Is this already in, Mr Holmes?

MR HOLMES: No, this is a new document. I think this document was obtained by you, Professor Handelsman, over lunch?

PROF. HANDELSMAN: That's right.

MR HOLMES: Could you tell the Tribunal what it shows and where it came from?

PROF. HANDELSMAN: This is an entry from the National - it's really where the PubMed comes from, the National C - I have forgotten what "C" is. Anyway, it's a very well established NIH based protein database centred in Washington. It's widely used as a way of identifying reliable information on various proteins - in this case Thymosin Beta-10 homo sapiens, meaning the human version - and it points out that it has 38 amino acids, and it's a single letter amino acid sequence, is at the bottom. We subsequently have the accurate molecular mass, which is - the accurate molecular mass is less than 4,000,

I think, from memory.

MR HOLMES: I will just show you this document.

PROF. HANDELSMAN: Sorry, the molecular mass is 4367.

MR HOLMES: Can I hand up four copies of that.

PROF. HANDELSMAN: I would add that the nature of amino acids is such that the smallest is a molecular weight of 75, the largest is 200, and adding or subtracting one would certainly be detectible based on that sort of molecular mass. But this figure of 4368, roughly, would be way separate from the peak in question.

CHAIRMAN: We might formally receive those, Mr Holmes.

#EXHIBIT AS-23 - Documents relating to Thymosin Beta-10.

MR HOLMES: Dr Vine, are you able to help us with the molecular weight of Thymosin Beta-15?

DR VINE: No, I don't know what it is off - - -

MR HOLMES: Did you look it up at all?

DR VINE: No, I didn't.

MR HOLMES: Did you download the same documents in respect of Thymosin Beta-15?

PROF. HANDELSMAN: Yes, I did.

MR HOLMES: Are they the molecular structure documents? I hand up four copies. Did you also conduct a search over the lunch break for the molecular weight of Thymosin Beta-15?

PROF. HANDELSMAN: Yes. That's on this document here. That figure is 5229, roughly.

MR HOLMES: I hand up four copies.

#EXHIBIT AS-24 - Documents relating to Thymosin Beta-15.

MR HOLMES: Is the peak we are talking about, in your view, referable to Thymosin Beta-10 or Thymosin Beta-15?

DR VINE: No, I don't think it is.

MR HOLMES: You then spoke about doing a search on the

ChemSpider database.

DR VINE: Yes.

MR HOLMES: Could you tell me what were the parameters of the search that you entered in the ChemSpider web page?

DR VINE: As stated in paragraph 15, I entered a mass range of 4955 to 4985 and asked it basically just to look for entries within that database with molecular weights in that range.

MR HOLMES: Professor Handelsman, did you do a search on the ChemSpider web database over the luncheon break?

PROF. HANDELSMAN: Yes, I did. I would say that we have a copy of it. It allows you to give a centred molecular mass, plus or minus a difference. So I wasn't able to get that kind of 30-dalton range that Dr Vine had, but nevertheless we have done a search on using the molecular mass of 4974 that he used, plus or minus 11.

MR HOLMES: All right. Is that the result of your search?

PROF. HANDELSMAN: That is correct, yes.

MR HOLMES: I tender that search.

CHAIRMAN: That will be AS-25. The search relates to - - -

PROF. HANDELSMAN: It's a search of the ChemSpider database putting in a known molecular weight on the basis that, if the figure from the readout was 4974, what other ones could be around that molecular mass.

CHAIRMAN: So it's a search based on a particular molecular weight?

PROF. HANDELSMAN: Correct, a range of molecular masses. A range of 22 on either side of 4974.

#EXHIBIT AS-25 - Professor Handelsman's ChemSpider database search.

MR HOLMES: Just going through it, in paragraph 11 in the last

sentence, Dr Vine, you say, "If the peak with the MZ is 4974 is really Thymosin Beta-4 then the mass spectrometer would appear to have a calibration error of approximately 10 daltons"; correct?

DR VINE: Yes.

MR HOLMES: So we go to the search. Professor Handelsman, you have entered that weight of 4974 plus or minus 11?

PROF. HANDELSMAN: Yes.

MR HOLMES: What did the result of the ChemSpider website show?

PROF. HANDELSMAN: I got 20 hits as opposed to Dr Vine's 28. I don't think that's a material difference. It's all a matter of how you specify the molecular mass range. We got 20 hits. I draw your attention to the second last one on the second last page, second from the bottom, which is Thymosin Beta-4 acetate. In other words, it identified Thymosin Beta-4 with the acetyl group attached within that range. But there was no other Thymosin identified, no other name Thymosin in that range.

MR HOLMES: So the ChemSpider website identifies all - is it all known substances or?

DR VINE: Perhaps I should say a few words about it. The ChemSpider database is a database of known chemical compounds compiled by the Royal Society of Chemistry. It currently stands I believe at something in the region of 22 or 23 million compounds. It's a database that's been compiled largely by chemists, and it's a database that isn't particularly I think replete with biological molecules, with proteins and peptides. It's more the more commonly accepted chemical compounds. So it is by no means a comprehensive biological database, but it does contain quite a large number of peptides and proteins.

It's a way of identifying materials on the basis of various properties that they might have. You can do individual searches such as the one that's been done here, which is a search based on molecular weight. So it's a way of finding possibilities when you - in this particular case, when you've run a mass spectrum, you have obtained a molecular weight, you can then go into ChemSpider and determine what substances have this molecular weight. As Professor Handelsman has pointed out and as you would expect, given that a fairly wide mass range has been put in and that mass range does encompass the molecular weight of Thymosin Beta-4 as the (indistinct) version, it did find what it calls Thymosin Beta-4 acetate, which is the same thing, which is what you would expect. It is in there. But the problem is that within the mass range that's indicated - and I agree with Professor Handelsman, I don't think there's a material difference. I used a slightly wider mass range. Professor Handelsman has used 11, but there are also a number of other compounds that are in there as well. So you can't distinguish between Thymosin Beta-4 and those other 20 compounds in that list based on the molecular weight.

PROF. HANDELSMAN: Could I add, though, that I think most of these compounds that are listed here do not necessarily - in fact, I doubt that any of them - occur in nature. They are just simply chemical structures that are used for identification purposes. In other words, they are artificially created. I think any one of those that is recognisable that occurs in nature would usually have the annotation as Thymosin Beta-4 does with a CAS number. Those are actually separately searched. So, as

I understand it, this means that the only recognised biological molecule in that range is actually Thymosin Beta-4 acetate.

DR VINE: Well, ChemSpider doesn't make that sort of distinction as to what sort of molecule it is. It only lists what it has in the database. The issue here is one of chemical identity. The proposition is that this material, the one that's mentioned in the letter of instruction that I was given, this material is Thymosin Beta-4. My thesis is simply the evidence does not support the identity of the material as Thymosin Beta-4. It is a possibility, but it isn't a certainty, not by a long way. Given that, as I said earlier, this database is not complete, from my experience of using it, it doesn't cover the area of proteins and peptides particularly comprehensively. It's been compiled mostly from chemical sources rather than biological sources. Given the nature of amino acids and the fact that, while there are naturally occurring amino acids, there are also potentially lots of non-naturally occurring amino acids, in fact probably many thousands of them, and the possibilities and combinations that could all add up to the correct molecular weight would be an enormous number. So it really goes down to whether one has confidence that the material analysed at Bio21 in 2012 was Thymosin Beta-4, and I say on the evidence, on the analytical data that we have before us, it's not that you can't be certain that it isn't Beta-4; I don't think you can really even conclude that it's probable. It's perhaps possible at best. But a lot depends on how well that instrument was calibrated, and we simply don't know that. So even that

possibility is tinged with that qualifier. Then, as I said earlier, the other qualifier is to what extent a mass spectrum with one peak in it can be said to identify any substance. If we were talking here about forensic identification in the case of a criminal matter or even identification in the case of identifying a drug for sports drug testing purposes, such an identification would simply not stand up. It wouldn't even be put forward. No reputable laboratory would claim they had identified a drug on the basis of a single peak in a mass spectrum.

MR HOLMES: Dr Vine, you have drawn the conclusion in paragraph 18 that it's not that of a Thymosin Alpha-1, correct, because the difference is too great?

DR VINE: Yes. Yes, I agree. I believe it is possible to draw that conclusion that it - even given the inaccuracy of the instrument and its lack of resolution, I think you can be pretty confident that the material that gives the peak at 4971 or 4974, whichever you want to use, that that isn't Thymosin Alpha-1.

MR HOLMES: May it also be concluded that the mass spectrum in figure 1 is not that of Thymosin 10, Beta-10?

DR VINE: I would say that's very probable too. I think the mass that we have been given here is out significantly. We are probably looking at something in the region of 600. We have 4367 as against 4965 or 4. So that's a very big difference. I doubt that the mass spectrometer would be out that far.

MR HOLMES: It may also be concluded that the Thy A-5 mass spectrum shown on figure 1 is not that of Thymosin Beta-15?

DR VINE: Yes, I think that's a reasonable conclusion too.

Again, you are talking of a mass difference of several hundred. So, again, despite the performance of the mass spectrometer, a mass difference of several hundred is sufficient for you to say it's not either of those two compounds.

MR HOLMES: May it also be concluded that the Thy A-5 mass spectrum is not that of a mixture of thymosins or peptides?

DR VINE: There is no evidence of a mixture because there is only one peak, although we have to say here, and I'm sorry if I sound repetitive, the peak is 10 daltons wide. If there were some other Thymosin with a very, very similar mass within a few mass units of the Thymosin Beta-4, it could be buried in there and we wouldn't know because the peak isn't able to resolve those materials. So we simply wouldn't know about that.

MR HOLMES: Wouldn't that Thymosin of an unnamed variety, other than Thymosin Beta-4, be brought up in your ChemSpider search?

DR VINE: It might be, and it might be one that doesn't have a trivial name, for all I know. Thymosin, as I understand it, is a generic term and there are any number of thymosins, I presume. I don't profess to be an endocrinologist, and the thymus gland is not my area of expertise. But I do appreciate that there are a lot of peptides and proteins in relation to that particular gland and how it operates. Whether they have all been established, whether they are all known, I don't know. My point is simply that on the data that we have we really can't be certain about identity.

MR HOLMES: Professor Handelsman, can you comment on that?

PROF. HANDELSMAN: I would add that thymosins are a family of peptides that are most expressed in the thymus. There is a limited number of them, and the sequencing of most of - of quite a large - probably all of them is known. When it comes to actually - and again context is important here. When it comes to actually purchasing through chemical manufacturers or so on, there's only really two that are actually ever advertised - that's Thymosin Alpha-1 and Thymosin Beta-4. There may be others that are available or could be synthesised on request, although heaven knows I don't think the parties involved in this would have the sophistication to ask to synthesise some other Thymosin which is not characterised at all biologically. So I think the fact that the ChemSpider search didn't turn up any other named Thymosin, it is most likely, and I haven't exhaustively tested each one of them, but it is certainly not Beta-10 or Beta-15. With more time, and I only really got to do this at lunchtime, I think we could check each one of these. But I would be very surprised if these aren't all artificial compounds which don't occur in nature, which aren't - are just not in the frame for thinking about ordering them and potentially using them the way in which the peptides involved in this case have been contemplated at least.

DR VINE: Am I able to make a comment to that, Mr Chairman?

CHAIRMAN: Yes, of course.

DR VINE: What I would say there is that certainly my experience with purchasing peptides and proteins has been an interesting one in that when you order these materials it is certainly necessary to check what you have ordered because you often find that what you have ordered isn't

what you expected. The industry as a whole, and we heard some of this this morning, contains a number of companies which produce materials of very dubious authenticity, and it could well be that if you have bought something which you think is Thymosin Beta-4 you have been provided with one of these things that the ChemSpider database, albeit an artificial substance, has produced. It may be some chemical company's failed attempt to make Thymosin Beta-4 or some analogue or some variant of it. The whole point of this is that you cannot be sure when you buy these materials. I think this is exceedingly important in the context that we are looking at here. When you are considering a material that's going to be formulated in some way and then injected into someone, I think it's incumbent upon whoever has sourced that material and will compound it to be absolutely certain that they know what it is, not to be, "Well, it probably is this because the mass is around about where it ought to be." From where I sit, if I'm on the other end of the syringe needle, on the sharp pointy end, I expect that whoever is putting it into me knows exactly what it is, not just same vague notion that it is probably the right thing. For that reason in my view it's fundamentally important that these materials are characterised properly, and that clearly hasn't been done in this case. Our experience, Racing Analytical Services, with these materials, we have done work on the ones we have bought ourselves. We have also done a lot of work for Australian Customs on materials that have been seized for one reason or another as potential prohibited imports, where we have found that it is quite a frequent occurrence for these materials not to

be what they are labelled to be. That can vary anywhere between being similar but not quite the same - I cite an example in here of a material that we found to be almost AOD-9604 except one amino acid had been changed; or it may be a totally unknown peptide with goodness knows what properties, or in fact there simply may be nothing there at all. So for me it is of vital importance that these materials are properly identified.

MR HOLMES: Can Professor Handelsman respond?

PROF. HANDELSMAN: I couldn't agree more in what Dr Vine has established, which is the proper standard the pharmaceutical companies follow. They wouldn't do anything like the sort of things we have talked about. If they ordered a peptide, they didn't make it themselves, they would sequence it probably several times in both directions to make sure that it is what it is and that it is highly purified. All of that is perfectly true. But I think what we are talking about in this particular discussion is really people who cut every corner, cut many corners, let's say. As Mr Ihle reminded me repeatedly, there's plenty of people who have less scruple than a pharmaceutical company. I think it is quite plausible that the compounding chemist or someone on his behalf ordered something called Thymosin and they simply wanted to do a check which of the two thymosins it might be. That's about all. I don't think they are following the pharmaceutical industry standards. They follow their own standards, and in some cases it is the shortcut of compounding pharmacists, and I think it doesn't exclude the possibility that this is Thymosin Beta-4 at all. In fact, the likelihood is, as we have identified in the

search, that it's the most likely candidate for that peak.

CHAIRMAN: In the end, gentlemen, those points you raise are very important and very valid. We ultimately have to put all that in the context of this case, which is a bit different from a very good scientific laboratory being operated here, Dr Vine, I can assure you.

MR HOLMES: I have no further questions.

CHAIRMAN: Mr Gleeson?

MR GLEESON: Thank you, Mr Chairman. Dr Vine, I might have misheard you, so please forgive me if I'm putting back to you something that you just didn't say, but I thought I heard earlier on during your evidence you say something to this effect, that as a mass spectrometerist you would reject that this was Thymosin Beta-4.

DR VINE: Yes. If I was given the data and I knew that the mass spectrometer was properly calibrated and had its resolution adjusted as well as it could be, I would reject it on two grounds: one, if it was properly calibrated, then the mass is wrong and therefore it can't be Thymosin Beta-4. It can't be out by 10 because the instrument is accurate, this says there is something there with a molecular weight of 4971 or 74, whichever we take as being the correct one, and that means it can't be Thymosin Beta-4 because we know that the molecular weight of Thymosin Beta-4 is - its monoisotopic weight is actually 4960, and then you add a proton for the MALDI process, so that would give you 4961. Then you have an isotopic distribution which actually gives you some additional peaks as well. However, on a more fundamental level, as I have also said, you would never base an identification on a single peak in a mass spectrometer. You need more

evidence than that to conclude that something's identity has been established.

MR GLEESON: That second point is a rather different point, isn't it? You are not saying by that second point that you would reject that it was TB4; that is, you can conclude that it is not TB4. The second point you are making is that you simply can't be sufficiently satisfied that it is TB4.

DR VINE: That's correct. There are two sides to that question. You would never be satisfied on the basis of a single - - -

CHAIRMAN: Just on the basis of that single analysis.

DR VINE: Particularly given the resolution of the instrument. The peak is 10 daltons wide. If you were to analyse Thymosin Beta-4 on a more modern mass spectrometer - the Bruker Microflex is a pretty outdated instrument. It is - one of my protein chemist colleagues refers to it as a bit of an outdated toy. Compared to the sort of instruments that we use routinely nowadays, it's not a very sophisticated machine. It doesn't have a lot of power. If you analyse it on the sort of equipment that we use in Racing Analytical Services laboratory, instead of seeing that blob 10 peaks wide what you would see in our laboratory, and we have done this because we have analysed a sample of Thymosin Beta-4 for Australian Customs - what you actually see are something of the order of 10 individual peaks, and they are the isotopic peaks of Thymosin Beta-4. We can resolve them all into a cluster, and there are 10 - set of 10 peaks. Even if you got that you still wouldn't be sure it was Thymosin Beta-4 because you have the fundamental issue that a single mass

spectrometric cluster of isotopic peaks doesn't constitute an identification.

CHAIRMAN: But it would be consistent?

DR VINE: But it would be consistent and it would be a much better indication. But it still would fall short of definitive. As I think Dr Watt said in his statement, really the only way to be sure this is Thymosin Beta-4 would be to actually do a sequence determination on it. You would - for a start you wouldn't just use mass spectrometry. You would use liquid chromatography mass spectrometry, which separates mixtures first and then introduces them sequentially into the mass spectrometer. You would treat the molecule with a digestive enzyme called trypsin, which will cleave it into smaller, more manageable bite-size pieces, and then you would analyse those individual pieces to ensure that the sequence of amino acids is the same, because what needs to be borne in mind is that even if you identify the molecular weight absolutely - and the instrument that I'm talking about that we use doesn't measure the molecular weight to one dalton. It actually measures the molecular weight to two thousandths of a dalton, which is what's called high resolution mass spectrometry. Even with that, you can't be sure it's Thymosin Beta-4 because you have the molecular weight, which means all the right amino acids are there but it doesn't mean they are in the right order. You can have a word and you can have all the letters in the word but unless the letters are all in the right order the word isn't there. That's how the system works. Even if all the amino acids are there, if they are not connected in exactly the right order, the molecule is not

Thymosin Beta-4. So, even if the mass was perfectly lined up, it wouldn't provide conclusive evidence.

PROF. HANDELSMAN: I just would like to add a bit of a reality check. This is really setting a standard of scientific perfection, which is certainly ideal, but I would also point out that even a calibration error of 10 in a molecular weight range of around 5000 is 0.2 of a per cent. It is not enormous. It is enormous maybe by the perfect standards that are alluded to. But this is still a working machine in a very high quality research institute that does very high quality work using that machine. If it were so defective it wouldn't be useful in medical research in which they do - have a huge throughput. So I would just say that perfect is the enemy of good. I think for the purposes that we are talking about the most plausible identification, it doesn't require that level of finesse.

MR GLEESON: Just returning to the first of the two reasons you advanced, Dr Vine, for the proposition that you would reject that this was TB4, if you assume that the spectrometer has a calibration error of approximately 10 daltons, then there would be no basis for rejecting that the product in question was Thymosin Beta-4; you would simply adhere, I assume, to the proposition that you can't be certain that it is Thymosin Beta-4?

DR VINE: Yes, that's right, if that were the case, but the trouble is we don't know whether that's the case or not.

MR GLEESON: So if I ordered Thymosin Beta-4 and I sent it off to the mass spectrom - that person.

DR VINE: Yes.

MR GLEESON: And I received the results as depicted in Thy A-5.

DR VINE: Yes.

MR GLEESON: And I knew that my spectrometer had a calibration error of approximately 10 daltons, I would say to myself "the results are consistent with what I ordered"?

DR VINE: You could say that to yourself, although I think my comment would be that if you are operating the mass spectrometer and you know you have a 10-dalton error then you are not a very good operator and you shouldn't be doing it. To knowingly operate an instrument when it is out of calibration is exceedingly unscientific and verging on negligent.

PROF. HANDELSMAN: Again, I'm sufficiently impressed that I will always send samples to Dr Vine because he has such high standards. But that is a standard of perfection that most machines - mass spectrometers are quite finicky machines and they do get out of calibration relatively often. They regularly need servicing and calibration and so on. I don't think an error of 10 daltons in 5000 is hugely material. It is not desirable. You wouldn't say it's satisfactory. But it is also not sufficient to reject the information out of hand.

MR GLEESON: Those are the only questions I have.

CHAIRMAN: Mr Ihle?

MR IHLE: Dr Vine, I would like to take you to JV-1, which is a copy of your curriculum vitae attached to your report.

DR VINE: Yes.

MR IHLE: Under "Qualifications", the last entry that you have there is "National Association of Testing Authorities, Australia, Assessor, 1992 and continuing"?

DR VINE: Yes.

MR IHLE: What does that role involve?

DR VINE: Perhaps I'd better start from the name of the - the National Association of Testing Authorities, Australia is a kind of a quasi government body now, I suppose, which is charged with the accreditation of laboratories for competence to do what they say they can do. So it's the sole body within Australia that provides accreditation of laboratories generally these days to various international standards, such as ISO 17025, which is the one most applicable to chemical laboratories. It works on the basis of assessing a laboratory in terms of their compliance obviously with the bureaucratic parts of the various international standards and then also with the technical requirements of being able to do what they claim they can do. It's very similar to GMP registration. It uses two sorts of assessors. NATA provide their own assessor, and then they use a set of scientific assessors who are called in for specific purposes. The scientific assessor's job is to look at the methodology of the laboratory, to examine its quality control procedures, all of its technical operations and effectively say, "Is it fit for purpose," I suppose is the most simple way of putting it. That's been my role as a technical assessor, to look at how laboratories operate and whether they can actually do what they claim they can do to the required international standard.

MR IHLE: I might get the acronym wrong, but the national testing measurement institute or the national - the testing measurement institute - - -

DR VINE: I'm not familiar with - I'm familiar with the National Measurement Institute, NMI.

MR IHLE: That's the one, NMI. Does your role involve any

involvement with NMI?

DR VINE: It does insofar as the Australian Sports Drug Testing Laboratory - that is the laboratory which ASADA use to carry out their drug testing, so that's the organisation that actually does the drug tests - is part of the National Measurement Institute. As a NATA assessor I have actually carried out their technical assessments since 1992 on - I'm not sure exactly - three or four occasions, and as well as that I have done desk audits of new methods from time to time again to assess whether the methods are fit for purpose.

MR IHLE: So when in paragraph 16 you say the following, "I'm unaware of any sports drug testing authority, human or animal, or regulatory agency, human, environmental or agricultural, which will accept identification on this basis", first of all, "this basis" is referring to that HPLC graph, as I understand it? Am I right there, when you say "this basis", is that what you are referring to?

DR VINE: It is referring to the mass spectrum.

MR IHLE: Yes, the mass spectrum. When you say you are unaware of any sports drug testing authority, does that include - do you take into that your experience as a NATA assessor?

DR VINE: Yes.

MR IHLE: That includes assessing the very laboratory that ASADA uses for its own drug testing purposes?

DR VINE: Yes.

MR IHLE: Can I take you then to paragraph 9 of your report, and this is something that's been touched on very briefly in relation to questions that have already been asked of you by Mr Holmes. In the first sentence of paragraph 9

you distinguish between what we see on the graph as 4971 and what you then go on to say, "it appears the peak has an Mz" - shorthand for molecular weight?

DR VINE: It's not exactly. One of the things that's not appreciated about mass spectrometry is that it appears as if the scale in a mass spectrometry is mass. In fact, the scale isn't mass. It's mass to charge ratio. It's just that in many mass spectrometers the charge is 1; that is, it's a single positive charge or sometimes a single negative charge. So mass to charge ratio is in fact the same as mass.

Often particularly in the mass spectrometry of peptides and proteins charges can be 2, 3, 4, 5, 10, 15, very large numbers. So in those cases you specify mass to charge ratio. So I always - you should always use M on Z rather than mass, but they are synonymous only when the charge is 1. In this spectrum the charge is 1.

MR IHLE: When you go on to say it's actually closer to 4974, by reference to the graph itself can you explain what you mean by that?

DR VINE: If we go to my figure 1 you can see the upper mass spectrum, there's a very, very small peak which has the number 4971.429 printed above it. While at first sight you might think that's the mass of the particular peak, when you expand that you get the trace shown at the bottom which shows in fact, or appears to show - and this may be where there's some issue with the Bruker Microflex software that I'm not aware of, but it appears to show 4971 isn't the centre of the peak, it is actually the front of the peak really, and the centre of the peak, if you use the scale along the bottom, might be more properly

estimated at about 4974. So that's where that sort of dichotomy comes in.

MR IHLE: Professor Handelsman, do you agree with that assessment of peaks in graphs?

PROF. HANDELSMAN: Yes, I do.

MR IHLE: Does that have any significance in the strength of opinion or otherwise that you are able to give to this Tribunal about what we can do with this analysis?

DR VINE: The comment you would make is 4974 is further away from our expected 4964 or 65 than is 4971. So it actually moves it a little bit further away. That's where my estimate of about 10 daltons of difference in mass comes from.

PROF. HANDELSMAN: And I would agree that that just encompasses the calibration error. If the calibration error is plus 10, in other words you take 10 away from it, it would coincide with exactly what was expected. So it is plausible at least that the calibration error explains that difference. It's not the only explanation, but it's a plausible one.

MR IHLE: Professor Handelsman, you heard Dr Vine say before that we don't actually know what the calibration error is here. Do you agree with that?

PROF. HANDELSMAN: He made an estimate of approximately 10, and I think that that's a reasonable estimate.

MR IHLE: Dr Vine, do you make that estimate here, or is that an estimate that you allow for should the substance actually be TB4? So if you start from the premise which is sought to be evidenced by this document, by this analysis, you can work backwards or you can work forwards. Do you actually think there has been a calibration error

of 10 or do you simply not know?

DR VINE: I think what I said originally was if we assume that - if that peak was Thymosin Beta-4 and we are measuring 4974, then the calibration error would be 10. But I think I also made some comment that we don't know what the calibration error is in fact. So that would only be an assumption based on assuming that the peak was Thymosin Beta-4.

The calibration error may well be much more than we know, perhaps less than we know. But the problem is the instrument appears to have - again, from Dr Watt's report, because I couldn't get - from the data I was provided I couldn't see the reference standards that Dr Watt referred to in his report with sufficient clarity to estimate how well their masses have been assigned. But he has I think more familiarity with the software than I do, and his report suggested that there was reasonable calibration of the instrument up to about 3000. But beyond that there was no evidence of any calibration standards that had been run. So beyond 3000 calibrations was pretty much unknown.

MR IHLE: You seem to be nodding, Professor Handelsman?

PROF. HANDELSMAN: I agree that it's uncertain rather than unknown. If the calibration up to 3000 is reasonable, it's likely - it's possible that there may be some error beyond that. But it's not likely to be enormous, if it is adequate up to 3000. Having said that, you can't say what it would be. But it wouldn't be enormous.

DR VINE: I don't know that you can say what it would be. If the calibration error progressed in a linear fashion, perhaps that might be true. But it may not progress in a

linear fashion. Mass spectrometer mass ranges often don't behave in a linear manner once they get towards the upper range that the instrument is capable of functioning at. It may well be that the change in calibration accuracy as you go to higher masses is not a linear, that is a straight line, relationship; it may well be an exponential relationship. We simply don't know with this particular instrument.

PROF. HANDELSMAN: I come back to Dr Watt's comment that the calibration appears to have been adequate up to 3000. In other words, there is no systematic deviation up to 3000. So to imagine that suddenly deviates beyond that is possible, things like that happen. But the most likely is that if it is in calibration up to 3000 it is not far out, although it may be out a little bit further or beyond that.

DR VINE: I would simply say we don't know. You would need to know the exact operating characteristics of the instrument to be sure about that. You simply can't be sure about it.

MR IHLE: Professor Handelsman, I just want to ask you about some of the documents you were able to obtain over lunch, specifically those in relation to Thymosin Beta-15 and Thymosin Beta-10.

PROF. HANDELSMAN: Yes.

MR IHLE: I don't know if you have the marked ones, but the protein information resource document.

PROF. HANDELSMAN: Yes.

MR IHLE: I have one which is marked AS-23. That's the one, as I understand it, the Thymosin Beta-10; is that right?

PROF. HANDELSMAN: Which number of residues has it got?

MR IHLE: Thirty-eight.

PROF. HANDELSMAN: Thirty-eight is Thymosin Beta-10, yes.
MR IHLE: Does thirty-eight residues indicate that there are 38 amino acids?
PROF. HANDELSMAN: Correct.
MR IHLE: Correct?
PROF. HANDELSMAN: Correct.
MR IHLE: And in relation to Thymosin Beta-15, number of residues, 45; that's on AS-24?
PROF. HANDELSMAN: Correct.
MR IHLE: That indicates that it's a chain of 45 amino acids.
PROF. HANDELSMAN: Yes, that's correct.
MR IHLE: Do you have a copy of your first report in front of you?
PROF. HANDELSMAN: Yes, I do somewhere. If you give me a second I will find it. Yes.
MR IHLE: Turn to page 13 of that report. You were asked questions about this the other day, you might recall.
PROF. HANDELSMAN: Yes.
MR IHLE: We will see the diagram in the bottom right-hand corner of page 13. Do you have that?
PROF. HANDELSMAN: Yes, I do.
MR IHLE: We have three substances listed with chains of what purport to be amino acids?
PROF. HANDELSMAN: Yes.
MR IHLE: We have Beta-4, Beta-10 and Beta-15?
PROF. HANDELSMAN: Yes.
MR IHLE: You may not recall - and I can take you to the transcript, but at page 339 of the transcript in reference to this diagram I took you to that in relation to both Beta-10 and Beta-15, and according to that diagram and your evidence on 12 January Thymosin Beta-10 was a 43

amino acid chain.

PROF. HANDELSMAN: Look, I recognise what you are saying. Beta-4 you mean or Beta-10?

MR IHLE: Beta-10.

PROF. HANDELSMAN: Look, I didn't have in my report anything about Thymosin Beta-10, and in fact the first time I really looked it up was today. So the correct figure at least from the NCBI protein database is 38. Now, I don't know that particular diagram. I can't explain that discrepancy off the top of my head. Just looking at the sequence - - -

MR IHLE: It also indicates that Beta-15 has 44 amino acids.

PROF. HANDELSMAN: All I can deal you is that this is a picture out of a review article by Harrer, which I didn't go into in any great depth. I just used it as a form of illustration. I actually meant to highlight what was at the bottom, which was the Thymosin Beta-4. The upper part just stayed in there more or less unintentionally, but specifically looking at those two thymosins in the NCBI protein database today that's the result that I circulated.

MR IHLE: That article that you pulled those two amino acid chains for Beta-10 and Beta-15 out would seem to be inaccurate in light of the information produced today?

PROF. HANDELSMAN: I would say that that's most likely, and without going into it further I can't account for that in detail at this stage.

MR IHLE: At least that's one example of where someone has represented something as Thymosin Beta-10 which, as we know from the chemical authority, is not actually Beta-10.

PROF. HANDELSMAN: I just haven't had time to go and look at

where the discrepancies are, and I don't quite understand that. But, yes, it's possible that there may be different forms of Thymosin Beta-10 too. Proteins are made in a sequence and there is a pro-sequence, a pre-pro, and it's variously chopped up before a final form is made. So it could be that that's what they call a pro Beta-10. In other words it's a slightly longer version which is cut down further.

MR IHLE: That amino acid chain of 43 which is represented as Beta-10 which is probably not Beta-10 - - -

PROF. HANDELSMAN: I don't know how far out it is. I would have to look at it side by side.

MR IHLE: We know it is out by at least five amino acids?

PROF. HANDELSMAN: Yes, apparently so, yes.

MR IHLE: That which has been represented in the diagram in your report would probably have a molecular weight in the vicinity of that which we see on the graph, would it not?

PROF. HANDELSMAN: It might have. But I think, as you yourself pointed out, probably the diagram is in error because the databases are more reliable sources of information. They are the standard source of information that people use for molecular weights and for structures of proteins and genes.

MR IHLE: The point is this, Professor Handelsman: even in learned articles which you yourself cite, people might get the sequence of Beta-10 and Beta-15 wrong.

PROF. HANDELSMAN: Look, it was not the object of my using the diagram to highlight Beta-10 or Beta-15; it was really the lower part. But, yes, you are right; people don't always get it right. There may be other explanations so that it is not wrong. For example, if it is a precursor form of

Beta-10 then there's no necessary inconsistency. But I can't account for that at this moment.

MR IHLE: In that instance, though, it would not be Thymosin Beta-10. If you had an amino acid peptide such as that represented in the diagram that you adopted that would not be Thymosin Beta-10.

PROF. HANDELSMAN: According to the protein database that would not be Thymosin Beta-10. It might be a precursor form of it.

MR IHLE: And Thymosin Beta-15 is the same as represented in the diagram.

PROF. HANDELSMAN: Yes. Well, there's a difference in the number of residues, that's right.

MR IHLE: Dr Vine, you gave a brief bit of evidence before in relation to the answers to the ChemSpider interrogation that you did, that you found that there were 28 and I think Professor Handelsman found 22 or 23 substances that fall within the molecular weight range that you identified. You have also identified the limits in relation to ChemSpider based on your experience. How often do you use ChemSpider?

DR VINE: Several times a week, I would think. Sometimes quite intensively and sometimes less so. But it would average several times a week.

MR IHLE: In your job how often are you looking by the way of mass spectrometry or otherwise at detection of peptides and other molecules?

DR VINE: Relatively frequently, I have to say increasingly frequently as these become more important as sports doping agents. When the ACCC report was released most sporting labs had almost no capacity to detect peptide doping

agents. Obviously since then we have put in a lot of work to change that situation, and that's necessitated a huge upgrading of the amount of work we do on biological molecules. So increasingly - and we see this too with the potential prohibited imports we get from Customs - they are peptides rather than the more traditional illicit substances that we have been used to seeing in the past. So it is very much a growth area and the number of things that come in that require you to identify proteins and peptides is increasing all the time.

MR IHLE: And in relation to those analyses that you conduct either by way of drug detection in horse racing or assistance to Customs or any other, do you have recourse to ChemSpider in those instances?

DR VINE: Yes. It's not so much in relation to the testing of the racing animals. In those tests we generally have a defined group of substances that we are looking for. But in terms of the Customs materials, yes, that's one of the sources we use. But we also use the other, if you like, more traditional sources of protein identification like BLAST searches and things like that and Swiss-Prot database. There are a number of international databases that you can have access to which you can use when you are trying to sequence a protein. There is a lot of software that's available that enables you to do that. So we make use of all of those tools. Going back to what I said about ChemSpider, ChemSpider tends not to be all that useful for proteins and peptides compared to the other more specific databases that we use.

PROF. HANDELSMAN: Can I - - -

MR IHLE: Professor Handelsman, do you use ChemSpider?

PROF. HANDELSMAN: No, I don't use it regularly, no.
MR HOLMES: I think Professor Handelsman said "can I".
PROF. HANDELSMAN: Can I actually come - - -
MR IHLE: Well, he can answer the question, with due respect, and if there is a matter that needs to be clarified - - -
PROF. HANDELSMAN: I'm just following on a question you asked me before and I have an answer now.
MR IHLE: Okay. Is this in relation to your diagram?
PROF. HANDELSMAN: Yes. As I suggested, if you look at the Thymosin Beta-10 and the diagram and compare it with the database there are five amino acids at the front end. That is very typically what you see in the way proteins are made. They are made in a long sequence and then it is chopped up into its final form. Presumably the 43 amino acid version in that diagram is a pro form of it with five amino acids at the front end.

The Beta-15 one has one amino acid less and that's a methionine which is often readily oxidised in the purification process. So my guess is that at that stage the purification wasn't reliable enough to identify that there's actually 45 and not 44. So I think in the end the databases are probably correct. They are the most up to date.

MR IHLE: So the database is correct. So it needs to have 38 in a particular order to be Beta 10?
PROF. HANDELSMAN: Yes.
MR IHLE: And it needs to have 45 in a particular order to be Beta 15?
PROF. HANDELSMAN: Correct.
MR IHLE: If there is something that comes in with the amino acid chain as depicted in those diagrams it would neither

be Beta 10 nor Beta 15?
PROF. HANDELSMAN: Yes.
MR IHLE: Going back to ChemSpider, are you in a position to agree or disagree with Dr Vine about how compendious ChemSpider is or is not in relation to peptides and proteins?
PROF. HANDELSMAN: I would defer to his much greater expertise in that sort of analytical chemistry and use of ChemSpider. I'm a very occasional user only.
MR IHLE: Professor Handelsman, do I understand the gravamen of your evidence to be that you really don't disagree with what Dr Vine says; rather you start from a different question which is, "If this analysis were to be applied on a dichotomous basis, is it one thing or the other, then by way of exclusion of one of them we are left only with the other?"
PROF. HANDELSMAN: Yes, that's how I phrased my report. If the question was the following, then it's clear. In fact the way the instructions went to Dr Vine were leaving the qualification out.
MR IHLE: Why did you insert the qualification?
PROF. HANDELSMAN: Because I think it represents the likely scenario. I think it represents the context in which these analyses were done by a compounding chemist.
MR IHLE: Why?
PROF. HANDELSMAN: Because a compounding chemist takes substances he or she orders from somewhere else and may - sometimes they don't bother to verify them, but in this case they may have decided to verify what it was.
MR IHLE: This is just guesswork on your part. You have seen no evidence as to why these were analysed?

PROF. HANDELSMAN: It is guesswork, but I'm trying to establish a context why this analysis was done, a plausible one given that it's a compounding chemist.

MR IHLE: I want to ask you this specifically. Have you been taken to any evidence or shown any evidence which suggests that the purpose for these analyses was to determine one of those two alternatives?

PROF. HANDELSMAN: No.

MR IHLE: So, based on what you have been asked, you have looked at these and you have made that assumption?

PROF. HANDELSMAN: Not quite. There were a number of things I was shown today, for example, like a catalogue that had the word "Thymosin" without any qualification. If someone ordered that they would then be obliged - I mean, commonsense, even a compounding chemist who will cut corners would be obliged to verify whether it is one or the other of the two that would be marketed.

MR IHLE: Dr Vine, what would you say about that in light of the types of assessments you have done for Customs when you might order one thing, it might be something close, or something different, or something completely different altogether?

DR VINE: I think that's very much the issue. It is all very well ordering something and it comes with an appropriate label and a certificate of analysis. But we have seen a couple of certificates of analysis mentioned today which don't seem to be really worth the paper they are printed on, and it is often the case that these materials are falsified. The production of peptides is very much a growth industry and there are a lot of cowboys out there who are just cashing in on the demand.

I don't really think you can put your trust in what is on the label unless you have established through experience whether your supplier is a reliable source of supply. To be fair, there are some companies out there that are very reliable sources of materials. The one in Australia, for example, Auspep, Auspep will make any peptide that you want them to make, and what they make is first-class material. It is spot-on what you order. It is expensive, but you can get it that way.

There are one or two other companies that we found to be useful sources of peptides, and invariably whatever we order from them turns out to be the right material. But even when we are ordering it for research purposes we will always verify it is the right material before we use it. Then there are a number of other compounding companies where simply it is a question of potluck whether you are going to get what you order.

I go back to my point earlier. I know these compounding chemists cut corners, but if you are compounding something to inject into someone I think you need a degree of certainty in terms of what you have and really the onus is upon you to establish you know exactly what the substance is.

MR IHLE: Professor Handelsman, I want to ask you a question which flows on from some questions that I asked you the other day but in light specifically of this evidence.

PROF. HANDELSMAN: Yes.

MR IHLE: Do I understand correctly that on or about 8 January you had a telephone conference with the lawyers for ASADA - - -

PROF. HANDELSMAN: We had a face-to-face meeting.

MR IHLE: You had a face-to-face meeting on 8 January?
PROF. HANDELSMAN: Yes.
MR IHLE: We have been provided with a note. I'm not sure whose note it is, but it purports to be of a meeting that you had on 8 January in relation specifically to this Bio21 documentation.
PROF. HANDELSMAN: We had a meeting on that day.
MR IHLE: I understand from the evidence that you gave on 12 January that you yourself don't tend to take notes during meetings.
PROF. HANDELSMAN: I do not, no.
MR IHLE: You rely on the notes taken by lawyers?
PROF. HANDELSMAN: No, I rely on my memory. But I ask people who have a particular point to raise or make to confirm it in email to me.
MR IHLE: Is it fair that on 8 January when you were shown these documents or this analysis that is really the subject of most of the questions you expressed a great deal of reservation - well, a deal of reservation both in relation to your expertise of analysing these types of graphs but also what could be determined from these types of printouts?
PROF. HANDELSMAN: Look, we had a meeting at which some documents were shown me across a table. I don't usually try to - I usually can't absorb them in that way and think about them properly on the spot like that. I usually take them away, and in this case got them to give them to me to think about it and then write the report. So whatever I said then was the sort of scepticism that comes that I haven't fully absorbed what's there.
MR IHLE: You were also shown the report of Dr Watt which is

now before this Tribunal.

PROF. HANDELSMAN: I saw little bits of it. I did not read the whole report and I only saw a couple of particular points in it. It was not given to me and I haven't read it, actually.

MR IHLE: So you haven't read it?

PROF. HANDELSMAN: No.

MR IHLE: Dr Vine, you have been provided with a copy of Dr Watt's report?

DR VINE: Yes, that's right.

MR IHLE: What do you say about Dr Watt's report? Do you agree with it, disagree with it, strongly agree, have reservations?

DR VINE: Fundamentally I'm in agreement with what Dr Watt says. I think he has reached the same conclusion that I have. There is something in that particular sample, but you can't be certain it is Thymosin Beta-4. The standard of the analytical evidence doesn't allow you to do that. I think he refers to it as a - I'm trying to think of the words he used. It won't come to me. Nothing better than a possibility anyway; I think that would be the gist of what he said, and I would concur with that. It is possible, but it is by no means established and you certainly can't rely on it. I think he called it a rough indication or words to that effect.

MR IHLE: Professor Handelsman, I'm trying to get a sense of this conference. You say there was a face-to-face meeting. This note that I'm about to take you to, the column is cut off, but it seems to say "teleconference with Professor Handelsman".

PROF. HANDELSMAN: We had a face-to-face meeting and someone

was on the phone. I can't remember who it was. So it was both face-to-face - it was mostly face-to-face; one person on the phone.

MR IHLE: In any event there was some discussion. That discussion involved Dr Watt himself.

PROF. HANDELSMAN: I think he was the one on the phone briefly, yes. But that was only for a short period.

MR IHLE: I'm going to hand this document down. It may or may not be something you have seen before.

PROF. HANDELSMAN: No, I have not seen this before.

MR IHLE: If you could hand those down. There is one for you and one for Dr Vine and there are three for the Tribunal. I will give you a moment just to read that document.

CHAIRMAN: Do you want to tender that?

MR IHLE: I will just ask a question or two about it, but I will be tendering it.

PROF. HANDELSMAN: I should say I'm struggling to read it.

CHAIRMAN: You are not on your own there, Professor.

PROF. HANDELSMAN: I thought it might have been my glasses.

MR HOLMES: The number is?

CHAIRMAN: It will be PG-16, Mr Holmes.

#EXHIBIT PG-16 - Diary note of 8 January 2015.

MR IHLE: Perhaps our learned friends could be good enough to tell us whose diary note it is.

MR HOLMES: Emily Fitton.

MR IHLE: I understand Emily Fitton is a solicitor with ASADA. Six lines down, "Handelsman is worried that we don't have the actual substance. We only have the files and the measurements."

PROF. HANDELSMAN: Yes.

MR IHLE: Is that an accurate record of something that you said

or represented?
PROF. HANDELSMAN: Well, it's close, but what I said was we would be far better off if we had the actual substance that had come from the compounding chemist or somewhere. Then we wouldn't have all the struggles we are going through. But, yes, that's the spirit of it, yes.
MR IHLE: You see there, "The Bio21 information is really just circumstantial evidence."
PROF. HANDELSMAN: Yes, I think that's fair enough because it wasn't ordered by ASADA or anybody competent. It was ordered by a compounding chemist. And so I was sceptical - just uncertain what to make of it. But bear in mind at this point I hadn't really looked at them, absorbed it or made any estimate of what it actually showed.
MR IHLE: The next reference, "Peaks don't match." Do you remember who said that?
PROF. HANDELSMAN: That wasn't me. I think that was probably Steve Watt.
MR IHLE: It goes on, "Steve has issues with calibration."
PROF. HANDELSMAN: Yes.
MR IHLE: The next entry, "Mass accuracy is really unknown." Do you remember who said that?
PROF. HANDELSMAN: I think that's Stephen Watt. It wouldn't have been me.
MR IHLE: Do you disagree with any of these three statements if they were Dr Watt's?
PROF. HANDELSMAN: No, I don't disagree. It's a matter of how much weight you put on them. But I wasn't in a position at that meeting to make a decision one way or the other.
MR IHLE: The next entry, "Analysis looks like rough check to

look at whether they've got the right number of amino acids there." Do you remember who said that?

PROF. HANDELSMAN: That's possibly me, but I just can't be certain. But it's quite possibly me, yes.

MR IHLE: I want to go down to just after point 5 of the page, there's a line that starts "Melissa". Two lines down from that - - -

PROF. HANDELSMAN: Sorry, where is "Melissa"? Yes.

MR IHLE: "Can give an opinion, but given his" - this is not in relation to Melissa; I was just using that as a hallmark, at point 5. Two lines below the line with "Melissa", "Can give an opinion, but given his lack of expertise in protein measurement he doesn't want to be pinned down on it." Is that a comment that's attributable to you, Professor?

PROF. HANDELSMAN: Look, I think it's a misstatement of what I said, which was that my expertise in mass spectrometry is in steroids and small molecules and not so much in proteins. I think that's just overstating it. But I was more - I had some discomfort in that this was mass spectrometry of proteins, yes. It is not my natural area of grazing, so to speak.

Q. I am done with those questions. This is a question to both the professor and the doctor. Included in the material that you were provided were another number of analyses that were conducted or ostensibly conducted on 9 May 2012 at Bio21; do you agree with that?

PROF. HANDELSMAN: I'm not sure what you are referring to.

DR VINE: I think it's the Thymosin Beta-4 and the Thymosin OOF.

MR IHLE: No. You were given a USB stick each, and on that USB

stick there were graphs in relation to a number of other substances that were tested on the very same day. Both of you have only referred to the one test on 12 May, but in the materials that were provided to you were documents relating to other tests conducted on the very same day.

DR VINE: This is presumably the Thy A-2 and Thy C and Thy C-2 you are referring to.

MR IHLE: Yes, I will provide you with copies for ease of reference.

MR HOLMES: Can I just ask a question of Professor Handelsman?

CHAIRMAN: Yes.

MR HOLMES: That question Mr Ihle is about to ask is preceded on an assumption that they were both given the same things on a USB stick, Mr Ihle, you are talking about?

MR IHLE: As I understand it. If necessary I can refer to a letter from the AGS.

PROF. HANDELSMAN: I have the documents and I print out the documents I was given. So I can refer to those. But that's all I have seen.

MR IHLE: Let me ask you this then . I will hand these to you. As I understand it, a disclosure notice was served on Bio21 in December of last year. In relation to that disclosure notice they produced, amongst other things, the document in electronic form the results of analysis, it's been provided on a USB stick, but also printouts. Are these documents you have ever seen before, Professor Handelsman?

PROF. HANDELSMAN: Let me just refer to the documents that I did receive. They do not appear to be among the documents I received and they don't look familiar to me. No, I don't believe I received them. I have the documents

I received printed out here, the original set, and it's not among those.

MR IHLE: There were documents that you were provided with, but there were also a number of documents you were shown during a conference, including the report of Dr Watt. Do you agree with that?

PROF. HANDELSMAN: I saw bits of his report. I did not read it fully. I was pointed to one or two things in it only.

MR IHLE: Do you want some time just to digest this?

PROF. HANDELSMAN: No, go ahead. I don't know if Dr Vine has seen these.

DR VINE: Yes, I have. I have also had access to the memory stick too. So I have looked at the data with the software.

MR IHLE: Do you want five or 10 minutes?

PROF. HANDELSMAN: No, go ahead. If I get to a point where I need to do that I will tell you. But otherwise - - -

MR HOLMES: Can I just object. There is an element of unfairness here where we are going outside the existing report. It is based on a USB stick and some materials which clearly Dr Vine has had time to examine but not to prepare a report on. This witness, Professor Handelsman, has not seen it, as I understand the gist of his evidence. So we are using the opportunity for Professor Handelsman being here at the hot tub to get him to look at materials that Dr Vine has already seen but has not put on a report for and to give opinions on the run. That is an extension of the proceedings which is unfair to the experts where Dr Vine has looked at it and decided not to give a report. That's the decision they make.

But now they want to give evidence on a topic

which we haven't been given any notice of, and it is quite unfair to the witness to now go into a new area where he's still only got the hard copies, not all the USB stick and looking at it on the screen and conducting the tests. Remember when I started my questions directed to Dr Vine he actually used the software and examined it on the screen. Now Professor Handelsman hasn't been given that opportunity.

CHAIRMAN: I understand all that. What's the relevance of this, Mr Ihle? If it was relevant one might have expected that it would have already been elicited.

MR IHLE: It is. These documents are referred to in Dr Vine's report.

CHAIRMAN: Where?

MR IHLE: At paragraph 14. In the body of the paragraph under the table he says, "Other materials analysed under the names Thy A-2, Thy C, Thy C-2 gave a mass spectra which did not contain significant peaks above 2,000. These materials clearly do not contain Thymosin Beta-4." The relevance is this. Professor Handelsman has identified that he has confined the question based on an assumption that he made. This is analysis of other substances saved under the file name "Thy" in May 2012, at the same time the analysis which has been the subject of most of the cross-examination.

We say the relevance is in relation to the question which Professor Handelsman has asked himself in the report. It is a very simple proposition that I seek to put forward and it is that really which is set out in paragraph 14 of Dr Vine's report; that there were five analyses that were done on 9 May 2012 purportedly by Vania

all in relation to Thy substances, only one of which returned a result anywhere near anything known as Thymosin.

PROF. HANDELSMAN: Can I say that I have checked - there are five pictures, screen shots, you have provided me with. The third one, the one with .0026, is the same as what I saw and what Dr Vine saw.

MR IHLE: Correct.

PROF. HANDELSMAN: But I have not seen the first, second, fourth or fifth before.

MR IHLE: All right. Do you want me to take you through them? If you think there is any unfairness, you can just say.

CHAIRMAN: Let's see how we go. We certainly have to, in terms of evaluating the evidence, take into account the fact that the professor hasn't seen these before.

MR IHLE: Can I also, to answer the objection that's being raised, provide the Tribunal and my learned friends with a letter from the Australian Government Solicitor dated 10 January under which these materials were served which said, "The report of Professor Handelsman considered the results of mass spectrometry analysis conducted by Vania Giordani on behalf of Como Compounding Pharmacy at the Bio21 facility. These analyses were obtained from Bio21 under a disclosure notice." That's these documents. If there's been any unfairness, we say it's because there might be a misrepresentation or at least - and I will cop this if it is on me - a misreading of that. But these documents were served as part of the bundle with which Professor Handelsman's report was served.

PROF. HANDELSMAN: I have here the letter that came to me from the Australian Government Solicitor.

MR IHLE: I accept that wholeheartedly. There is not going to be an in-depth analysis here. There is a very simple set of questions.
MR HOLMES: The objection is based on the unfairness. There are two sentences there under that square box in paragraph 14. They have not been cross-examined upon. They have not been asked questions on. They are not disputed. But now, having got the witness here, the witness not having seen the material until now and seeing it in a small form, they are going to go beyond that and use that as a springboard to ask - I don't know.
MR IHLE: I can tell you exactly what I'm going to ask.
MR HOLMES: It is not in the report and it's not been cross-examined or asked questions of.
CHAIRMAN: What are you going to ask, Mr Ihle?
MR IHLE: I'm going to ask him to look at each of these analyses and say if he can exclude, based on these analyses, any form of known Thymosin.
CHAIRMAN: Based upon - - -
MR IHLE: Let's say Alpha-1 and Beta-4, which is the - - -
CHAIRMAN: Let's see how we go. The circumstances under which this has arisen, particularly in relation to the position of Professor Handelsman, we will take into account.
MR IHLE: Thank you, Mr Chairman.
CHAIRMAN: Professor, are you able to - - -
PROF. HANDELSMAN: I'm quite happy to go ahead on that basis.
CHAIRMAN: On that basis, with that caveat that I have just stated.
PROF. HANDELSMAN: Yes. Okay.
MR IHLE: Professor Handelsman, you will see the printout which is numbered 22 in the corner, saved under the file name

which ends "Thy A-2".

PROF. HANDELSMAN: Yes, I see.

MR IHLE: That does not tend to indicate the presence of either Thymosin Alpha or Beta-4, does it?

PROF. HANDELSMAN: Around 3,000 there could be an error, some little blips there, but there is certainly nothing around 5,000. So, no. But we don't know what these represent. These could be just running control fluids just to test the machine to see if there is any carryover from a previous analysis. I don't know what these are. But they don't appear to have much in the way of the target anolytes in them.

MR IHLE: Turning to page 24 in the corner - just so we can be clear the odd numbered pages have a tabular breakdown of what the peaks are.

PROF. HANDELSMAN: Yes.

MR IHLE: Do you agree with that?

PROF. HANDELSMAN: Yes.

MR IHLE: Although you say there may be something around 3000, the table hasn't picked anything up other than 346 and 522?

PROF. HANDELSMAN: No, that's correct.

MR IHLE: So that would exclude both Alpha and Beta-4?

PROF. HANDELSMAN: Yes. But, as I said, I don't know what these are. These could be control injections for all we know with nothing in them deliberately.

MR IHLE: And at 0024?

PROF. HANDELSMAN: Yes, same. Nothing there.

MR IHLE: Thy A-5?

PROF. HANDELSMAN: Thy A-5 was the one we saw before.

MR IHLE: I want you to go back to 0024.

PROF. HANDELSMAN: Yes.
MR IHLE: Do you see in the filename at the top that's called "Thy A-5".
PROF. HANDELSMAN: Yes, so it is.
MR IHLE: Again that doesn't seem to show any substance in the range of Thymosin Alpha-1 or Beta-4?
MR HOLMES: Does that have the same number up the top on the right-hand side? I'm just asking that. Is that a different number?
PROF. HANDELSMAN: You are right that there is nothing in that range, but it also doesn't go up. The one with 0024 doesn't go up to 5,000. So you have no idea. There could be Thymosin Beta-4 in it. I would say there's no Thymosin Alpha-1 in it, but there could be Thymosin Beta-4. It just doesn't go up high enough in the mass to charge ratio.
MR IHLE: The one at 26 is the one that we have been talking about for most of the afternoon?
PROF. HANDELSMAN: Yes, we have seen that before.
MR IHLE: The one at 28 doesn't show anything in the range of Alpha or Beta-4?
PROF. HANDELSMAN: Beta 4 is not in the range.
MR IHLE: There is nothing to indicate the presence of either?
PROF. HANDELSMAN: No, that is not true. There is nothing to indicate the presence of Alpha-1. It doesn't go up to even test whether - Beta-4 could be there. Dr Vine might comment on whether that's true or not.
MR IHLE: Dr Vine?
DR VINE: The mass range that's printed in those diagrams appears to only go up to mass 4,000. So if there was something above that you simply wouldn't see it.

PROF. HANDELSMAN: It is the same with the last one, too.
DR VINE: I don't know what the criteria that are applied by the instrument's computer are for listing peaks in tabular form. The tabulated peaks on the following page don't seem to go above 1,000. I'm not sure whether that means that there really isn't anything above there or whether that's subject to the same limited range. So what I'm saying is the range that's on the sheet of paper may not be the range that was acquired by the mass spectrometer. It may be the range that's just been displayed in that graph or it may be that that was the range that was acquired. You can't tell.
CHAIRMAN: The problem is all we have is that piece of paper.
PROF. HANDELSMAN: Yes.
DR VINE: Yes.
CHAIRMAN: So, in terms of what it can tell us, it doesn't seem to be very much.
DR VINE: No.
CHAIRMAN: Working purely off that document.
DR VINE: I'm not sure if this is admissible, Mr Chairman, but in my paragraph 14 I say there aren't any significant peaks. That comment was made on the basis of examining the files themselves, that I think they did go beyond 4,000 but I couldn't see anything in them. That's my recollection, but I would need to recheck that.
CHAIRMAN: That's not on the diagram obviously?
DR VINE: It wasn't on the diagrams printed, no.
MR IHLE: Just so we can be clear, in relation to each of those under acquisition parameter, the date of acquisition for each one is 9 May 2012?
PROF. HANDELSMAN: Yes.

MR IHLE: I tender those documents.
MR HOLMES: I maintain the objection.
CHAIRMAN: It will be subject to that objection, Mr Holmes. PG-17. No doubt we will hear submissions as felt necessary. How would we describe these, Mr Ihle?
MR IHLE: They would be described as the documents - - -
CHAIRMAN: Documents referred to in paragraph 14 of - - -
MR IHLE: They are documents produced by Bio21 pursuant to a disclosure notice served upon them by ASADA on 17 December 2014.
MR HOLMES: I don't think it is all of the documents.
MR IHLE: It is not all of the documents. But we might say they are marked ASA-2.0074 - - -
CHAIRMAN: Marked 0022, 24, 26, 28 and 30.
MR HOLMES: The odd numbers are on the back.
CHAIRMAN: So just 22 to 30.
#EXHIBIT PG-17 - Documents marked 0022 to 0030 produced by Bio21 pursuant to a disclosure notice served by ASADA on 17 December 2014.
MR IHLE: Thank you, Mr Chairman. I have no further questions.
MR CLELLAND: Nothing from us, Mr Chairman.
CHAIRMAN: Is there anything further that we need to trouble our learned experts with? Professor, thank you very much for your assistance now over a couple of weeks. No doubt you have an aeroplane to catch and we want you to catch it. So we won't hold you anymore. Dr Vine, thank you very much for your attendance. It's appreciated. Otherwise we will adjourn until 10 o'clock tomorrow.
ADJOURNED UNTIL THURSDAY, 22 JANUARY 2015 AT 10.00 AM