Medical Report (4)

Re: Wayne Douglas – Benzodiazepine Dependence

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Prepared for: Tokyo High Court

Date: 27/7/11

Signature:

Contents

Introduction

I have been invited to write this additional report with regards to Wayne's patient file held by us, which was released to him, upon his request, from our Quality Risk Control Department on 28th June 2010.

Further to Report 3, which focused mainly on Wayne's Benzodiazepine dependence in relation to the patient files from Japan, in this report I would like to focus mainly on the patient files from New Zealand and how Wayne's dependence diagnosis was initially determined.

In addition, I would like to take this opportunity to advance my opinion with regards to prescribing issues, informed consent and monitoring in Wayne's case. This is because I will be busy with various hospital commitments over the next several months and I understand the court proceedings present various time constraints as well.

This report consists of 4 main sections as follows:

1. Confirmation of Prescriptions (Diazepam equivalents)
2. Diagnosis & DSM-IV TR (initial assessment)
3. Differential Diagnosis (additional information based on NZ files)
4. Prescribing, Informed Consent, Monitoring

Section One looks at confirming the exact doses that Wayne was prescribed and the Diazepam equivalents.

Section Two looks at the grounds upon which I made my initial dependency diagnosis, including the application of the DSM-IV TR, and the symptoms that Wayne presented with.

Section Three provides additional information regarding the differential diagnosis based on Wayne's previous history contained in his New Zealand medical records.

Section Four looks at prescribing, informed consent and monitoring based on Wayne's case in relation to recommendations outlined by the World Health Organization and other general prescribing guidelines.

Once again, the reference numbers to evidence items lodged in the court were provided to me by Wayne and his lawyer and I have not been able to verify them firsthand, however, I trust they are consistent with the court records.

Section One

1. Confirmation of Prescriptions

1.1 Diazepam Conversions

1.1.1 Below is a breakdown of the Diazepam equivalents supplied by Mental Health & Addiction Services. Further to my first Report 1, which covered simple prescription history, I would like to clarify the converted Diazepam equivalents of the Benzodiazepines that were prescribed to Wayne. Below is a breakdown for the Benzodiazepine component of the prescriptions (daily dosage):

Prescribing Doctor (Hospital)	Period	Prescription Drugs		Dose (mg)		Diazepam Equiv (mg)
		Trade Name	Chemical Name			
Dr. [redacted] ([redacted] Clinic)	5/7/00 ~ 22/1/01	Contol	Chlordiazepoxide	15		6
		Rivotril	Clonazepam	0.9		9.0
		Grandaxin	Tofisopam (10%)	150		6
Total Diazepam						**21**
Dr. [redacted] ([redacted])	23/1/01 ~ 8/4/01	Rivotril	Clonazepam	1.2		12
		Constan	Alprazolam	1.2		12
Total Diazepam						**24**

NB: As we do not deal with Tofisopam in New Zealand, we have no conversion rate for this drug. Subsequently, the rate included above was based on the Japanese source supplied by Legal Counsel [redacted] below in Article 1.1.2, as this drug is more commonly used in Japan.

1.1.2 Below is a breakdown of the Diazepam equivalents supplied by Legal Counsel [redacted]

Prescribing Doctor (Hospital)	Period	Prescription Drugs		Dose (mg)	Conv Rate (5)	Diazepam Equiv (mg)
		Trade Name	Chemical Name			
Dr. [redacted] ([redacted])	5/7/00 ~ 22/1/01	Contol	Chlordiazepoxide	15	10	7.5
		Rivotril	Clonazepam	0.9	0.25	18
		Grandaxin	Tofisopam (10%)	150	125	6
Total Diazepam						**31.5**
Dr. [redacted] ([redacted])	23/1/01 ~ 8/4/01	Rivotril	Clonazepam	1.2	0.25	24
		Constan	Alprazolam	1.2	0.8	7.5
Total Diazepam						**31.5**

1.2 Reasons for Differing Diazepam Conversions

1.2.1 The rate used for converting Diazepam equivalents tends to differ from source to source. This is because individual variation in clinical responses to "equivalent" doses can vary so close monitoring of patient response to substitution is necessary when converting from one Benzodiazepine to another.

1.2.2 The source of conversion rates used by us here at the Mental Health & Addiction Services is based on the ASAM and TRANX guidelines.

1.2.3 The rate used by Legal Counsel [redacted] gives a slightly higher Diazepam conversion than the rate used by us here at Mental Health & Addiction Services. However, it is not unusual to have a slight variation in conversion ranges and more importantly, it does not by any means alter the fact that Wayne became dependent to the doses that were prescribed to him.

1.3 Tofisopam

1.3.1 I understand the defense is claiming that Tofisopam is non-addictive. As mentioned above, we do not deal with Tofisopam in New Zealand, however, Professor Ashton has provided the following information with regards to this.

"All the benzodiazepines are non-selective and act on all types of GABA/benzodiazepine receptors. Valium acts on exactly the same receptors as Klonopin etc. The main reason that benzodiazepines have somewhat different structures is not so much that they act on different receptors (they don't) but so that the drug companies can call them different drugs. They remain chemically benzodiazepines (a chemical name). Although they may differ in binding affinity for the receptors, potency, elimination time, etc., they all act on all subclasses of benzodiazepine receptors. Animal studies have consistently shown that all benzodiazepines are capable of inducing physiological dependence after chronic administration."

"The drug Tofisopam is a benzodiazepine derivative manufactured in China. It has anxiolytic properties but is said not to have sedative, anticonvulsant, or muscle relaxant properties. I have no experience with this drug but it is almost certain that in some doses within the therapeutic range the drug will turn out to be addictive and, if used long-term, will cause withdrawal symptoms. Non-benzodiazepines which have been claimed to have specific effects (such as zopiclone) have turned out to have all the same actions as benzodiazepines, including dependence (addiction) and withdrawal effects. Furthermore, any drug that alleviates anxiety, (e.g. alcohol, barbiturates and the earlier tranquillizers) is almost certain to cause dependence in some people. Even antidepressant drugs which relieve anxiety cause withdrawal effects when stopped."

1.3.2 Even if in the case that Tofisopam was not addictive, this argument does not by any means alter the fact that Wayne became dependent, as he was prescribed other Benzodiazepines as well. That is to say, even if the Tofisopam was removed from the equation, the remaining Diazepam equivalent was still sufficient enough to form dependence.

1.4 Addictiveness of Benzodiazepines

1.4.1 As outlined in Article 2.1 of my 3rd report, Professor Ashton has confirmed that it is possible to develop tolerance and dependence on minimal therapeutic doses as low as 2.5~5mg of Diazepam.

1.4.2 It is often assumed that when Benzodiazepines are prescribed legally they must be safe. However, this is not necessarily the case.

1.4.3 Below is a quotation from Professor Malcolm Lader (Professor Lader is an adviser to the World Health Organisation on drugs used in psychiatry).

"It is more difficult to withdraw people from benzodiazepines than it is from heroin. It just seems that the dependency is so ingrained and the withdrawal symptoms you get are so intolerable that people have a great deal of problem coming off. The other aspect is that with heroin, usually the withdrawal is over within a week or so. "With benzodiazepines, a proportion of patients go on to long term withdrawal"

1.5 Breakdown of Reduction Attempts

1.5.1 Below is a breakdown of Wayne's attempts at reduction.

No.	Time	Type of Attempt (Stopping or Reducing)	Result	Evidence	Doctor
# 1	Late Nov 2000	Attempt at stopping (2 consecutive doses)	Unsuccessful	• See Report 3, Article 2.5.2 • Pg 8, Article 9 of Wayne's first statement	Dr. [redacted]
# 2	1st Mar 2001	Attempt at reducing (1 single dose)	Unsuccessful	• See Report 3, Article 2.3.4 • Pg 10 of [redacted] patient file (Evidence Koh A6)	Dr. [redacted]
# 3	27th Mar 2001	Attempt at stopping (2 consecutive doses)	Unsuccessful	• See Report 3, Article 2.3.6 • Pg 11 of [redacted] patient file (Evidence Koh A6)	n/a
# 4	28th Mar 2001	Attempt at reducing (1 single dose)	Successful, but suffering withdrawal	• Pg 3 of Dr. Whitwell's file (having problems with withdrawal)	Dr. Whitwell

Dr. Whitwell's patient file supports Report 3, Article 2.3.4 because it shows that Wayne had continued taking the drugs 3 times a day following his 2nd unsuccessful attempt at reduction under Dr. [redacted], despite showing an awareness that they were likely causing harm.

1.6 Formal Reduction History Breakdown

Mth	Date	Day	Morn (mg)	Noon (mg)	Night (mg)	Dzm Eq (mg)	Notes
Mar	25th	Sun	0.4/0.4	0.4/0.4	0.4/0.4	24	Wayne returned to NZ on 0.4mg Clonazepam / 0.4mg Alprazolam 3 x day
Mar	26th	Mon	0.4/0.4	0.4/0.4	0.4/0.4	24	
Mar	27th	Tue	0.4/0.4			8	Wayne reports 3rd attempt at stopping
Mar	28th	Wed	0.4/0.4		0.4/0.4	16	Wayne reduced to twice a day
Mar	29th	Thu	0.4/0.4		0.4/0.4	16	← Wayne approached Dr. Whitwell, as he was having difficulty with withdrawal. Dr. Whitwell explained that Benzodiazepines are addictive and proceeded with a reduction plan encouraging Wayne to maintain a reduction at twice daily doses.
Mar	30th	Fri	0.4/0.4		0.4/0.4	16	
Mar	31st	Sat	0.4/0.4		0.4/0.4	16	
Apr	1st	Sun	0.4/0.4		0.4/0.4	16	
Apr	2nd	Mon	0.4/0.4		0.4/0.4	16	
Apr	3rd	Tue	0.4/0.4		0.4/0.4	16	
Apr	4th	Wed	0.4/0.4		0.4/0.4	16	
Apr	5th	Thu	0.4/0.4		0.4/0.4	16	
Apr	6th	Fri	0.4/0.4		0.4/0.4	16	
Apr	7th	Sat	0.4/0.4		0.4/0.4	16	
Apr	8th	Sun	0.4/0.4		0.4/0.4	16	
Apr	9th	Mon	0.25		0.5	7.5	← Wayne was further encouraged to reduce and was prescribed Clonazepam (0.5mg x 45 tabs) only. He started taking ½ morn, 1 night. He was then referred to our service as he was having trouble with withdrawal.
Apr	10th	Tue	0.25		0.5	7.5	
Apr	11th	Wed	0.25		0.5	7.5	
Apr	12th	Thu	0.25		0.5	7.5	
Apr	13th	Fri	0.25		0.5	7.5	
Apr	14th	Sat	0.25		0.25	5	Wayne self reduced to ½ tab twice daily
Apr	15th	Sun	0.25		0.25	5	
Apr	16th	Mon	0.25		0.25	5	
Apr	17th	Tue	0.25		0.25	5	
Apr	18th	Wed	0.25		0.25	5	
Apr	19th	Thu	0.25		0.25	5	Wayne presented to us (nurse assessment)
Apr	20th	Fri	0.25		0.25	5	← I saw Wayne for the first time and a treatment (reduction) plan was discussed. We also provided info on Benzodiazepines and the nature of withdrawal. Although, Wayne showed a strong determination to stop, we encouraged him to stay on his current dose to allow his body to readjust.
Apr	21st	Sat	0.25		0.25	5	
Apr	22nd	Sun	0.25		0.25	5	
Apr	23rd	Mon	0.25		0.25	5	
Apr	24th	Tue	0.25		0.25	5	
Apr	25th	Wed	0.25		0.25	5	
Apr	26th	Thu	0.25		0.25	5	
Apr	27th	Fri	0.25			2.5	Wayne self reduced to ½ tab morn (estimated time)
Apr	28th	Sat	0.25			2.5	
Apr	29th	Sun	0.25			2.5	
Apr	30th	Mon	0.25			2.5	← Follow-up consultation. Wayne noticed the worsening of some of his symptoms, however, he remained determined to stop and a plan was made to reduce his drug intake to nil over the following 2 weeks.
May	1st	Tue	0.25			2.5	
May	2nd	Wed	0.25			2.5	
May	3rd	Thu	0.25			2.5	
May	4th	Fri	0.25			2.5	
May	5th	Sat	0.25			2.5	
May	6th	Sun				0	Wayne had stopped his drug intake
May	21st	Mon	A follow-up consultation was conducted. Wayne was experiencing additional withdrawal symptoms, which he provided in list form (See page 22 of Mental Health & Addiction Services patient file). The nature of withdrawal was discussed again and he was discharged back to his GP, Dr. Whitwell.				

1.7 Clarifications of File Content

(1) Drug Names

1.7.1 On page 6 of the Mental Health & Addiction Services patient file, it says:
"Came over from Japan on Rivotril (Clonazepam) 1.2 mg od 24mg Diazepam
Librium (Chlordiazepoxide) 1.2 mg od Equivalent"
(NB: od = once daily)

1.7.2 I can confirm that the drug name "Librium (Chlordiazepoxide)" above was a mistake and that Wayne was in fact taking "Constan (Alprazolam)", this is confirmed in the entry by our detox nurse (page 16).

1.7.3 This is also consistent with the following records:
1) Page 10 of the [redacted] patient file (Evidence Koh A6)
2) Page 2 of Dr. Whitwell's patient file
3) GP referral form

1.7.4 Subsequently, I can confirm that he came over from Japan on the following prescriptions:
1) Rivotril (Clonazepam) 0.4mg 1 TDS after meals (3 x daily) = 1.2 mg daily
2) Constan (Alprazolam) 0.4mg 1 TDS after meals (3 x daily) = 1.2 mg daily

1.7.5 The conversion rate used for determining the Diazepam equivalent of 24mg in Article 1.7.1 above was as follows:

Clonazepam	1.2mg × 10 =	12mg
Alprazolam	1.2mg × 10 =	12mg
		24mg

(2) Prescription Changes

1.7.6 On page 6 of the Mental Health & Addiction Services patient file, it says:
"End of March Seen GP No change"

1.7.7 This refers to the fact that Dr. Whitwell did not change Wayne's prescriptions when Wayne first presented to him on 29th March 2000.

(3) Reduction Amounts

1.7.8 On page 16 of the Mental Health & Addiction Services patient file, there is an entry on 19th Apr 2001, which says "Clonazepam 0.5 mg BD" (NB: BD = 2 times a day)

1.7.9 I can confirm that this was the total amount of tablets that had been prescribed to Wayne by Dr. Whitwell, but in fact Wayne was only taking half in the morning and half in the evening at the time of he presented to us on 19th Apr 2001. This is shown in the next sentence, where it says "Has since in the last week reduced his own dose to Clonazepam 0.25 mg BD"

(4) Weekly Use

1.7.10 The weekly use recorded on page 12 of the Mental Health & Addiction Services patient file refers to the week leading up to Wayne's presentation at the A&D service (See Article 1.6 above).

1.7.11 The wording "last week" refers to one week's time leading up to the day of Wayne's presentation – not a calendar week. This is consistent with her other entry made the same day on page 16, which says "Has since in the last week reduced his own dose to Clonazepam 0.25 mg BD"

1.8 Previous History of Drug Use

1.8.1 As outlined in Report 1, Article 1.2, when Wayne presented to our service, both the detox nurse and I carried out a detailed series of questions with regards to Wayne's history of drug use.

1.8.2 Subsequently, it was noted that Wayne had no prior hallucinogen use, no history opiate use, no history of solvent use and no history of stimulant use (See page 5 of patient file).

1.8.3 As outlined in Report 1, Article 1.2.3, he did however acknowledge that he used cannabis between ages of 15 and 21, but had no cannabis since the age of 21. Wayne reported that he smoked about 1 marijuana cigarette between about 5 people at parties.
NB: On page 5 of the patient file it says from age 17.

1.8.4 On page 4 of the patient file it says "Counsellor visited once at a school. Decision was to stop cannabis. No Cannabis since age 21." Wayne reports this took place at age 21 (in 1987), after which he stopped.

1.8.5 I have been informed that Wayne's history thereafter has also been entered into the evidence. Wayne says that after distancing himself from untoward peer pressure and associated cannabis use, he decided to take advantage of a government initiative to return to school, as an adult student in 1990. After this, he began studying at university, where he excelled in learning Japanese, and apparently went on to represent New Zealand in a scholarship tour of Japan. I understand that he also went on to receive numerous accolades for his work in the field of international relations in Japan. This history is consistent with the note in the patient file on page 13, where it says "Only as teenager, smoking dope. Rebuilt life. Since no problems."

1.9 Findings

1.9.1 Wayne's history does not suggest that he has an addictive personality and that he indeed had a substance free history with exception of the cannabis use that was mentioned.

1.9.2 The only history of note with Wayne regarding substance use was the Benzodiazepine regime that he was initially prescribed by Dr. [redacted] in 2000.

1.9.3 As outlined in Report 3, Article 1.3, we can determine that there was at least a 50~100% chance that Wayne was dependent simply based on the duration and dosages of his prescriptions alone – before we even look at the overall clinical picture or the application of the DSM-IV TR.

1.9.4 Further, regardless of the differences in Diazepam conversions mentioned above, the overall amounts were still sufficient enough to form dependence, as confirmed by Professor Ashton, who has observed the development of tolerance and dependence in patients on minimal therapeutic doses as low as 2.5~5mg of Diazepam (Report 3, Article 2.1).

Section Two

2. Diagnosis & DSM-IV TR

Below is an explanation of how we were able to determine Wayne's initial dependency diagnosis based on the information we had in our files before the proceedings for compensation commenced.

NB: As a result of Wayne's legal case for compensation, more and more questions have been asked, and subsequently, a lot of additional information has surfaced after the fact, such as the content of the patient files from Japan. Most of this additional information was considered and applied to the dependency diagnosis in Report 3. Although a lot of the additional information retrieved after the fact actually supports the dependency diagnosis, in this section of Report 4, I would like to focus on the method used in making the initial dependency diagnosis upon Wayne's presentation to our service in April 2001.

2.1 Diagnostic procedure

Refer to Report 1, Articles 2.1.1~4 for explanation of this.

2.2 Original Grounds for Diagnosis (Etiology)

2.2.1 As explained in Report 1, one of the first things we did was to consider the referral form from Wayne's GP, Dr. Whitwell. Noted in this referral was the fact that Wayne had a very strong desire to stop and yet was having difficulty reducing. This is evident where it says "attempting reduction without complete success. Patient very keen to get off these meds".

2.2.2 Noted in Wayne's history upon presentation was the fact that he had been prescribed multiple combinations of Benzodiazepines and a tricyclic antidepressant for almost a 10 month period by the time he was assessed at our service. Subsequently, we were able to determine that there was at least a 50~100% chance that he was dependent simply based on the duration and dosages of his prescriptions alone.

2.2.3 Based on the interviews with Wayne, we were able to form the initial overall clinical picture (Report 1, Article 2.2). Through these interviews we were also able to determine the fact that Wayne did not have an addictive personality. This was made evident by his keenness to distance himself from the Benzodiazepine regime and his history (See page 5 of patient file).

2.2.4 Also taken into consideration was the application of the DSM-IV TR (See next page).

NB: We also carried out some tests including thyroid function test, blood glucose test and full blood count (See page 17 of patient file). These were done to check if there was any other reason that could have explained his feeling of "lousy". I usually do these to rule out more common forms of tiredness, which I was able to do in Wayne's case. Also done at the time were U&E (check renal function), LFT's (check liver function) and all results did come in the normal range.

2.3 DSM-IV TR Based on Initial Assessment

2.3.1 The DSM-IV TR criteria can be applied to Wayne's initial assessment, as follows:

(1) Tolerance

Tolerance was evident in the fact that Wayne reported some settling of his symptoms, but soon afterwards his symptoms started to return along with others. This is supported by the comment on page 3 of Wayne's typed notes upon presentation to our service (page 9 of the patient file) where it says "Although my condition had stabilized to a certain extent (initially), I continued to suffer from most of the aforementioned symptoms....Furthermore, additional symptoms began to appear..."

Further, as outlined in Report 3, Article 2.1, the fact that Wayne produced withdrawal symptoms upon reduction at our service also confirms that he had developed tolerance. This is due to the fact that withdrawal and tolerance are interrelated because if a patient does not have tolerance, then there is no neuro-adaptation, and thus no withdrawals will occur (Report 2, page 1).

NB: Refer to Report 3, Article 2.1 for additional information regarding the application of the criteria for Tolerance.

(2) Withdrawal

2.3.2 As mentioned in my first letter, dated 10 Sep 2004, when Wayne first presented to our service on 19th Apr 2001, he had a full comprehension of his history and presented it to both myself and the Detox Nurse in typed form (See pages 7~11 of patient file). It was noted that many of the symptoms contained in this history were consistent with Benzodiazepine withdrawal and or side effects.

2.3.3 As outlined in Report 1, Article 2.3 – 2, in Wayne's case, as he had been prescribed Benzodiazepines ongoing for almost 10 months by the time he was reviewed at our service, it was very likely that he would have had withdrawal symptoms simply based on the length of time he was prescribed Benzodiazepines for.

2.3.4 Wayne met the criteria for withdrawal, which was made evident by the following symptoms, which either initially emerged during the course of his treatment due to tolerance (Report 3, Article 2.2.3) or initially got worse or first developed on reduction of his overall dose as recorded in the patient file and shown below:

No.	Withdrawal Symptoms Outlined in Report 3, Article 2.2.9	Correspondence to Patient File (Initial Assessment)
1	Tingling sensation over face	Pg 22
2	Loss in coordination	Pg 22 (arm & hand)
3	Myoclonic jerks	Pg 22 (involuntary movements)
4	Oily smell in body odour	Pg 22 (increased hypersensitivity)
5	Increased joint pains	Pg 22
6	Tightening of muscles	Pg 18 (21/5/01) & Pgs 21~22
7	Worsening of dizziness	Pg 18 (30/4/01)
8	Worsening of pulsating temporal arteries	Pg 18 (30/4/01)
9	Worsening of visual disturbances	Pg 18 (21/5/01) & Pg 21
10	Increase in emotional instability	Pgs 10~11 (Feel on brink of having nervous breakdown)
11	Increased palpitations	Pg 10
12	Tightening in chest	Pg 11
13	Flushing	Pg 10
14	Hypersensitivity	Pg 10 (hyper and nervy)

2.3.4 As outlined in Report 1, Article 3.1.6, our service provided Wayne with information on Benzodiazepines at his first consultation on 19th Apr 2001. This included information on what they are prescribed for, how they work, the nature of side-effects and withdrawal and how to identify the symptoms.

2.3.5 With this increased awareness, Wayne was able to identify several other withdrawal symptoms, which he provided by way of a typed list at his final consultation on 21 May 2001 (See pages 21~22 of patient file). This list of withdrawal symptoms included those that he had first developed during the drug treatment and new ones that he developed after stopping completely on 5 May 2001.

NB: In my letter to Dr. Whitwell, dated 5th June 2001, I mentioned that when Wayne reduced his dosage he noticed the symptoms of dizziness, pulsating temporal artery, and headaches returned, but they quickly settled over the following five days after reduction. This means that the symptoms had settled back to the level they were before the previous step in reduction – it does not mean they settled completely.

To explain further, this refers to the fact that each time Wayne reduced, he experienced a worsening of symptoms. He also had numerous other withdrawal symptoms in addition to the above (See pages 10, 11, 21, 22 of file) and many of them did not begin to settle completely until after about 6 months following complete cessation. This is supported by the entry in Dr. Whitwell's patient file in November 2001, where it says "slow improvement in most areas" and again in January 2002, where it says "Symptoms – most improving except ocular". Also noted in January 2002 was the fact that Wayne's pulse rate had returned to 68 (normal) from 90 (tachycardia) recorded on page 3 of the [redacted] patient file.

NB: Refer to Report 3, Article 2.2 for additional information regarding the application of the criteria for Withdrawal.

(4) Loss of Control

2.3.6 Regarding the criteria for loss of control, it was noted in Dr. Whitwell's referral form to our service that Wayne was "attempting reduction without complete success" (See page 23 of Mental Health & Addiction Services patient file).

NB: One can see the following entry made by Dr. Whitwell in his patient file on 9th April 2001.

Tired	–	on	Alprazolam	0.4mg 1 bd
			Rivotril	0.4mg 1 bd

Having problems with withdrawal
Control
~~Add Fluoxetine 20mg~~
?? look at home detox

This supports Article 2.3 of Report 3 for Loss of Control.

Further, this is consistent with Article 2.3 of Report 3, which highlights the fact that Dr [redacted] was also not sure whether or not to reduce Wayne's intake from 3 to 2 times a day because of the symptoms worsening.

2.3.7 Other unsuccessful attempts at reduction became clear after proceedings for compensation had commenced (See Article 1.5.1 above).

NB: Refer to Report 3, Article 2.3 for additional information regarding the application of the criteria for Loss of Control.

(6) Impact on Life

2.3.8 When Wayne presented to our service, it was clear that he had suffered an impact on his life due to the fact that he was no longer able to work.

2.3.9 As outlined in Report 2, of particular note was the fact that he was still able to work in Japan, albeit on light duties, before the treatment began, but he struggled to complete his contract during the course of the treatment (subsequently cut short), after which he ended up in a state where he was unable to work at all again for over one year.

NB: Refer to Report 3, Article 2.4 for additional information regarding the application of the criteria for Impact on Life.

(7) Continued Use Despite Knowledge of Harm

2.3.10 As outlined in Report 3, Article 2.5.1, the fact that Wayne always produced detailed notes regarding his condition upon consultation shows that he is the type of person who is aware his condition.

2.3.11 Noted in the history that Wayne presented to our service was the list of additional symptoms that he developed following approximately 4 months of drug treatment. Further, after showing awareness that he had developed these new symptoms, he endeavoured to seek alternative help from another hospital (See page 10 of patient file).

2.3.12 Despite showing awareness that the drugs were possibly causing him harm, he continued to use, which supports the criteria for Continued Use Despite Knowledge of Harm.

NB: Refer to Report 3, Article 2.5 for additional information regarding the application of the criteria for Continued Use Despite Knowledge of Harm.

2.4 Symptoms on Presentation

2.4.1 Also taken into consideration upon Wayne's presentation to our service was the list of symptoms contained in his typed notes (See pages 10~11 of patient file). I note that the symptoms contained in this list are consistent with those referred to in Report 3, Article 2.1.3 / Evidence Koh A12, and Article 2.2.3 / Evidence Koh A26.

2.4.2 I also note that there are some slight variations. For example; according to Evidence Koh A12, Wayne first developed the palpitations following 1.5 months of Benzodiazepine exposure, but according to his typed note on page 10 of the patient file, he developed palpitations from October.

2.4.3 Also, on page 2 of Wayne's typed notes (page 8 of patient file) he lists "jaw pain" under the group of symptoms as at 16th May 2000, following his initial vertigo attack. Wayne in written communication has since reported that this was a mistake and that he did not develop any tightness in his jaw until about October 2000, when it started to lock up and was accompanied by a general stiffening of muscles encompassing his entire body (Report 3, Article 3.3.17).

2.4.4 This is consistent with the fact that there is no mention of jaw pain / stiffness in any of the other documentation, including any of the patient files, before it was first noted in Wayne's handwritten note to Dr. [redacted] in December 2000 (Report 3, Article 2.2.3 / Evidence Koh A26).

2.4.5 According to Wayne's first statement (Page 8, Article 7), he did not bring the psychological symptoms (that he developed during the treatment) to the attention of Dr, [redacted] for fear of being committed to a psychiatric institution in a country different from his own.

2.4.6 However, he did complain of these symptoms upon presentation to our service. These included feelings of being hyper and nervy, emotional instability, (chronic) anxiety, feelings of being on the verge of having a fit / going mad, mood swings, (chronic) depression, feelings of having a nervous breakdown and confusion (See page 21 of patient file).

2.4.7 The mood swings and aggressiveness were also noted in statements from friends and family (Report 3, Articles 2.4.3~4).

2.4.8 The panic attacks were initially described as episodes of being hyper and nervy, emotional instability, being on the verge of having a fit etc, but were not recognized as being panic attacks as such until after most of Wayne's other symptoms had subsided and after he had learnt more about the untoward effects of Benzodiazepine dependency through various publications and through our follow-up discussions at the time of writing Report 1.

2.4.9 As outlined in Report 3, Article 1.2, when determining a diagnosis for dependence, it is not sufficient enough to simply analyze symptoms, rather everything needs to be considered in context including; the patient background / history, overall clinical picture, application of the DSM-IV TR criteria and the combined relationship of this information.

2.5 Recovery (additional information)

2.5.1 It was noted in Report 3, Article 3.1.2, that Wayne recovered from most of his symptoms within the first year of cessation with many symptoms subsiding within the first 3 months. It was also noted in Article 11 of the summary that he "recovered from most of his symptoms within about 3 months of completing the initial withdrawal phase". Given that the initial withdrawal phase took several months, and that many of his symptoms started to improve 3 months after that, it would mean that he was starting to show signs of recovery after about 6 months of stopping.

2.5.2 This can be confirmed by the entry made in Dr. Whitwell's file on 1st November 2001, where it says "slow improvement in most areas".

2.5.3 Further, the fact that Wayne continued to make a steady recovery with time is supported by the entry made in Dr. Whitwell's file on 8th January 2002, where it says "Symptoms – most improving except ocular. Is looking at going back to work".

2.5.4 As outlined in my first letter, dated 10 September 2004, when I saw Wayne again in January 2003 and again in April 2003, it was apparent that he had been making a significant improvement in his state of overall physical and psychological health since he was first referred to our service. This is supported by the entry made by Psychologist Alan Guy, which says "Presented looking very well + reporting a stable increased weight than when last seen here. No obvious mood disorder". Also, noted was the fact the he had remained Benzodiazepine free since he was discharged back in May 2001 (See Mental Health & Addiction Services patient file, page 19).

2.5.5 Further, when I saw Wayne again in September 2004, it was apparent that his condition continued to improve in the absence of Benzodiazepines. This was noted in the file where it says "Today he is healthier & fitter than before (April 2003). Wayne looks well in appearance - bench presses 180 kg".
NB: Wayne has since informed me that he was actually squatting 180 kg, and bench pressing over 100kg. Nonetheless, it was a significant improvement considering that he was having difficulty just walking when we first saw him.

2.6 Records

2.6.1 You will note that my consultations with Wayne were recorded in the Mental Health & Addiction Services patient file as far as 8th 2004.

2.6.2 All of the additional work done regarding Wayne's case for compensation since then has been done on a volunteer basis in my own time. Subsequently, no hospital records regarding Wayne's case were maintained after September 2004.

Section Three

3. Differential Diagnosis (Additional Information Based on NZ Patient Files)

3.1 Dr. ter Haar' File – History of Complaints (9 Mar 1989 ~ 18 Jun 1996)

3.1.1 Below is a list of complaints taken from Wayne's history under Dr. ter Haar that may be used to try and rule out certain symptoms associated with his Benzodiazepine dependence. Subsequently, I would like to take this opportunity to differentiate between these previous complaints and the dependency symptoms in 2000 ~ 2001.

(Pg.1: Low back pain)

3.1.2 We know that Wayne had a previous history of periodic lower back pain since straining his back lifting heavy lumber in March 1989 (discussed in Article 3.3.17 of Report 3).

It may be argued that the "muscle stiffness" Wayne experienced during the drug treatment in 2000 ~ 2001 was attributable to his previous episodes of "low back pain".

As mentioned in Report 3, the "muscle stiffness" associated with the dependence was not localized or limited to one area; rather it encompassed his entire body. This general all over "muscle stiffness" is supported by the fact that Wayne began a course of regular full-body deep tissue massage from November 2000 (following 4~6 months of Benzodiazepine exposure) at a local physiotherapy clinic in Saitama to help try and alleviate this. NB: I have been informed that the physiotherapy clinic has supplied Wayne with a letter explaining this muscle stiffness and subsequent course of full-body massage therapy.

(Pg.1: Left shoulder pain)

3.1.3 Wayne suffered from recurring left shoulder dislocations following a sporting incident in 1985. This continued to cause him discomfort until after he had recovered from the subsequent operation done by orthopedic surgeon, Tim Astley, in 1991.

It may be argued that the additional "shoulder stiffness" (Report 3, Article 2.1.3 / Evidence Koh A12) Wayne experienced during the drug treatment in 2000 ~ 2001 was attributable to his previous dislocations and subsequent operation.

However, the pain associated with the above, had already resolved itself following a course of strengthening exercises and physiotherapy before Wayne travelled to Japan in 1999. This is supported by the entry on page 4 of Dr. ter Haar's patient file, where it says "Good result from shoulder repair". Further, the pain associated with the shoulder dislocations, was limited to the left side only. The "muscle stiffness" associated with the dependence, however, included, not only both shoulder areas, but the entire body, as explained above.

3.1.4 We can see from the above history, a number of Wayne's previous complaints occurred as separate individual cases, under different circumstances at different periods in time, and were not accompanied by other groups of symptoms.

Whereas, the dependency symptoms all occurred under the same circumstances at the same time and were accompanied by other symptoms consistent with dependence. Further, all of the symptoms associated with Wayne's dependency increased again during the withdrawal process and then they improved after the drugs had been removed.

3.1.5 Considering the above within context of the overall clinical picture (Report 1, Article 2.2) and the fact that Wayne met 5 criteria of the DSM IV-TR within the same 12 month period, it is clear that Wayne's previous history was not a contributing factor to his condition in 2000 ~ 2001, rather it was caused by Benzodiazepine dependency.

NB: Wayne was a regular patient of Dr. Barry ter Haar from 9 Mar 1989 ~ 18 Jun 1996.
He then travelled to Japan in July 1996 to undertake a public relations job.
After, he returned in August 1998, he relocated to Waitara and subsequently, became a regular patient of Dr. Whitwell from 4 Sep 1998 (See below).

3.2 Dr. Whitwell's File – History of Complaints (4 Sep 1998 ~ 1 May 2002)

3.2.1 Below is a list of complaints taken from Wayne's history under Dr. Whitwell that may be used to try and rule out certain symptoms associated with his Benzodiazepine dependence. Subsequently, I would like to take this opportunity to differentiate between these.

(Pg.3: Long History of Slightly Stiff Neck)

3.2.2 We know that Wayne had a previous history of periodic neck pain, which according to Wayne, first developed in late 1997 whilst doing prolonged desk work using a laptop computer with poor ergonomics at the Miyazaki Local Government Office (discussed in Article 3.3.17 of Report 3). NB: Dr. ter Haar's patient file above shows that Wayne had no history of neck pain prior to 1997.

It may be argued that the "muscle stiffness" Wayne experienced during the drug treatment in 2000 ~ 2001 was attributable to his "long history (3 years) of slightly stiff neck"

However, once again, the "muscle stiffness" associated with the dependence was not localized or limited to one area; rather it encompassed his entire body and had worsened to the degree that his jaw began locking up.

(Pg.3: Pain in between shoulder blades)

3.2.3 On 4th September 1998 Wayne also complained of "pain in between shoulder blades (leading up to neck)".

It may be argued that the "muscle stiffness" Wayne experienced during the drug treatment in 2000 ~ 2001 was attributable to this "pain in between shoulder blades"

However, as with previous muscular complaints, this was localized, whereas, the "muscle stiffness" associated with the dependency encompassed his entire body. Further, Wayne reports that the episodes of "pain in between shoulder blades" are periodic in nature and are triggered only by strenuous exercise, which is supported by the note in Dr. Whitwell's patient file where it says "Lifting weights at gym".

(Pg.3: Long History Mild Lower Back Pain)

3.2.4 Refer to Article 3.1.2 above for discussion on this.

(Pg.3: Long Standing Anxiety Depressive Problem)

3.2.5 On 29th March 2001, there is an entry saying "long standing anxiety depressive problem", which may suggest that Wayne's anxiety symptoms were caused by an underlying anxiety condition. Also, there are several other entries throughout Dr. Whitwell's patient file referring to anxiety and depression symptoms.

3.2.6 I would agree that Wayne was suffering from anxiety symptoms; however most of the symptoms he presented with to our service in April 2000, were likely caused or exacerbated by Benzodiazepine dependency and not an underlying anxiety condition. The reasons for this are as follows:

1. Wayne's prior history, spanning 10 years (including Dr. Whitwell's file) shows that he had no previous psychological conditions (including any anxiety problems) or neurological complaints prior to travelling to Japan in 1999 documented in his available medical notes.

2. Benzodiazepines can cause simple stress symptoms to worsen, and can lead to the development of panic attacks etc during the treatment, which is well documented in the literature (Report 3, Article 3.3.15).

3. The fact that Wayne's condition worsened during the treatment to the point where he was unable to work.

4. Like his other dependence symptoms, the anxiety and depression type symptoms intensified again during the formal reduction process, and like his other dependence symptoms, the anxiety and depression type symptoms continued to improve following completion of the initial withdrawal phase of his formal withdrawal program – in the absence of Benzodiazepines, although, many symptoms did wax and wane for several months, which is consistent with a protracted withdrawal syndrome.

5. Wayne has since been able to make a return to living and working in Japan, and despite being under considerable more stress on this occasion with his ongoing case for compensation, he continues to maintain a much better state of health.

(Findings)

3.2.7 There is no question that Wayne had symptoms of anxiety and depression in 2000 ~ 2001. The only question is: to what degree were these symptoms (anxiety / depression) patient related and to what degree were they caused by Benzodiazepine dependency.

3.2.8 Based on the aforementioned reasons, and the reasons outlined in Report 3, Article 3.3.12, it is most likely that the majority of Wayne's anxiety type symptoms upon presentation to our service were caused by Benzodiazepine dependency.

3.2.9 The one exception to Wayne's recovery from these symptoms following his abstinence from Benzodiazepines was that he did continue to suffer from panic attacks, albeit to a lesser degree over time. However, this needs to be analyzed taking into consideration the long term effects including; protracted withdrawal, the trauma of the dependence experience, and the additional pressures of his subsequent case for compensation.

3.2.10 We do know, however, that Wayne had no history of panic attacks before being exposed to Benzodiazepines.

3.2.11 The difficulty of being able to differentiate between symptoms of anxiety and those of dependency is one of the big problems with Benzodiazepines because it often results in the overprescribing of these drugs. Quite often, the formation of dependency is overlooked, resulting in doctors thinking that the patient's anxiety condition has worsened. The patient's prescriptions are sometimes increased followed by a temporary alleviation of symptoms; however, this often leads to the compounding of the dependency problem.

3.2.12 In addition to the above, when put into context of the overall clinical picture (Report 1, Article 2.2) and considering the fact that Wayne met 5 criteria of the DSM IV-TR within the same 12 month period, it becomes clear that most of the (chronic) anxiety and (chronic) depression symptoms Wayne had in 2000 ~ 2001 were most likely caused or exacerbated by Benzodiazepine dependency.

3.3 Mental Health & Addiction Services – History of Complaints

(Pg.8: Depression)

3.3.1 On page 2 of Wayne's typed notes upon presentation to our service (page 8 of the Mental Health & Addiction Services patient file) there is a list, which corresponds with that on page 12 of Dr. [redacted]'s patient file under the title "NB".

3.3.2 We can see there is an additional comment included in this list, which was not originally included in the version given to Dr. [redacted]. This additional comment is: "Have started to feel depressed and closed in since vertigo attack."

3.3.3 Wayne reports that following his initial vertigo attack and subsequent balance problem, he had some difficulty going out and socializing, as he usually would.

3.3.4 Subsequently, it may be argued that the "Impact on Life" outlined in Article 2.4 of Report 3, was caused by the initial vertigo attack and balance problem thereafter, as opposed to Benzodiazepine dependency.

3.3.5 However, once again, this needs to be considered in context. For example, we know that Wayne was still able to work in Japan, albeit on light duties, before the Benzodiazepine treatment began and during the early stages of the treatment, but following more than 4~6 months of Benzodiazepine exposure, his condition continued to deteriorate and eventually he ended up in a state where he was unable to work at all again for a period exceeding one year.

3.3.6 This suggests that the Benzodiazepine dependency had the greater impact because Wayne was still able to work following his initial complaint of vertigo and subsequent balance problem, but he was not able to work following his drug treatment.

(Pg.17: Counseling)

3.3.7 On page 17 of the patient file, there is an entry on 30th April 2001 saying that Wayne had requested general counseling as opposed to specialist D/A (Drug & Alcohol) counseling.

3.3.8 Wayne in written communication has reported that the reason why he requested general counseling was because, after having been briefed on the nature of Benzodiazepines, including dependence and withdrawal, he felt he knew what needed to be done as far as stopping was concerned, and subsequently, did not feel that he needed any extra counseling for this. Rather, he wished to seek advice regarding grief etc. with regards to his situation at the time.

(Pg.25: Stressors)

3.3.9 In my letter to Dr. Whitwell, dated 5th June 2001, I mentioned that Wayne was encouraged to look at alternative relaxation techniques to help him cope with some of the stressors he had described. These stressors refer to the previous work related stress at his job in Shizuoka in late 1999 / early 2000, the fact he suffered from an undiagnosed vertigo attack that had left him with a ongoing balance problem for a period, and the fact that he had been suffering from Benzodiazepine dependency, which had subsequently impacted on his life including his ability to work.

(Pg.22: Visual Disturbances)

3.3.10 Further to Articles 3.3.16~21 of Report 3, which gave examples on how some of the symptoms relating to Wayne's original complaint (muscle stiffness and hypersensitivity) worsened in the presence of Benzodiazepines, the worsening of visual disturbances gives another example of this.

3.3.11 Page 11 of Dr. [redacted]'s patient file shows that Wayne was experiencing sensitivity to light and flickering in his vision following his initial vertigo attack.

3.3.12 However, we can see from the notes on page 21 of the Mental Health & Addiction Services patient file that Wayne later complained of an <u>increase</u> in light sensitivity, colour flashes, exaggerated after images, flashes, staggered focus etc following 4~6 months of Benzodiazepine exposure. This worsening of visual symptoms is also suggestive of withdrawal.

Section Four

4. Prescribing, Informed Consent, Monitoring

4.1 Prescribing Issues

4.1.1 Below are some contributing factors, which would have increased the risks regarding the forming of dependence in Wayne's case.

1. Prolonged prescriptions
2. Multi-prescribing
3. Suitability of prescriptions
4. Informed consent (See Article 4.2)
5. Monitoring (See Article 4.3)

(1) Prolonged Prescriptions

4.1.2 As mentioned in Report 3, and in previous reports, the risk factor with regards to the forming of dependency in Wayne's case would have increased by about 50~100% simply based on the prolonged period of the prescriptions.

(2) Multi-prescribing

4.1.3 As mentioned in Report 3, and in previous reports, the above risk factor would have increased yet even further, based on the fact that Wayne was prescribed multiple combinations of Benzodiazepines. This is because Benzodiazepines do not mix well, and when they are mixed, there is an increased possibility of side-effects and dependency forming.

(3) Suitability of Prescriptions

4.1.4 Firstly, in order to help determine the suitability of the drugs that were prescribed to Wayne, we should consider the reason why they were prescribed to begin with.

4.1.5 Regardless of their potency, speed of elimination or duration of effects, the therapeutic actions of all Benzodiazepines are virtually the same, as follows:

- Anxiolytic (relief of anxiety)
- Hypnotic (promotion of sleep)
- Myorelaxant (muscle relaxation)
- Anticonvulsant (control fits convulsions)
- Amnesia (sedation for surgical procedures)

4.1.6 We know from the evidence that Dr. [redacted] diagnosed Wayne as having "Sylvian Aqueduct Syndrome". Also, we know that Neurologist, Dr. [redacted] from the [redacted] Hospital, who saw Wayne initially, and Neurologist, Dr. Hutchinson, who saw Wayne later, both suspected a "vestibular problem".

4.1.7 With regards to the therapeutic effects of Benzodiazepines as a suitable means of treatment for either of these diagnoses, Dr. Hutchinson, supplied the following information in his letter, dated 11 Feb 2008.

"I would agree with doctors at the [redacted] Hospital that Mr Douglas most likely had an episode of Acute Vestibulopathy in May 2000."

"A range of neurological conditions (for example, cerebellar infarction, multiple sclerosis) can mimic Acute Unilateral Peripheral Vestibulopathy, but all are excluded or made very unlikely if the brain MRI scan is negative. Methylprednisolone significantly improves the recovery of peripheral vestibular function in patients with Acute Unilateral Peripheral Vestibulopathy[3]. Patients are sometimes also administered intravenous fluids and anti-emetics."

"The Sylvian Aqueduct Syndrome is rare and seldom encountered in modern neurological practice. A literature search in February 2008 (Pubmed) using the expression "Sylvian Aqueduct Syndrome" yielded just 23 articles since 1966, with only 3 articles in the past 20 years. It refers to a syndrome whose features include vertical gaze restriction, abnormal pupillary reaction, upper lid retraction, and convergence–retraction eye movements. Paralysis of convergence and skew deviation may also occur. Sylvian aqueduct syndrome usually occurs in patients with shunted hydrocephalus whose shunts become blocked[4]. Single case reports have also described the syndrome in patients with midbrain infarction[5], multiple sclerosis[6], thalamic haemorrhage[7], tumours in the pineal region[8] and unilateral midbrain lesions[9]. Mr Douglas apparently did not have the above constellation of neurological signs, but more importantly his brain MRI scan did not show hydrocephalus or any other disorder which can produce the Sylvian Aqueduct Syndrome."

"I do not know of any reason, theoretical or otherwise, why benzodiazepine medication would have had a role in the treatment of Mr Douglas in 2000. Benzodiazepine drugs do not have useful anti-emetic or anti-vertiginous properties and have no clear role in the treatment of Acute Unilateral Peripheral Vestibulopathy. Further, benzodiazepine drugs would not be effective in treating hydrocephalus or any of the other conditions which may produce the Sylvian Aqueduct Syndrome."

4.1.8 With regards to the therapeutic effects of Benzodiazepines as a suitable treatment for anxiety, they are effective for the short-term treatment of acute trauma (for not more than about 2 ~ 4 weeks); however, they are not suitable as a means of long term regular treatment, due to the fact that dependence can be rapidly formed.

"The Committee on Safety of Medicines and the Royal College of Psychiatrists in the UK concluded in various statements (1988 and 1992) that benzodiazepines are unsuitable for long-term use and that they should in general be prescribed for periods of 2-4 weeks only." (See Benzodiazepines: How They Work and How to Withdrawal. Prof. C. H. Ashton. Revised August 2002 – Chapter 2, Page 2/10 of online version).

4.1.9 Subsequently, regardless of the reason why these drugs were prescribed, whether it was for treating anxiety or Sylvian Aqueduct Syndrome, Wayne's treatment cannot be considered as ideal, and over a prolonged period, it ultimately led to the formation of Benzodiazepine dependency.

4.2 Informed Consent

4.2.1 Below are some indicators that would suggest Wayne was not given adequate informed consent with regards to his multiple prescriptions of Benzodiazepines.

1. Dr. [redacted]'s diagnosis did not include anxiety
2. Reported reason for prescriptions (during mediation)
3. Efforts to seek drug related information
4. Dr. Whitwell's patient file
5. Presentation to our service

(1) Dr. [redacted]'s Diagnosis Did Not Include Anxiety

4.2.2 Firstly, 4 out of the 5 drugs that were prescribed to Wayne are used in the treatment of anxiety, including 3 different kinds of Benzodiazepines and 1 tricyclic antidepressant.

However, Dr. [redacted]'s patient file clearly shows that there was no diagnosis made regarding an anxiety, condition, nor was there any entries made in his patient file relating to the treatment of anxiety for the entire the duration of the treatment.

This supports Wayne's verbal reports that there was never any discussion regarding the treatment of anxiety.

(2) Reported Reason for Prescriptions (During Mediation)

4.2.3 I have been informed that when asked during mediation why the 3 different kinds of Benzodiazepines and 1 tricyclic antidepressant were being prescribed, Dr. [redacted] responded by saying "Acute vertigo attacks are scary and are often accompanied by a sense of anxiousness and so, a decision was made to "add a little something" into the prescriptions for this".

To use the words "add a little something" seems to be quite an understatement. This is because, once again, the majority of the drugs prescribed were for the purpose of treating anxiety, and therefore, Wayne should have been given adequate informed consent with regards to this, together with an explanation of the possible risks and alternative options, at the time of his very first consultation - before the treatment began.

(3) Efforts to Seek Drug Related Information

4.2.4 Wayne reports that from about October 2000, when his condition started to deteriorate more notably, he began making various efforts to seek information about the drugs that had been prescribed to him by Dr. [redacted]

4.2.5 These efforts included making inquiries to the dispensary used by Dr. [redacted], asking family and work colleagues to see what they could find, and later getting information from the dispensary at the [redacted]

NB: Wayne says that he has copies of the information he received as a result of the above research.

4.2.6 The fact that Wayne was making efforts to seek information about the drugs is further suggestive that he did not receive, what Wayne would consider, adequate information during his consultations.

(4) Dr. Whitwell's Patient File

4.2.7 The referral form to our service from Dr. Whitwell, dated 10 April 2001, says "he (Wayne) says these (the drugs) were prescribed in Japan without informed consent".

Wayne reports that after learning of the addictive nature of Benzodiazepines from Dr. Whitwell, he felt surprised that he had not been told this at any stage under Dr. [redacted], and subsequently, responded by making the above comment.

NB: One must also consider that at this point in time, Wayne's only concern was with getting well again. He had absolutely no thoughts of pursuing litigation, and therefore, had no other reason for saying that he had not been given informed consent, apart from that actually being the case.

(5) Presentation to Our Service

4.2.8 Upon presentation to our service it was clear that despite the efforts above (4.2.4~6) Wayne knew very little about the nature of the drugs and the reason why they had been prescribed. As far as he knew, all of the drugs, including the 3 different kinds of Benzodiazepines and 1 tricyclic antidepressant had been prescribed as a means of treatment for "Sylvian Aqueduct Syndrome".

NB: Upon learning about the nature of Benzodiazepines Wayne showed a tremendous desire and commitment to stopping, which further supports the fact that he does not have an addictive type personality. Subsequently, had he been properly informed, as to the nature and potential risks of Benzodiazepines, it is possible that Wayne may have chosen to look at alternative options instead.

4.3 Monitoring

4.3.1 Below are some indicators that would suggest Wayne's Benzodiazepine treatment was not monitored sufficiently.

1. The Formation of dependence
2. Reported admission of "inadequate knowledge" during mediation
3. Signs of tolerance were overlooked
4. Withdrawal symptoms were overlooked
5. Given authorization to drink alcohol
6. No records of monitoring for dependence

(1) The Formation of Dependence

4.3.2 The simple fact that Wayne had formed dependence suggests that the monitoring was not adequate.

(2) Reported Admission of "Inadequate Knowledge" During Mediation

4.3.3 I have been informed that when Legal Consul [redacted] asked Dr. [redacted] during mediation if he knew what to look for with regards to recognizing when a patient is forming dependence, the answer was "No".

4.3.4 To know what to look for and to be able to recognize when a patient may be forming dependence, is a fundamental responsibility for any doctor prescribing Benzodiazepines.

4.3.5 Further, they should also inform the patient about what to look for and ask the patient to report immediately any changes in their condition (any new symptoms etc).

(3) Signs of Tolerance Were Overlooked

4.3.6 As outlined in Article 2.1 of my 3rd report, Wayne was showing signs of tolerance after about 1.5 months of treatment. Had there been an appropriate monitoring system in place, this could have been detected and the treatment reassessed accordingly.

4.3.7 According to Wayne's statement, when he complained of developing palpitations in August (following about 1.5 months of treatment), Dr. [redacted] responded by saying "Don't drink cold water directly after taking a bath" and "Don't fill the bath water over your chest". In response to Wayne's deteriorating appetite, Dr. [redacted] responded by saying "You need to eat more". Over the months that followed, other responses made to Wayne's complaints about his deteriorating condition included "You're probably feeling worse because of recent bad weather" and "You have to toughen up"

4.3.8 The above comments support the noted admission made by Dr. [redacted] during mediation with regards to not knowing what to look for when a patient is forming a state of dependence.

(4) Withdrawal Symptoms Were Overlooked

4.3.9 As outlined in Article 2.2 of my 3rd report, Wayne was developing symptoms of withdrawal due to tolerance following about 4~6 months of treatment. Had there been an appropriate monitoring system in place, this could have been detected and the treatment reassessed with a view to implementing a controlled reduction.

(5) Given Authorization to Drink Alcohol

4.3.10 Wayne reports that When Dr. [redacted] made the first prescription, he advised that it was okay to consume alcohol whilst taking the drug treatment.
NB: This is consistent with the entry made in Dr. [redacted]'s patient file, where it says "Drinking alcohol once a week" (See page 10).

4.3.11 However, contrary to this advice, patients should be advised to avoid alcohol and they should be informed about the potential risk of additive effects and increased side effects.

"Benzodiazepines have additive effects with other CNS depressants, including other hypnotics, sedative antidepressants, neuroleptics, anticonvulsants, sedative antihistamines, and alcohol. The combined disinhibitory effects of alcohol and benzodiazepines may also be additive and contribute to aggressive behaviour. Patients prescribed benzodiazepines should be warned of these interactions." (See Toxicity and Adverse Consequences of Benzodiazepine Use. Prof. C. H. Ashton. Page 2/12 of online version).

(6) No Records of Monitoring for Dependence

4.3.12 Dr. [redacted]'s patient file contains no records of monitoring for potential drug dependency, which further supports the fact that the monitoring was insufficient and ultimately resulted in the formation of Benzodiazepine dependency in Wayne (Evidence Otsu A1).

4.4 Clinical Considerations

Below is a list of considerations regarding prescribing, informed consent and monitoring. Most of these are based on examples in accordance with New Zealand law, and recommendations established by the World Health Organization. As I am not familiar with Japanese law, I am unable to make reference with regards to the guidelines in Japan; however, I am sure that Wayne's lawyer will be able to clarify this.

4.4.1 As outlined in previous reports, it is recommended that Benzodiazepines should not be prescribed for any longer than 2 ~ 4 weeks as dependence can be rapidly formed. (See reference in Article 4.1.8)

4.4.2 Benzodiazepines are highly addictive drugs that can produce many adverse reactions including tolerance, withdrawal, side-effects and dependency. Subsequently, when prescribing any medication, unless managed properly, some prescriptions have the potential to cause difficulties for the patient, their families, their work and others around them.

4.4.3 For this reason, in principle, the patient has the fundamental right to be informed of the risks before being prescribed Benzodiazepines, so that they may be able to make an informed decision regarding their health and well-being.

4.4.4 This includes an explanation of his or her condition, an explanation of why the proposed medication is considered suitable for treating their condition, an explanation of the options available, including an assessment of expected risks, side effects and cost of each option.

NB: In the case of New Zealand, this outlined by the Medical Council of New Zealand Information and Consent April 2002. These rights are also consistent with the WHO (1994, 2000) "Guide to Good Prescribing, a Practical Manual".

4.4.5 Further, when doctors prescribe addictive drugs, they need to keep in mind and monitor for the development, or management of potential drug dependency.

NB: This is a requirement of the Medical Council of New Zealand and it is also consistent with guidelines developed by other countries e.g. Hong Kong (Hong Kong college of psychiatrist 1997), USA (Principles of Addiction Medicine, Benzodiazepine Prescribing Guideline Work Session, Maine).

4.4.6 The WHO (1994, 2000) "Guide to Good Prescribing, A Practical Manual" gives an outline of the process of rational treatment / prescribing of medication. It defines 6 steps as follows:

1. Define the problem
2. Specify the therapeutic objective
3. Verify the suitability of the prescription
4. Give information, instructions & warnings
5. Start the treatment
6. Monitor treatment

4.4.7 To expand further on step 4 (information, instructions and warnings), necessary provision of information includes the following:

1. A description of the effects of the drug (which symptoms will disappear and when; how important is it to take the drug; what happens if it is not taken)
2. Side effects (which side effects may occur; how to recognize them; how long they will remain; how serious they are; what to do if they occur)
3. Instructions (when to take; how to store; how long to continue the treatment; what to do in case of problems)
4. Warnings (what not to do; maximum dose; the need to continue treatment)
5. Next appointment (when to come back; when to come back earlier)
6. Make sure everything is clear to the patient.

NB: As with the prescribing of any medication, you need to consider whether the patient is on any other medication and if there is a possibility of drug interactions, especially when multi-prescribing.

4.4.8 As Benzodiazepines are highly addictive drugs that can produce many adverse reactions, "Monitoring" is necessary when prescribing these drugs.

4.4.9 Monitoring should include the following (WHO Guide to good prescribing, a practical guide 1997):

1. Regular observations to see whether the illness is cured.
   NB: When it is, the treatment should be stopped.

2. Regular observations to see whether the treatment is effective.
   NB: If it is, but the illness is not yet cured, then the prescribing doctor should include in their review of the patient; a review of any side effects and if serious, the treatment should be reassessed.

3. Regular observations to see whether the treatment is ineffective.
   NB: If it is, the treatment should be reviewed.

4.4.10 Good medical practice dictates that monitoring is needed, as outlined above, to ensure that the patient does not suffer from any adverse reactions as a consequence of the treatment.

4.4.11 Monitoring should involve regular reviews of the patient to ascertain whether the medication is still needed and if there are any unintended effects occurring as result of the medication.

4.4.12 Below is a list of appropriate measures that need to be taken when a patient exhibits signs that they may be forming a state of Benzodiazepine dependence (based on WHO Guide to Good Prescribing, A Practical Manual, 1997).

1. Review diagnosis
2. Review therapeutic objectives
3. Review suitability of treatment for this patient
4. Review whether the drug was correctly prescribed
5. Review whether the patient understood the treatment correctly and whether they took the drug correctly
6. Review whether the patient was correctly monitored

4.5 Findings

4.5.1 The aforementioned evidence clearly shows that Wayne was not given adequate informed consent with regards to the prescriptions. There was no explanation / information given with regards to treating symptoms of anxiety, nor were there any explanations / information given with regards to why the proposed medication was considered suitable for treating Wayne's condition. As far as Wayne knew, based on the information he had been given, the prescriptions were for the sole purpose of treating "Sylvian Aqueduct Syndrome".

4.5.2 The fact that Dr. [redacted] overlooked signs of tolerance and the development of symptoms consistent with withdrawal also suggests that the monitoring was inadequate, and that Wayne was not adequately advised with regards to the possibility of dependency and side-effects, what the signs are, and what to do should they occur.

4.5.3 Dr. [redacted]'s patient file clearly shows that there was no monitoring system in place for detecting potential dependency. As a result, vital signs were overlooked, and the opportunity to review the treatment was missed.

4.5.4 Subsequently, the appropriate measures (outlined in Article 4.4.12 above) were not taken, and despite Wayne's efforts to draw attention to his deteriorating condition, he was continuously given repeat prescriptions of Benzodiazepines resulting in the compounding of his drug dependency.

Cumulative Summary / Conclusion

Below is a cumulative summary based on the evidence outlined in both Report 3 and this Report 4.

1) In 1999, Wayne traveled to Japan in good health with no previous history relating to psychological conditions (including any anxiety problems) or neurological complaints.

2) In late 1999, he developed some stress symptoms whilst working at a stressful job in Shizuoka, which are recorded on pages 12~13 of the [redacted] ENT patient file and include fatigue / lethargy, pressure in temple areas, swelling of temporal veins, shortness of breath, sleep disturbances.

3) Wayne subsequently changed jobs in late March 2000 and reported that he really liked his new job, which was also noted on page 13 of the [redacted] ENT patient file.

4) On 11th May 2000, he suddenly awoke at 2am with an attack of vertigo, which left him with an ongoing balance problem – unsteadiness in gait.

5) Wayne was initially seen at the [redacted] Hospital and underwent a series of tests including an MRI scan, all of which showed up negative. Neurologist, Dr. [redacted], who saw Wayne initially, and Neurologist, Dr. Hutchinson, who saw Wayne later, both suspected a "vestibular problem".

6) Wayne began to develop feelings of anxiousness over not being able to receive a clear diagnosis for his vertigo attack and the balance problem that followed.

7) In June 2000, he decided to get a referral to see Dr. [redacted], who specializes in balance problems.

8) Dr. [redacted] diagnosed Wayne as having "Sylvian Aqueduct Syndrome". Anxiety was not included in his diagnosis.

9) Dr. [redacted] began prescribing multiple drugs including 3 different kinds of Benzodiazepines (anxiolytic drugs) and 1 tricyclic antidepressant for over a 6 month period without any change in dosage.

10) This prolonged prescribing of multiple Benzodiazepines would have increased the likelihood of Wayne becoming dependent to about 50~100%.

11) According to information supplied by Neurologist, Dr. Hutchinson, Benzodiazepines would not have been suitable for treating either "Sylvian Aqueduct Syndrome", or a "vestibular problem", and neither are they suitable for the long term treatment of stress symptoms due to the fact that dependence can be rapidly formed.

12) Dr. [redacted] did not inform Wayne as to the reason why the drugs (3 different kinds of Benzodiazepines and 1 tricyclic antidepressant) were being prescribed. As far as Wayne knew, these drugs were being prescribed as a means of treatment for "Sylvian Aqueduct Syndrome" and he had no idea that they were Benzodiazepines or what Benzodiazepines are designed for.

13) Wayne showed signs of developing the early stages of tolerance following about 1.5 months of treatment, which was evident in that some of his symptoms settled initially and then returned along with the development of others including palpitations.

14) This was further compounded by several more months of daily dosing, after which, Wayne developed several more new symptoms that were consistent with tolerance and withdrawal (following about 4~6 months of prescriptions).

15) In response, to these complaints, including the palpitations, Wayne reports that he was told not to drink cold water directly after taking a bath, not to fill the bath water over his chest, he needed to eat more, he was probably feeling worse because of recent bad weather, and that he had to toughen up.

16) Following about 4~6 months of treatment, when Wayne's condition was deteriorating, his friends began voicing their concerns regarding his wellbeing.

17) Feeling concerned for his wellbeing, Wayne reports that he tried unsuccessfully to stop his drug intake in late November 2000.

18) Soon after this attempt, Wayne returned to see Dr. [redacted] at the [redacted] Hospital on 13th December 2000 to request a re-referral to another hospital.

19) Wayne then began to make a list of new symptoms, dated 18th December 2000, so that he could better convey his concerns regarding his deteriorating condition to Dr. [redacted] Many of the symptoms contained in this list were consistent with withdrawal due to tolerance.

20) Subsequently, we can estimate that Wayne had likely developed Benzodiazepine dependence following about 4~6 months of treatment, which based on statistics, is a typical timeframe for dependence to form (See reference on page 13 of Report One).

21) After having lost faith in Dr. [redacted] and his treatment, Wayne decided to change hospitals. At his final consultation he asked for information about the drugs that he was being prescribed to serve as future reference, which was refused.

22) Soon after changing hospitals, a reduction plan was negotiated with Dr. [redacted] In accordance with this plan, Wayne made a second unsuccessful attempt at reduction.

23) Following this attempt, Wayne decided to return to New Zealand one week short of completing his employment contract, where he made another unsuccessful attempt at stopping.

24) Dr. Whitwell declared him unfit to work and referred him to our service for professional help, as he was having problems with withdrawal.

25) During the formal reduction program, his symptoms intensified again along with the development of other withdrawal symptoms.

26) Wayne made a steady recovery from most of his symptoms following about 3 months of completing the initial withdrawal phase of the reduction program (6 months following cessation). Other symptoms took up to 1 year to recover from gradually improving over time, which is suggestive of a protracted withdrawal syndrome.

27) Following completion of the reduction program, Wayne was able to make a gradual return to recreational activities, where he made significant gains in weight, strength and stamina, which was made apparent by his ability to later return to work as an adventure tour guide and yardman.

28) He has since been able to make a return to living and working in Japan, and despite being under considerable more stress on this occasion with his ongoing case for compensation, he continues to maintain a much better state of health.

29) After reviewing the notes, I can confirm that 5 of the 7 DSM-IV TR criteria can be applied to Wayne's initial dependency diagnosis based on the information we had in our files before proceedings for compensation began.

30) Further, the additional information that surfaced later, as a result of Wayne's legal case for compensation, including the patient files from Japan, does not detract from the fact that Wayne met these 5 criteria.