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PHARMACEUTICAL REPORT

Prepared at the request of:

SOLICITORS

for

The Court

Presented by

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Fellow, American College of Clinical Pharmacology, 1991
Fellow, Faculty of Pharmaceutical Medicine, 1993
Fellow, Royal College of Physicians, 1996

BSc Upper 2nd Class Hons. Physiology 1970 (Cardio-Respiratory and Neurology)
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Membership of the Royal College of Physicians, 1976
Joint Committee on Higher Medical Training Certificate in General (Internal) Medicine. 1982
GMC Registration as Specialist in General Medicine. 2004

Law Society approved as Expert Witness, 2004
Registered: UK National Crime Operations Faculty, 2004
National Police Improvement Agency Expert Adviser Database 2009

Member Drug Information Association. 1984
Member American Academy of Pharmaceutical Physicians. 1993
Member International Stress Management Association. 1997
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The Boden Memorial Award for Medicine, Haberdasher's Aske School, Elstree, 1967
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BMA undergraduate Research Award, 1972
Elected member of European 500 Dynamic Entrepreneurs, 1995

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30 papers and articles on stress
Editor in Chief: Dilemmas and Solutions in Global Drug Development – PJB Publications
Author: Good Clinical Practice for Investigators
Author: Standard Operating Procedures for Investigators

Medical Advisor to Release (the drug assistance charity) 1973 – 1978

With assistance from:

Gary Sutton, Head of Drug Services at Release (CV attached – ref 1)

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Throughout this report, where I quote from papers supplied, this will be entered in italics, whenever I am giving my opinion throughout the body of the report; this will be typed in bold.

INTRODUCTION

1. I am instructed in this matter by solicitors for the defendant in their letter of 26 July 2010. In this I am told that:

'We act on behalf of the above named client who is charged with production / cultivation of Cannabis.

Police attended The defendant' address and found a number of plants, recorded as being Cannabis.

The defendant has stated to us that although he admits to growing the plants seized at his address, he has done so to self-medicate after suffering excruciating pain from a long-standing spinal injury. The defendant has stated that he uses cannabis for pain relief and that the side effects from this use are far less than those suffered from prescribed medication.

We therefore ask that a report be prepared for use at Court to deal with the following issues:

1. *Is Cannabis used for or useful to deal with pain as a relief?*
2. *If so for what types of illness and / or pain relief is it suitable?*
3. *When addressing this defendant would his injuries fall into a category that Cannabis would help?*
4. *Is Cannabis used in other countries as a legal pain relief and if so, what others countries and in what context is it used?*
5. *Does this country (England/Wales) have any legal uses for Cannabis and if so what are they?*

6. *Does this country have any legalised / Government run Cannabis farms and what are they used for?*
7. *What are the side effects of Cannabis, ranging from low levels of plant strength to high level of "skunk" type plants? (So far there is no level of strength for the plants found)*
8. *What are the side effects of prescribed pain relief?*
9. *In your expert view does Cannabis have benefits which outweigh the use of prescribed medication and are the side effects mentioned above greater or less for Cannabis than for prescribed medication.'*

2. I have been sent to read the following documents:
    1. *Terms of engagement for instruction of Experts letter.*
    2. *Indictment.*
    3. *Witness Statements pages 1-24.*
    4. *Exhibits pages 1-30.*
    5. *Unused Material.*
    6. *Defendant's previous convictions.*
    7. *Defendant's Proof of Evidence.*
    8. *Legal Aid Order*
    9. *GP's chronology*
    10. *Letter for NHS trust'*

    which I confirm I have looked at.
3. I am told by solicitors that '*The defendant knows that currently Possession of Cannabis is illegal and therefore growing Cannabis is also illegal'.*
4. At 8.30 on the morning of Thursday, 12 August 2010, I was informed that the defendant had decided to plead guilty and that this report would be used in mitigation.
5. I was assisted in my research for the report by Mr Gary Sutton, Head of Drug Services at Release which is a charity, founded in 1967, to give advice and guidance in relation to drugs and the Law to people who misuse drugs, their families and professional bodies working in the field. Release employs five qualified full time lawyers and three specialist drugs workers all of whom work on information provision, direct advice and

policy. He is responsible for writing, co-authoring or editing all information put out by Release in printed or electronic form, including their website.

6. I acknowledge his assistance in writing the report and his CV is attached, reference 1. I am, however, the only signatory to the report and take responsibility for it in its entirety, as would be expected of a medically qualified expert witness.

7. The essence of this report is to:

   i) Outline the legal status of medicinal cannabis use in major territories and to support its use with regulatory documents. This includes both medicinal cannabis use and the use of Sativex, a prescription medicine developed by GW Pharmaceuticals which comprises delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD).

   ii) Review published academic articles in peer reviewed journals.

   iii) Identify statements made by the developers and manufacturers of Sativex, the approved combination of delta-9-Tetrahydrocannabinol and cannabidiol, which received its regulatory approval in the UK as recently as 16 June 2010.

   iv) Identify statements of the product licence holders in the UK, Bayer Pharmaceutical and in Spain, Almirall.

   v) Comment on the defendant's medical condition as detailed in his General Practitioner submissions.

   vi) Identify specifically the evidence for use of cannabis and cannabinoids in pain associated with spinal injury such as he has.

   vii) In addition to all the above, I place the evidence into context using my own education, training and experience in these areas.

   viii) The experience of Gary Sutton of Release has been helpful.

8. The court should be aware that this is a fast moving and developing field, because after a long history of the use of illegal cannabis in medical conditions (**which was initially tried because of the personal experience of cannabis users**), there is now a growing body of published scientific work on the subject. There is also the increasing legality of medicinal cannabis use, particularly in the US, Canada and

Catalonia. (**Catalonia in Spain has some autonomous regulations regarding healthcare**.)

9. There are now regulatory approvals of Sativex in Canada, the UK and Spain. The UK approval was mid-June and the Spanish approval at the very end of July.

10. Thus the literature and knowledge in the public domain will be increasing in an exponential fashion. This is due to a number of factors:

    i) The developers and product licence holders and their licensees across the world will slowly add territories and indications to their regulatory approved uses around the world.

    ii) The majority of the developmental work will slowly be published in peer reviewed journals as opposed to being in the in-house confidential data of the developers.

    iii) I expect GW Pharmaceuticals and Bayer in the UK to slowly disclose further information to me when it is in the public domain. I have currently asked not to be supplied anything under confidence.

    iv) Development and the issuing of an investigational new drug application in the US, by the developers to the FDA, will mean that data will be increasingly available more openly than in Europe under their Freedom of Information Acts and will be accessible on the internet.

    v) When the product is officially launched to doctors in the UK by Bayer, as the licensees of GW Pharmaceuticals and the product licence holder, there is likely to be a great deal of press.

    vi) Further work on Sativex will be published and the indications will be expanded to cover other areas which are currently in Phase Two and Three research and development.

11. Additionally, other cannabis extracts and agonistics of the cannabis receptors are in development and there will be publications on them and possibly even approvals I am not aware of.

12. My report therefore is likely to be superseded on an ongoing basis. Public funding limitations will not allow me to update the report at each end every opportunity,

however, I will inform the solicitors for the defendant of any major changes and should I ever be asked to present an opinion to or before the courts, will repeat due diligence and use my own increasing knowledge. A total review like this, which may need to be compiled, would however be subject to public funding being available.

13. In producing this report, for Sativex, I have relied on:

- The Summary of Product Characteristics (SPC), which is a legal document drafted by the product licence holder and approved by a regulatory body. In the UK, this would be the MHRA - the Medicines and Healthcare Products Regulatory Agency.
- The Public Assessment Report of the decentralised procedure which is the UK's assessors report at the MHRA which allowed them to grant a product licence.

14. In relation to Nabilone and Marinol, two additional cannabinoids licensed in the UK and USA, I have relied as appropriated on:

- The Summary of Product Characteristics (SPC), which is a legal document drafted by the product licence holder and approved by a regulatory body. In the UK, this would be the MHRA - the Medicines and Healthcare Products Regulatory Agency.
- The MHRA adverse events Yellow Card system, which is a spontaneous reporting system and does not always take into account cause and effects, additionally even for serious adverse drug reactions there is a great deal of under reporting with no more than 10% of even serious adverse drug reactions being reported.
- Martindale, which is published by the British Pharmaceutical Society and is the standard text to which all doctors should refer.
- The Physicians' Desk Reference, containing the product information and product insert which is a document written by the manufacturers in conjunction with the Federal Drugs Administration in the US and is referred to as product labelling.

15. I have additionally relied on:

    - The website of GW Pharmaceutical, the initial developers and attach copies of the website with the download date on the right hand corner. This is needed as the website will constantly be updated. (Please see attached reference 2.)
    - My own and Release's extensive literature on the subject of cannabis.
    - Regulatory documents where available from other healthcare agencies such as Health Canada.

16. The legal status of cannabis in the US has been updated from www.procon.org, a respected specialist US source of political information which gives advantages and disadvantages of changes of important legal issues in the US. These have been cross referenced against other sources of information and I cannot detect inaccuracies. I rely on the published House of Lords '*Science and Technology Science and Technology – Ninth Report'* on cannabis, Parliamentary copyright 1998.

17. Other information is referenced when used.

18. As is my usual practice, I have set up alerts at the National Institute of Health Bethesda, Maryland, using their search engine, PubMed using the keywords '*clinical trials'* and *'cannabis'.* I have also set up Google alerts for '*Sativex regulatory approvals*'.

19. I am also in contact with and am awaiting a response from GW Pharmaceuticals and Bayer.

[B L A N K]

EVIDENTIAL BUNDLE

20. In view of the fact that the defendant has pleaded guilty, I will not review this in any great detail and trust that although myself and Gary Sutton may take issue with some of the points, we have not been asked to give our opinion on it nor would it be useful to the court.

[B L A N K]

PROOF OF EVIDENCE OF THE DEFENDANT

21. I have read this which runs to 4 pages, is unsuperpaginated, undated, unsigned and is similar to all relevant information as per the General Practitioner's witness statement and correspondence. I do not quote from it here and privilege may be claimed.

[B L A N K]

WITNESS STATEMENT OF GENERAL PRACTITIONER 31.05.10

22. The witness statement of the defendant's GP is dated 31/05/2010, is superpaginated 23, 24 and signed.

23. In this statement and the open letter of 21 May 2010, I am told of the defendant's medical substance dependence and abuse, and spinal medical history. It states '*in 1982 The defendant suffered a back injury when he fell from a three foot high trestle. It was found at the time that he also had congenital spondylolithesis. He needed time off work from August until November that year.*

In October 1985 he had back rehabilitation at Hospital.

In July 1988 he was admitted for back pain and a diagnosis of Grade 2 spondylolithesis was made; he stayed in hospital for three days.

In July 1989 he underwent lumbosacral spinal fusion to stabilise his spine. .....

During the times he has been seen for the pain in his back there is mention in the letters by various Orthopaedic Consultants and Pain Clinic Consultants that he uses cannabis to help the pain in his back.....

In 1996 he had a revision operation with work done on the screws holding some bones of his lower spine in place.

In January 2002 he was seen at Hospital and it was noted that he may have a crack in one of the rods connecting part of the spine together but he concluded that as the wires were solid, no action needed to be taken.

In June 2002 it is documented that he had a four week sick certificate for back pain.

In August 2002 it is documented that he had a five day episode of back pain.

In October 2002 and in November he had further sick certification for back pain.

In April 2008 he had some hip pain.

In October 2009 he was seen and prescribed muscle relaxants for back pain.

In October 2009 he was referred back to Hospital for his back pain and states in a clinic letter 'as far as his back is concerned his pain is very variable at times; he is pain-free and other times he is in severe pain. Today he was pretty good, his spine is

quite mobile and non-tender and x-rays simply show an intact spinal fusion from L4 to the sacrum with pedicle screws in situ and there is no evidence of loosening of the screws, in short, he has an intact spinal fusion that is structurally sound and, as such, there is no further orthopaedic surgery that should be offered to this man. I have shown him the x-rays and explained that this fusion is sound. If he does have further severe episodes of back pain then he may benefit from a referral to a Pain Specialist for discussion about his analgesic requirements. There is no further orthopaedic surgery that would be appropriate here'.

24. In so far as it relates to this case, I am only highlighting those issues related to his back. (**I am however told in his statement of proof that he has the presence of severe pain after an infection of herpes, this is likely also to be helped by the medicinal use of cannabis.**)

25. I also attach, for the sake of brevity, an open letter written by a Consultant Orthopaedic Surgeon, dated 1 March 2010 which is quoted by the GP in full. (Please see attached reference 3.)

[B L A N K]

OTHER PAPERS SEEN

26. I have read, but do not detail in case the prosecution does not want to adduce bad character, the printout of summary convictions etc.

27. I have seen legal aid representation and my fees are covered by granting of prior authority, dated 15 July 2010.

[B L A N K]

SUMMARY OF INFORMATION SUPPLIED

28. The defendant admits the charges against him (**I do not know if the indictment has changed**) and I believe he will say that he was growing his own marijuana so that he may self-medicate the pain from his severe spinal condition as detailed extensively in his medical records.

[B L A N K]

CANNABIS CURRENTLY APPROVED BY REGULATORY AGENCIES IN WORLDWIDE RESPECTED MARKETS – UK, EUROPE, AMERICA & CANADA

NABILONE

Summary of Product Characteristics

(Please see attached reference 4)

29. The Summary of Product Characteristics for Nabilone, (**a synthetic cannabinoid**) in section 4.1 entitled '*Therapeutic indications'* states '*Nabilone is indicated for the control of nausea and vomiting, caused by chemotherapeutic agents used in the treatment of cancer, in patients who have failed to respond adequately to conventional antiemetic treatments.*'

30. All other information is in the Summary of Product Characteristics which may be relied on as it is approved by the MHRA.

MHRA

(Please see attached reference 5)

31. The adverse experiences reported in the UK to the MHRA are shown in the Drug Analysis Prints which are attached and may be relied on.

Martindale

(Please see attached reference 6)

32. Martindale is published by the British Pharmaceutical Society and is the standard text to which all doctors should refer. It states that Nabilone is '*a synthetic cannabinoid with antiemetic properties, is used for the control of nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetics'.*

[B L A N K]

MARINOL

Physicians' Desk Reference

(Please see attached reference 7)

33. Marinol is approved in the USA by FDA, but not in the UK. It contains Dronabinol, which is a cannabinoid.

34. In the US it has regulatory approval for:

    1. *'anorexia associated with weight loss in patients with AIDS; and*

    2. *nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments'.*

35. The entirety of the product information, which is approved by the FDA, may be relied on.

[B L A N K]

SATIVEX

Summary of Product Characteristics

(Please see attached reference 8)

36. Sativex contains '*2.7 mg delta-9-tetrahydrocannabinol (THC) and 2.5 mg cannabidiol (CBD). Each 100 microlitre spray also contains up to 0.04 g alcohol'*.

37. Sativex has been in development for 12 year by GW Pharmaceuticals and is licensed in the UK to Bayer. The Summary of Product Characteristics has had regulatory approval and therefore may be relied on.

38. In section 4.1 of the Summary of Product Characteristics, entitled '*Therapeutic Indications'* it states '*Sativex is indicated as add-on treatment, for symptom improvement in patients with moderate to severe spasticity due to multiple sclerosis (MS) who have not responded adequately to other anti-spasticity medication and who demonstrate clinically significant improvement in spasticity related symptoms during an initial trial of therapy'*.

39. The product has been reviewed by the MHRA assessors prior to its granting of the product licence. This report is now publically available on the web and is called the Public Assessment Report (PAR).

Public Assessment Report

(Please see attached reference 9)

40. The document '*Public Assessment Report, Decentralised Procedure, Sativex Oromucosal Spray, UK/H/2462/001/DC, UK licence no: PL 18024/0009, GW Pharma Limited*' is available on the MHRA website and runs to 129 pages

41. This report has been read by me and comments have been made to GW Pharmaceuticals and Bayer on its contents and it may be relied on.

[B L A N K]

US SITUATION

(Please see attached reference 10)

42. I attach the printout downloaded from ProCon.org for the legal status and regulatory status related to medical marijuana (**I do not address the use of cannabis as an illegal substance or the legality surrounding its use in the USA and the states separately**).

43. There are currently 15 states which have voted to some degree for its medical use. Table 1 shows the states, the year the regulation was passed, how the vote went through, the necessary ID card payments and the limits of possession. Some states accept ID cards from other states, but some do not.

[B L A N K]

44. Two additional states have passed laws which are favourable to medical marijuana, but do not legalise it, these are Arizona and Maryland.

'14 Legal Medical Marijuana States and DC - Laws, Fees, and Possession Limits

Fourteen states and DC have enacted laws that legalize medical marijuana:

State	Year Passed	How Passed (Yes Vote)	ID Card Fee	Possession Limit	Accepts other states' registry ID cards?
1. Alaska	1998	Ballot Measure 8 (58%)	$25/$20	1 oz usable; 6 plants (3 mature, 3 immature)	Unknown *
2. California	1996	Proposition 215 (56%)	$66/$33	8 oz usable; 18 plants (6 mature, 12 immature)**	No
3. Colorado	2000	Ballot Amendment 20 (54%)	$90	2 oz usable; 6 plants (3 mature, 3 immature)	No
4. DC	2010	Amendment Act B18-622 (13-0 vote)	***	2 oz dried; limits on other forms to be determined	Unknown
5. Hawaii	2000	Senate Bill 862 (32-18 House; 13-12 Senate)	$25	3 oz usable; 7 plants (3 mature, 4 immature)	No
6. Maine	1999	Ballot Question 2 (61%)	****	2.5 oz usable; 6 plants	Yes
7. Michigan	2008	Proposal 1 (63%)	$100/$25	2.5 oz usable; 12 plants	Yes
8. Montana	2004	Initiative 148 (62%)	$25/$10	1 oz usable; 6 plants	Yes
9. Nevada	2000	Ballot Question 9 (65%)	$150 +	1 oz usable; 7 plants (3 mature, 4 immature)	No
10. New Jersey	2010	Senate Bill 119 (48-14 House; 25-13 Senate)	*****	2 oz usable	Unknown
11. New Mexico	2007	Senate Bill 523 (36-31 House; 32-3 Senate)	$0	6 oz usable; 16 plants (4 mature, 12 immature)	No
12. Oregon	1998	Ballot Measure 67 (55%)	$100/$20	24 oz usable; 24 plants (6 mature, 18 immature)	No
13. Rhode Island	2006	Senate Bill 0710 (52-10 House; 33-1 Senate)	$75/$10	2.5 oz usable; 12 plants	Yes
14. Vermont	2004	Senate Bill 76 (22-7) HB 645 (82-59)	$50	2 oz usable; 9 plants (2 mature, 7 immature)	No
15. Washington	1998	Initiative 692 (59%)	******	24 oz usable; 15 plants	No

*[**Editor's note:** 12 of the 14 states require proof of residency to be considered a qualifying patient for medical marijuana use. Only Oregon and Montana have announced that they will accept out-of-state applications. Karen O'Keefe, JD, Director of State Policies for Marijuana Policy Project (MPP), told ProCon.org in a July 27, 2010 email that "Patients and their caregivers can cultivate in 13 of the 14 states. Home cultivation is not allowed in New Jersey or the District of Columbia and a special license is required in New Mexico."]'*

45. The two latest additions are new Jersey and DC (District of Columbia, the US capital city) some sources do not include one or both of these at the moment.

SPAIN

(Please see attached reference 11)

46. In the last week of July, the Spanish Health Authorities granted approval for Sativex, a Oromucosal Spray as an add-on therapy for the treatment of moderate to severe spasticity due to Multiple Sclerosis (MS) in patients who have not responded adequately to other anti-spasticity medication the first new treatment for MS-related spasticity in decade.

47. Prior to this the autonomous government region of Catalonia launched a program of therapeutical use of Sativex for 600 patients of a wide set of illnesses, from MS to cancer. The product is presented as an atomizer to be taken orally, and it will be delivered at drugstores inside some hospitals.

48. The complete list of indications for the Catalonian government's sponsored use as stated on the GW Pharmaceuticals website states:

'*Sativex was prescribed to patients with the following therapeutic:*

- *Neuropathic pain due to MS*
- *Spasticity due to MS*
- *Neuropathic pain due to different medical conditions (other than MS)*
- *Anorexia-cachexia syndrome due to cancer or AIDS, and*
- *Nausea and secondary vomiting due to chemotherapy treatment.*

The study was restricted to patients who were unable to respond to, or unable to tolerate, currently available treatments and whose medical condition and quality of life were considered to be poor. The published results showed that half of the patients who received Sativex responded well by reporting improvement of their symptoms. Patients with MS reported an improvement of their pain and/or their spasticity. Patients with neuropathic pain from other causes also experienced improvement of their pain. The majority of patients with anorexia – cachexia syndrome showed improved appetite and patients undergoing chemotherapy reported an improvement of their nausea and vomiting.

Sativex has also been trialled in two pilot Phase II trials in post-operative pain which have shown encouraging results.' (Please see attached reference 2*)*

CANADA

49. Marijuana remains an illegal drug in Canada. The paper on the Legal Status of Medicinal Cannabis, as attached (please see attached reference 11), states *'However, on July 30, 2001, the Narcotic Control Regulations was amended and the Marihuana Medical Access Regulations came into force. These regulations established a compassionate framework to allow the use of marijuana by people who are suffering from serious illnesses and where the use of marijuana is expected to have some medical benefit that outweighs the risk of its use. In Canada, the cannabis is distributed by Health Canada under the brand name of CannaMed to patients who fit into certain categories. These categories (see below) include end-of-life patients or those with a debilitating medical condition. It is prescribed in order to help with epileptic seizures, severe pain associated with either HIV/AIDS, arthritis, cancer, multiple sclerosis or a spinal cord injury or disease.*

In (2003), a court again declared Canada's Marihuana Medical Access Regulations unconstitutional "in not allowing seriously ill Canadians to use marijuana because there is no legal source of supply of the drug." In effect, this means that Canadians cannot be prosecuted for using marijuana medically because the Marihuana Medical Access Regulations gives patients the right to do so, but does not set up any legal apparatus for obtaining cannabis.'

50. I attach from the Health Canada website details of the people whom are able to obtain authorisation to possess marijuana. There are two categories of people. Category 1 includes people whom have severe pain from spinal cord disease and from spinal cord injury.

'Category 1: This category is comprised of any symptoms treated within the context of providing compassionate end-of-life care; or the symptoms associated with the specified medical conditions listed in the schedule to the Regulations, namely:

- *Severe pain and/or persistent muscle spasms from multiple sclerosis;*

- *Severe pain and/or persistent muscle spasms from a spinal cord injury;*
- *Severe pain and/or persistent muscle spasms from spinal cord disease;*
- *Severe pain, cachexia, anorexia, weight loss, and/or severe nausea from cancer;*
- *Severe pain, cachexia, anorexia, weight loss, and/or severe nausea from HIV/AIDS infection;*
- *Severe pain from severe forms of arthritis; or*
- *Seizures from epilepsy.*

Applicants must provide a declaration from a medical practitioner to support their application.

Category 2: This category is for applicants who have debilitating symptom(s) of medical condition(s), other than those described in Category 1. Under Category 2, persons with debilitating symptoms can apply to obtain an Authorization to Possess dried marihuana for medical purposes, if a specialist confirms the diagnosis and that conventional treatments have failed or judged inappropriate to relieve symptoms of the medical condition. While an assessment of the applicant's case by a specialist is required, the treating physician, whether or not a specialist, can sign the medical declaration.'

(Please see attached reference 12)

51. The doctor has to be cleared to prescribe cannabis but the court rules set down by the Canadian Supreme Court means that they have to have a very good reason to refuse this. There are two schedules - one for people with serious illnesses like MS, Cerebral Palsy and Spasticity patients, patients with AIDS as well as patients with chronic Hepatitis C and glaucoma.

52. The second schedule is for pain patient, people with more diffuse symptoms but again most applications are granted. You can nominate a grower or else get the government weed grown in an abandoned mine which is very low grade so no one wants it. Most people go to a compassion club or else ask permission to grow it themselves.

53. Additionally Canada has:

i) Approved Sativex for the relief of neuropathic pain in Multiple Sclerosis

ii) Approved Sativex as an adjunctive analgesic treatment in adult patients with advanced cancer who experience moderate to severe pain during the highest tolerated dose of strong opioid therapy for persistent background pain.

[B L A N K]

REST OF THE WORLD

(Please see attached reference 11)

54. We have gathered this information to the best of our abilities, obviously we do not have sight or primary legislation in any of these countries. I attach it for:

- Australia
- Belgium
- Austria
- Germany
- Norway
- Portugal
- Finland
- Romania
- Denmark
- Israel
- India
- Jamaica
- Mexico
- New Zealand
- Pakistan/Peshawar
- Cameroon
- Uruguay

[B L A N K]

WEBSITE OF GW PHARMACEUTICALS

(Please see attached reference 2)

55. As GW Pharmaceuticals is a regulated UK based pharmaceutical company, their website would be subject to the Medicines Act and they have a licence to cultivate cannabis, they would be cautious in their claims. They also would be subject to pharmaceutical self-regulation such as in the Association of the British Pharmaceutical Industry's code of practice.

56. I attach the medical section of the website of GW Pharmaceuticals who were the developers of Sativex, however, they have licensed to major pharmaceutical companies around Europe, the US and the rest of the world.

57. Their research, clinical studies and their regulatory activities have been over a 12 year period.

Multiple Sclerosis

(Please see attached reference 2)

58. The GW Pharmaceuticals website states that the major indication is Multiple Sclerosis, at which they are targeting both the spasticity and pain. The pain is neuropathic (**nerve pain in nature**) and these patients responded inadequately to other conditions.

59. They note the approval for MS spasticity in the UK and for the relief of the neuropathic pain of MS in Canada.

60. **Currently even they do not mention their Spanish approval in their website, as at 11.08.2010, although by the time this report is served, they may have updated it.** They note that for other European country's regulatory applications are expected to be made under '*the Mutual Recognition Procedure in the second half of this year'.*

Cancer Pain

(Please see attached reference 2)

61. Currently patients are prescribed opioids for cancer pain, but the undesirable side effects of constipation, sedation, respiratory depression, tolerance, abuse, dependence and withdrawal all contribute to the desire of physicians in cancer and terminal care to look for alternatives with less drastic and severe side effects.

62. I have noted previously the Canadian approval for this. GW Pharmaceuticals currently have many ongoing studies, some of which are published.

63. They state '*Sativex is approved in Canada as an adjunctive analgesic treatment in adult patients with advanced cancer who experience moderate to severe pain during the highest tolerated dose of strong opioid therapy for persistent background pain. Cancer pain is also the lead target indication for approval of Sativex in the US'.*

Neuropathic Pain

(Please see attached reference 2)

64. The Canadian approval has already been noted. This is a very difficult pain to treat and one often has to use complex combinations of antiepileptic drugs, mood stabilising drugs, antidepressants, morphine type opiates and newer agents such as Gabapentin and Pregabalin.

65. The website of GW Pharmaceuticals states '*Sativex is approved in Canada for the treatment for central neuropathic pain due to MS. Sativex has also been used in a number of Phase II and III clinical trials in various models of peripheral neuropathic pain, from which a body of positive data has been generated'*.

GW Pharmaceuticals other indications

66. There is published evidence of an early placebo controlled trial showing improvements in pain and other measures in people with rheumatoid arthritis.

67. There is also ongoing work in postoperative pain. The list of publications from their website is attached (please see attached references 13), as is the abstract sourced by me from PubMed for the treatment of pain in rheumatoid arthritis which concluded '*In*

the first ever controlled trial of a CBM in RA, a significant analgesic effect was observed and disease activity was significantly suppressed following Sativex treatment. Whilst the differences are small and variable across the population, they represent benefits of clinical relevance and show the need for more detailed investigation in this indication.' (please see attached references 14)

[B L A N K]

UK PARLIAMENTARY HOUSE OF LORDS SELECT COMMITTEE ON SCIENCE & TECHNOLOGY

(Please see attached reference 15)

68. The UK Parliamentary House of Lords Select Committee on Science and Technology, Ninth Report, chapter 5, published in Parliament, copyright 1998, shows the position as of then and my review above shows what great strides there have been in the regulatory approved use of cannabis substances since that time.

69. It acknowledged the use in MS, which is where the first approvals have been obtained, and they also took evidence of users growing themselves and states under 5.5 '*An increasing number are growing their own cannabis, "primarily to avoid problems of impurity", or buying in bulk to ensure consistency of dose; either course exposes them to stiffer sentences, if caught, than the frequent purchase of small quantities (cp IDMU p 261). Medical users typically take cannabis as frequently as, but in smaller quantities than, recreational users'*

70. It is interesting that it notes under 5.6 that the '*medical purposes is sometimes connived at by the medical professions*' whom are now embracing this treatment.

71. It notes the use of Nabilone and Dronabinol.

72. They also took evidence of the unlicensed use of Nabilone in intractable pain in conditions such as MS, cancer, peripheral nerve damage and spinal lesions. This is of particular importance to the defendant, The defendant.

73. They also note, in relation to spinal injury, which this defendant has '*The ACT also know of 50 users with spinal injury, and 20 with other conditions. A survey conducted by the newspaper Disability Now in 1997 among its disabled readers revealed, among 200 respondents, 40 people taking cannabis for MS, 40 for spinal injury, 35 for back pain, 27 for arthritis and 64 for other conditions. IDMU's surveys of 2,794 regular cannabis users have revealed 78 whose main reason for using it is medical*.'

74. In addition to all the areas that GW Pharmaceutical are researching, there has been suggestion of its use in other conditions, these have included epilepsy, glaucoma and asthma.

75. Other people have noted it's possible use in health issues where there are abnormal tremors such as Parkinson's Disease.

[B L A N K]

CANNABIS

76. Cannabis is, in its botanical definition a genus of plant that includes three sub species Cannabis Sativa (L.), cannabis Indica (L) and the less favoured cannabis ruderalis (L). There are a large number of hybrids, which have been genetically engineered to promote the most desirable characteristics of each type, in order to increase, yield, THC content, durability etc. These however remain cannabis plants when they grow. Generally when cannabis used in this report it refers either to the genus and where necessary we have specified if it is a plant compound, a metabolite or one of the sought after extracts of the (mature) plant.

77. Marijuana refers to a mixture of the leaves and flowering tops of the cannabis plant. Generally, the upper leaf and mature female bud contain the highest levels and most sought after THC.

78. Hashish is a term that applies to the resin extracted from marijuana. Terminology alters between countries, and ethnic groups. The strength of marijuana is less than that of hashish and both are less than an oil that may be extracted. The percentage by weight of THC from Police seizures in the UK ranges from 0.5 to 8% for marijuana, 2 to 8% for the resin (and over 50%+ for the oil, which is extremely rare and requires careful extraction). With 'hydroponic' cultivation of genetically altered cannabis, grown in ideal light and feed by nutrient materials, without soil, commonly, if less than completely accurately, called 'Skunk,' the marijuana upper leaf /bud may be 7 to 18% THC. A form of cannabis known as 'sinsemilla' ('without seeds', sp.) which again, is the unfertilised flowering heads of the female plant, traditionally the 'sativa', separated from male plants and may contain levels of Delta9THC as high as 'skunk' variants. 'Skunk' was initiated in Holland in 1979 and most hybrids have since adopted the title. Virtually every report from the Forensic Science Service on upper leaf/bud seizures refers to this part of the plant as 'skunk'. It is very pungent and due to its potency smaller amounts are needed to attain a 'high'.

79. A large number of chemicals may be extracted from the drug, these are called cannabinoids. The most important being Delta-9-THC, Delta-8-THC, Delta-9-THC-Acid and all these may be psychoactive.

80. Cannabinol (CBN) and cannabidiol (CBD) may be present in large amounts, but have little euphoric activity. Cannabidiol may have some relaxant effect on muscles, does decrease the anxiety that cannabis may provoke, may be protective to the paranoid psychotic effects of cannabis, and may have some analgesic actions itself, or synergistically enhances those of 9THC. The amount of Delta-9-THC, the main active substance, may be present in amounts as little as 0.5% in marijuana and as much as 70% in refined cannabis oil.

81. Different plants have different ratios of THC and CBD (cannabidiol).

82. If the THC levels are greatest, the effect is one of a euphoric high, however if there is a greater amount of CBD, people believe the effects are more of one of relaxation and sedation.

83. There are studies which show that 9-THC increases anxiety as well as intoxication, sedation and psychotic symptoms, and this anxiety and the psychotic symptoms may be reduced by CBD.

84. Indeed the two substances have distinct effects on neuro psychiatric physiology and psychology.

85. There has even been a suggestion that CBD could be developed as an anxiolytic or antipsychotic.

86. CBD is a sedative primarily, as well as having some analgesic properties.

87. It has been postulated that the reason why people who smoke cannabis get less airways irritation and inflammation than those who smoke nicotine is because of a protective effect of CBD.

88. When smoked, cannabis produces an almost immediate reaction peaking in 20 to 30 minutes and lasting three to four hours.

89. When taken by mouth, absorption is slow and irregular. Effects are usually first seen within 30 minutes to one hour and peak between one and three hours and can persist for up to eight hours.

90. THC is widely distributed in the body and is actively metabolised in the liver to an active compound being the 11-Hydroxy derivative. In the liver, it is metabolised by an important member of the P450 enzyme, namely, CYP3A3/4 of which all the cannabinoids are enzyme inhibitors.
91. It is excreted in the urine over a prolonged period of time.
92. Blood concentrations of THC do not correlate well with the reported psychoactive effects due to the fact that 11-Hydroxy, Delta-9-THC is also psycho active.
93. The plasma elimination half-life is of THC is between 28 and 56 hours depending on the individual's metabolism and use of cannabis.
94. The tissue half-life is about seven days because THC binds to fat in the body and complete elimination may take up to 30 days.
95. The most widely used forensic test is 9 Carboxy THC, which is a metabolite of Delta 9 THC, but is itself not psychoactive. The most widely used confirmatory test identifies 11-nor-9-carboxy-delta-9-Tetrahydrocannabinol (THC COOH) at above 15ng/ml as a cannabis positive test. Lower detectable levels could be caused by passive inhalation.
96. There are many different types of cannabinoids 9THC produces the high, cannabinol is not psychoactive and is thought by many to be protective to the schizophrenic-like symptoms people who smoke cannabis may get.
97. There are many different types of cannabinoids in cannabis plants and all their effects may be slightly different and genetic modification may alter the cannabinoids and thus the effects.
98. The main psychical effects of cannabis are increase in heart rate, changes in blood pressure, reddening of the eyes, dry mouth and increase in appetite. There may be changes in motor coordination and psychomotor function and cannabis may affect driving.
99. Psychological effects include relaxation, euphoria, elevation of mood, distortion of time and space, disturbances of memory and judgment, sleepiness, sedation, alterations in consciousness increased sensation of all types.
100. Many people find that sensuality and sexuality are increased due to relaxation, some degree of disinhibition and an increased sensation. Paradoxically, some people may

become irritable and aggressive. With severe intoxication there may be disturbances of perception and thought and in extreme cases hallucinations and psychosis and very rarely unconsciousness.

101. I identify below some of the major and minor cannabinoids in cannabis.

Major Constituents:

- (-)-[delta 1]-3,4-trans-tetrahydrocannabinol
- (-)-[delta 6]-3,4-trans-tetrahydrocannabinol
- tetrahydrocannabitriol (aka cannabitriol)
- cannabidiolic acid
- cannabidiol
- cannabinol
- THC acids A and B (inactive unless smoked)

Minor constituents:

- cannabigerol
- cannabigerolic acid
- cannabichromene
- cannabichromenic acid
- cannabicyclol (aka cannabipinol)
- cannabicyclolic acid
- cannabicitran
- cannabielsoic acids A and B
- cannabinolic acid (neutral cannabinoid)
- cannabichromanon
- cannabifuran
- dehydrocannabifuran
- 2-oxo-[delta 3]-tetrahydrocannabinol
- cannabigerol monomethyl ether
- cannabidiol monomethyl ether
- cannabinol methyl ether

Compiled from "*The Botany and Chemistry of Hallucinogens*" by Schultes & Hofmann and '*Medical marijuana and its use by immunocompromised individuals*.' (McPartland and Pruitt, 1997)

[B L A N K]

MEDICAL USES OF CANNABIS

Review of the literature

102. I attach seven papers on the medical use of cannabis, published from 2000 to 2009.

- **Medicinal use of cannabis in the United States: historical perspectives, current trends, and future directions.**

  J Opioid Manag. 2009 May-Jun;5(3):153-68.

  Aggarwal SK, Carter GT, Sullivan MD, ZumBrunnen C, Morrill R, Mayer JD.

  (Please see attached reference 16)

- **Allowing the medical use of cannabis.**

  Med J Aust. 2001 Jul 2;175(1):39-40.

  Hall WD, Degenhardt LJ, Currow D.

  (Please see attached reference 17)

- **An approach to the medical marijuana controversy.**

  Drug Alcohol Depend. 2000 Feb 1;58(1-2):3-7.

  Hollister LE.

  (Please see attached reference 18)

- **Human studies of cannabinoids and medicinal cannabis.**

  Handb Exp Pharmacol. 2005;(168):719-56.

  Robson P.

The review by Robson in 2005 reviews the evidence for:

- Review of clinical research
- Symptomatic relief in Multiple Sclerosis and spinal cord injury
- Symptomatic relief in other neurological conditions
- Chronic pain
- Appetite stimulation

- Appetite suppression in obesity
- Glaucoma
- Epilepsy
- Psychiatric disorder
- Asthma

(Please see attached reference 19)

- **Medical marijuana and the developing role of the pharmacist.**

  Am J Health Syst Pharm. 2007 May 15;64(10):1037-44.

  Seamon MJ, Fass JA, Maniscalco-Feichtl M, Abu-Shraie NA.

  (Please see attached reference 20)

- **Treatments for chronic pain in persons with spinal cord injury: A survey study.**

  J Spinal Cord Med. 2006;29(2):109-17.

  Cardenas DD, Jensen MP.

  (Please see attached reference 21)

- **Cannabinoid-based medicines for neurological disorders--clinical evidence.**

  Mol Neurobiol. 2007 Aug;36(1):129-36. Epub 2007 Jun 29.

  Wright S.

  (Please see attached reference 22)

[B L A N K]

FUTURE OF CANNABINOIDS IN MEDICINE

103. Now the two cannabis receptors have been identified, pharmaceutical companies will be looking to both develop cannabis plants to deliver different combinations of cannabinoids and also try to develop synthetic alternatives to both stimulate the receptor and block it.

104. One of the things stopping pharmaceutical companies going down this route, and was a challenge taken on by GW Pharmaceuticals, was the illegal status of cannabis and thus its medical use would require major changes in the law.

105. This hurdle has now been crossed with the first, and ongoing approvals in Europe, approvals in Canada, the filing of an investigational new drug application to do studies in America and worldwide acceptance.

106. There are many other substances in development which are undergoing research, but it is not the place of this report to list them all here.

107. Other substances have been approved in the past, but have been taken off the market due to toxicity. These include the drug Rimonabant, which is a CB1 receptor blocking drug which was used for obesity. This is the opposite effect of stimulant drugs on increasing appetite, which is a known side effect of illegally smoked cannabis, known as the *'munchies'*.

[B L A N K]

LEGAL CANNABIS FARMS IN THE UK

108. GW Pharmaceuticals have isolated four genetic alleles in the cannabinoid genome and are attempting to alter this to produce plants with different combinations of cannabinoids. Their cultivation in farms is licensed and their cultivation controlled.
109. The geographical location of the farms is a matter of top secrecy. It is believed that other people have licences to cultivate cannabis, although the Home Office appears to be circumspect in giving this information out.
110. I am sure the court could find out, using its powers, if this was deemed to be important at all to this, or future cases.
111. We believe that Kew Gardens and the Royal Botanical Society must have a licence as the plants are grown there. We understand the LGC, which is the Laboratories of the Government Chemist, did, should and do have a licence.
112. Mr M, who has given expert evidence in many cannabis cases and is associated with Gary Sutton, had a licence for one year in 2008, before it was revoked one year later. He was given this licence to help in his medical expert witness work. We also believe Aberdeen University may have a licence but as pharmaceutical chemists from GW Pharmaceuticals are associated with this department, it may be covered by their licence.

[B L A N K]

CANNABIS IN NEUROPATHIC PAIN RESULTING FROM SPINAL INJURIES

113. We have mentioned previously the indication for Sativex in Canada, where it is licensed for '*the adjunctive treatment for the symptomatic relief of neuropathic pain in multiple sclerosis in adults'*. I attach the Health Canada information. (Please see attached reference 23)

114. I have also noted previously the cancer pain indication and the approval in Canada for central neuropathic pain.

115. Comen et al in 2008 wrote a review of the pathological implications of cannabinoids in neuropathic pain (Please see attached abstract reference 24).

116. The year previously Wright published the paper:
'Cannabinoid-based medicines for neurological disorders--clinical evidence'
on the use of cannabinoids in neurological disorders, particularly pain (Please see attached reference 22)

117. In 2009 Aggarwal et al published a paper entitled:
'*Medicinal use of cannabis in the United States: historical perspectives, current trends, and future directions'*
(Please see attached reference 16)
Aggarwal et al noted that in Washington State neuropathic pain was the reason for access of medical cannabis in 89 people, discogenic back pain 72, and osteoarthritis 37.

118. Cardenas DD, Jensen MP, 2006, a paper entitled:
'Treatments for chronic pain in persons with spinal cord injury: A survey study'.
(Please see attached reference 21)
Cardenas et al did a survey of treatments for chronic back pain and noted the inadequacies of current treatments and in this survey 73% of people had tried at least one alternative pain treatment outside of licensed medical products.
The most frequently tried were massage, marijuana and acupuncture. He concludes that '*many patients are not finding adequate pain relief from commonly prescribed*

medications. Alternative therapies should be considered as additional treatment options in this population'.

119. Croxford JL

'Therapeutic potential of cannabinoids in CNS disease'

Croxford in 2003 highlighted the therapeutic potential of cannabinoids in CNS disease and notes that '*indeed, in clinical trials of postoperative and cancer pain associated with spinal cord injury, cannabinoids have proven more effective than placebo but may be less effective than existing therapies'*.

(Please see attached abstract reference 25)

120. Doctors in the US are now going public on the potential for cannabinoids to treat spinal cord injury symptoms based on the growing evidence of their positive effect in the various conditions already discussed, such as neuropathic pain, spinal injury, rheumatoid arthritis and other types of pain.

121. On the GW Pharmaceuticals website, it notes that they have completed a Phase Two study in spinal cord injury, results of which have been summarised as '*new positive data from GW's Phase Two clinical trials in Multiple Sclerosis and Spinal Cord injury is provided in the preliminary results announced separately today. This encouraging data shows significant improvements in a range of symptoms'*. (Please see attached reference 26) This also reviews other neuropathic pain trials.

122. A recent study in 2006 by Dr Anita Holdcroft showed that cannabis was useful at relieving pain after major survey. (Please see attached reference 27)

[B L A N K]

SIDE EFFECTS OF CANNABIS

(Please see attached abstract reference 28)

123. I attach the section from Myler's Side Effects of Drugs.

SIDE EFFECTS OF OPIOIDS

(Please see attached abstract reference 29)

124. I attach the monograph from Myler's Side Effects of Drugs.

MARTINDALE, CANNABIS AND OPIOIDS

125. The adverse effects of cannabis treatment relate to physiological effects and psychological effects.

126. Nausea and vomiting may be the first effects of cannabis taken by mouth, despite the fact that when inhaled or used as a spray, they relieve this.

127. The most frequent physical effects of cannabis intoxication are an increase in heart rate with alterations in blood pressure, conjunctival congestion, dry mouth, and increased appetite. Deterioration in motor coordination is common and cannabis has been reported to affect driving.

128. The psychological effects include elation, distortion of time and space perception, irritability, and disturbances of memory and judgement. Anxiety or panic reactions may occur, particularly in inexperienced users. These reactions do not usually require specific therapy; diazepam may be necessary for severe reactions.

129. Psychotic episodes of a paranoid or schizophrenic nature, and usually acute, have occurred in subjects taking cannabis, especially in large doses or after the use of varieties bred for a high yield of cannabinoids (so called skunk).

130. Cannabis may also have other effects on the cardiovascular system, and in relation to the central nervous system, the effects include alterations in cognition, anxiety and depression, and psychosis, including schizophrenia.

131. It also has many interactions, however, they are of little relevance to this report, although clinically are important.

OPINION

132. This gentleman has pleaded guilty (**I do not know if the indictment has changed**) to the offence, however, in my opinion, from what I have read, there could easily be mitigating circumstances. From a biophysical and pharmacological perspective there are a number of points where the patients suffering as substantially documented over a considerable period of time appears to be substantially mitigated by pain killing properties of cannabis. There is an ever increasing evidence base concerning this which I will now address.

133. I give this judgement based on what I have read about his condition and my pharmacological and medical knowledge of the ability of cannabis to relieve pain when it is not relieved by other medications.

134. Additionally, the use of cannabis, although not without side effects and possible long term mental health sequelae, appears devoid of the debilitating side effects of the other pain relieving medicines used for severe and intractable pain.

135. The side effects of the opioids are well known and not only include dependence, abuse, withdrawal and addiction, but also include the side effects shared by all the opioids including:

- nausea and vomiting (particularly in initial stages)
- constipation
- dry mouth
- spasm of the biliary ducts leading from the liver to the gut resulting in severe biliary colic (**abdominal pain**) and possibly even jaundice
- muscle spasms
- low blood pressure
- most severely and importantly, a depression of respiration

136. Opioids have many other side effects, such as:

- low or fast heart rate
- palpitations of the heart
- fluid retention in the lower limbs resulting in puffiness

- oedema
- alterations of blood pressure
- hallucinations
- vertigo
- dizziness
- euphoria
- dysphoria
- mood changes
- dependence
- dizziness
- confusion
- drowsiness
- sleep disturbances
- headache
- sexual dysfunction
- difficulty with passing water
- urinary retention
- ureteric spasm
- visual disturbances
- sweating
- flushing
- rash
- urticaria
- pruritus

It is also, of course, dangerous in overdose.

137. The use of opioids in non cancer pain is thwart with difficulties because of the dangers of dependence, misuse and abuse, withdrawal, addiction and people becoming used to their effects. All these and the psycho-active nature of their effects lead patients to attend more than one doctor to try to get excess supplies, as well as diversion into the illegal market. This is of such major importance that there are extensive guidelines

given to doctors in the UK and the US as well as other territories to guide their use. An example of UK guidance is attached. As well as two examples from the US (available on request), it is an important enough topic for the Royal College of General Practitioners in their training manuals for GP's to give individual guidance. (Please see attached references 30 and 31.) In patients with acute spinal injury and possibly pain due to pressure on nerves or the spinal cord, the patient can become so anaesthetised that further damage may be caused without the patient being aware, that they literally, cannot feel their bodies warning them not to adapt certain positions which may cause further damage.

138. Thus due to their adverse effects including addiction, physical and neuro psychiatric consequences and difficulties in use, it is thought that prescription cannabis will be a significant advance.

139. This is shown by despite the illegal nature of cannabis, a growing worldwide recognition that it may be used relatively safely in a variety of conditions, as I have indicated in my report.

140. Neuropathic pain from the spine, which is what the defendant appears to suffer from, on good medical evidence, is one of these.

141. The increasing regulatory approvals and increasing number of medicinal substance laws, particularly in the US, Canada and Spain, and the new regulatory approvals in the UK, are testament to the medical opinion moving substantially forward from its position of ten years ago.

142. One of the difficulties is that because of the lack of prescription cannabis, many people with the condition suffered by the defendant, have turned to illegal cannabis and as the evidence presented to the House of Lords suggests, grow their own in a not infrequent nature. They have to be aware of crop morbidity and mortality. A power cut for example can destroy in a day, many weeks of careful effort. It is certainly not uncommon to experience wildly differing yield per plant in the same crop. Experience and facilities will of course have a bearing on this. The Court may consider that this uncertainty would be a factor in an individual deciding to grow a crop. It may also be a factor that some individuals supply themselves to eschew the illegal market.

143. It is not surprising, with the increasing knowledge of cannabis growth, that these people often indulge in cultivation associated with water pumping, which the police sometimes call '*hydroponics'*, although this truthfully means the growth in a non-soil mixture with controlled supplies of nutrients and water, it is well know that you need intense light to mature the plants and because the patient needs to have a continuing supply, they also indulge in rotation.
144. None of the things by themselves would lead someone to believe it is being done for profit. The quantity of substances found may do, as may the yield, which is highly variable dependant on the strain on the plant used and the condition it is used in.
145. I have not read of the defence putting forward a challenge to the evidence of the police, and as The defendant has pleaded guilty, this is not a matter for this report. However, there would be experts other than me who could do this and would I believe disagree with the police.
146. It would be tempting to presume that with the ability of doctors to now prescribe the legal medicinal substance Sativex, that it would be an easy evolution for patients dependant on illegal cannabis to have their needs met by substituting illegal cannabis for Sativex. Only time will tell if this is a useful therapeutic option.
147. The doctor would need to either use Sativex on a named patient basis, sharing responsibility with the pharmaceutical company, who are unlikely to do this in my experience in this way, for substitution of illegal substances. Alternatively they would need to prescribe outside of the product licence, which clinical pharmacologists do on a frequent basis. If a doctor does this, they are then taking a much fuller responsibility for their actions than when they prescribed within a product licence approved indication. My experience is that GP's do not take on this challenge readily. Whether drug addiction units will take on this challenge remains to be seen. Addiction units already overburdened with clients on class 'A' drugs, in reality have little time for cannabis users. Indeed they have little time for addiction to prescription drugs either.
148. There will be further complications in that from my knowledge of cannabis use and my pharmaceutical knowledge of Sativex, the two do not immediately appear to be similar or inherently consistently substitutable, although they may be in some cases.

149. It only contains two cannabinoids and in a fixed proportion. Other cultivated cannabis is not so purified and has many, many more cannabinoids with differing effects possible, differing in their course of actions and differing interactions. Without entering the realms of speculation, as I do not know the cannabis type in this case, it appears that there are some cannabis seeds available that are sold as containing higher amounts of CBD or other compounds. A look at the seed stores advertising on the internet shows that they claim that the effects of different hybrids are carefully graded. Clearly, I cannot condone this of course, indeed I counsel against buying any substance be it legal or illegal off the internet. I am however bringing to the Court's attention that some illegal users may believe they can mimic the effects of Sativex by selecting from seed suppliers who appear to, and claim to, advise on such matters. It would be detrimental if illegal suppliers made much of their similarity to Sativex.
150. Although not in the Summary of Product Characteristics, but in the MHRA public assessment report, is the pharmacokinetic curve for Sativex which is the blood concentration across time after one or multiple doses. It is immediately obvious from figure 1, the profile is completely different and it may even be wondered by many how such low levels have been shown to have such profound effects.
151. There is also a great deal of individual variability between patients' responses, both pharmacokinetically and pharmacodynamically and also, as we know from nicotine replacement therapy and the inhalation of smoke, it is hard to place inhalation of smoke with other ways of delivering actively pharmaceutical substances.
152. It would certainly, however, be useful for the defendant to consult with his doctor who can then make an informed choice based on information from Bayer.
153. This report is by necessity incomplete, as I have not had the opportunity to read any of the defendant's medical records, seen any X-rays, consulted with defendant or had direct contact with any of his medical practitioners.

[B L A N K]

ADDRESSING THE SOLICITORS' POINTS OF INSTRUCTION

1 Is Cannabis used for or useful to deal with pain as a relief?

154. As detailed in my report.

2 If so for what types of illness and / or pain relief is it suitable?

155. As detailed in my report.

3 When addressing this defendant would his injuries fall into a category that Cannabis would help?

156. As stated I have not consulted with the defendant nor seen the entirety of his General Practitioner or hospital records. Neither have I discussed the case with them, nor have I examined him or seen any investigations either historical or current. However, from reading the submissions of his GP and the letter from his Orthopaedic Surgeon (which considering the complexity of his case are not adequate for a complete opinion) there are a number of possible reasons why the defendant's injuries would fall into the categories, and that the evidence suggests he would get relief. These include:

i) his original spinal injury

ii) possible damage to the spinal cord

iii) the original and continuing structural anatomical damage and changes to the bones and surrounding areas which may cause pain

iv) the insertion of orthopaedic devices to correct his injury

v) all the structural changes resulting from the original injury and his operative intervention would destroy the anatomy enough to get nerve entrapment as well as exacerbation of this by inflammation and swelling. This could result in both spinal pain, neuropathic pain and pain due to nerve entrapment all of which would respond to cannabis.

4 Is Cannabis used in other countries as a legal pain relief and if so, what others countries and in what context is it used?

157. As detailed in my report.

5 Does this country (England/Wales) have any legal uses for Cannabis and if so what are they?

158. As detailed in my report.

6 Does this country have any legalised / Government run Cannabis farms and what are they used for?

159. As detailed in my report.

7 What are the side effects of Cannabis, ranging from low levels of plant strength to high level of "skunk" type plants? (So far there is no level of strength for the plants found)

160. As detailed in my report, the greater the concentrations of active substances, the greater the degree of both benefit and adverse effects. Although the police state that they found '*skunk type plants'* it is our experience that they use this term almost generically now. The developers of Sativex believe they have dissociated the effect of cannabinoids on pain and spasticity from the euphoric effects and adverse effects of cannabis.

8 In your expert view does Cannabis have benefits which outweigh the use of prescribed medication and are the side effects mentioned above greater or less for Cannabis than for prescribed medication.

161. This is the crux of the matter. I have mentioned in my opinion the difficulties of the use of opioids in some detail and these all count against the use of opioids in non-cancer pain. Additionally, it is increasingly noted that prescription opioids may cause

more mortality than illegal opioids and I attach the abstract and paper by Dahlla which shows the increasing mortality noted in Canada (please see attached reference 32).

162. Additionally, when Professor David Nutt et al reviewed the risk of dependence and side effects of substances at the time, he was suggesting the development of a rational scale to assess the harm of drugs of potential misuse. He noted that cannabis was less of a problem than even alcohol and tobacco when considering both dependence and physical harm. This was published in the Lancet, Volume 369, page 1047, and was far less a problem than the illegal opioids and thus probably the legal opioids.

163. Primm et al in 2004 have addressed the problems of managing pain in the US with opioids and I attach their abstract and article from 2004 (please see reference 33).

164. It will also be seen from my report that the side effects of cannabis, both prescription and from the plant substances, is far less than those of the opioids. It would be my view that in many patients the benefits of cannabis, in prescription form and also in illegal form, may be beneficial compared to prescribed medication such as opioids. However, illegal use although possibly beneficial to patients, cannot be supported by a registered medical practitioner while it remains illegal.

165. It is for this reason that I and many other registered practitioners are so excited about the possibility of cannabinoids being legally prescribed using Sativex.

166. Nothing in my report should be taken to believe that I support the illegal use of cannabis, this is particularly so as the concentration of active substances has increased over recent years, children are smoking it at a younger age when their brains are in development and they are using it more frequently.

167. The increasing evidence of young people possibly suffering from depression and psychotic symptoms in general and also when they are predisposed to them is very concerning.

168. It is to be hoped that Sativex will allow the legal use in appropriate people and also that it itself does not become a prescribed medicine of abuse. Many believe this is unlikely to happen because of the low concentrations it delivers to the blood where you get the beneficial effects on cannabis receptors to produce the positive effects without overt evidence in most patients of the psychoactive effects which drive people to use it recreationally.

[E N D]

STATEMENT OF TRUTH

Declaration

I confirm that insofar as the facts stated in my report are within my own knowledge I have made clear which they are and I believe them to be true, and that the opinions I have expressed represent my true and complete professional opinion.

I believe that the facts I have stated in this report are true and that the opinions I have expressed are correct.

I understand that my primary duty is to the Court both in preparing reports and in giving oral evidence.

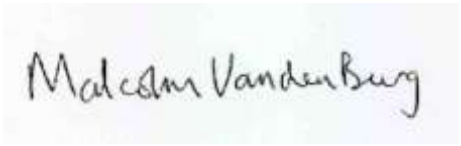
I have set out in my report what I understand from those instructing me to be the issues in respect of which my opinion as an expert is required.

I have endeavoured in preparing this report to be accurate and complete. I have included all matters, which I regard as relevant to the opinions I have expressed.

I have drawn to the attention of the Court all facts of which I am aware which might affect my opinion.

At the time of signing the report I consider it to be complete and accurate. I will notify those instructing me if for any reason I subsequently consider that the report requires correction or qualification.

This report is the evidence that I am prepared to give under oath subject to any correction or qualification I may make before swearing or affirming to its correctness.



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Malcolm VandenBurg
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