No. T-2030-13

FEDERAL COURT

BETWEEN:

NEIL ALLARD
TANYA BEEMISH
DAVID HEBERT
SHAWN DAVEY

PLAINTIFFS

AND:

HER MAJESTY THE QUEEN IN RIGHT OF CANADA

DEFENDANTS

EXPERT REPORT OF DAVID W. PATE

I, DAVID W. PATE, Ph.D., M.Sc., of 280 – 1857 West 4th Avenue, Vancouver, British Columbia, MAKE OATH AND SAY AS FOLLOWS, THAT:

(*a*) Issues addressed in the report.

1. This report addresses (a) basic botanical information regarding the *Cannabis* plant; (b) the location and components of the therapeutically active compounds found in the *Cannabis* plant; (c) methods of extracting these compounds from the plant material; (d) methods of ingesting these compounds by humans; (e) differences between the ingestion methods including differences in potential harms, onset and duration of effect and efficacy for therapeutic use.

(*b*) Description of qualifications.

2. I am currently the Director, Canadian Advanced Studies Institute Ltd. in Vancouver, British Columbia. I graduated in 1974 with a Bachelor of Arts degree in science, with a major in Biology and a minor in Chemistry from Webster University in St. Louis, Missouri in 1974 and then a Masters of Science degree in Biology, from the

University of Missouri – St. Louis at St. Louis, Missouri in 1979. I have also obtained a Doctor of Philosophy degree in Pharmaceutical Chemistry from the University of Kuopio, Finland in 1999. A significant amount of my research and experience has been in relation to the medicinal use of cannabis (marihuana) and cannabinoids.

3. Now produced and marked as Schedule "A" to my report is a list of my publications as of July 15th, 2011 showing the various topics I have researched and studied and again indicating significant research in relation to cannabis (marihuana).

4. I appeared and was qualified as an expert in botany and pharmacology in the Supreme Court of British Columba in the case of ***R. v. Owen Edward SMITH (2012 BCSC 544)*** before the Honourable Mr. Justice Johnson in which the court ruled on April 13th, 2012 that on the evidence there had been a violation of liberty and security rights of the medical marihuana users protected by s.7 of the ***Canadian Charter of Rights and Freedoms*** and remedied the breach by deleting the word "dried" wherever it appeared in the ***Marihuana Medical Access Regulations.*** As a consequence the definition of "dried marihuana" became superfluous and was also deleted from those Regulations, leaving in place the balance of the Regulations but removing what the Court described as an arbitrary restriction on the lawful use of marihuana to its dried form. As I understand it, the British Columbia Court of Appeal recently upheld the trial court's decision in that case in ***R. v. Owen Edward SMITH (2014 BCCA 322).***

(c) *Curriculum Vitae*

5. A copy of my current CV is attached as Schedule B.

(*d*) Facts and assumptions on which the opinions in the report are based.

6. The facts and assumptions upon which the opinions in this report are based are the expert's personal and professional experiences and qualifications as a biologist and chemist.

7. I understand that the Government of Canada in the Marihuana for Medical Purposes Regulations (*MMPR*), and by amendments to the Narcotic Control Regulations (*NCR*) is limiting possession and distribution of cannabis (marihuana) to its

"dried form" and therefore precluding the use of this substance in less harmful and more effective ways through the use of it in forms other than "dried" such as in its natural form as a green plant or extracts such as oils and tinctures and concentrates.

8. Further facts upon which the opinions in this report are based are set out in the Affidavit of David W. Pate attached to and incorporated herein as Schedule C, and in particular the facts set out in paragraphs 6 to 37 of that affidavit that was accepted in and used in the ***Smith*** litigation referenced above. I hereby depose to the same information contained therein as part of my evidence in this expert report and verily believe the contents of Schedule C continue to be true and accurate with the following minor amendments:

a. In paragraph 6 "...is a dieocius plant in the family Cannabacae" is amended to "...is a dioecious plant in the family Cannabaceae.";

b. In paragraph 9 "This is scientifically inaccurate as the glandular trichomes manufacture, contain and surround the resin itself" is amended to "This is not strictly accurate scientifically as the glandular cells reside as a rosette at the base of the spherical resin reservoir which contains and surrounds the secreted resin"; and,

c. In paragraph 37 "An added benefit is the elimination of psychoactive side effects" is amended to "An added benefit is the elimination of psychoactive side effects, depending possibly on dose concentration and application location."

(e) Summary of opinions.

9. In my expert opinion:

a. Restricting patients to consumption of dried marihuana only by way of restricting their possession to dried marihuana only and prohibiting the production of cannabis resin, or cannabis-based medicine serves no valid medical purpose;

a. Patients consuming medical cannabis benefit medically from having lawful access to a wide range of methods of ingestion;

b. The *Cannabis* plant is harvested for the medicinal resin compounds found inside the glandular trichomes of the plant.

c. There is no medical utility to the dried plant matter.

d. In essence, the plant is no more than a carrier for the glandular trichomes that are, themselves, a manufacturing site and reservoir for the resin that contains the cannabinoids and terpenes.

e. There are negative effects associated with ingesting whole *Cannabis* plant matter, either orally or by smoke inhalation, which can range from minor to serious.

f. Ingesting the resin by means of smoking would be less harmful to the patient than smoking the dried plant matter which bears the resin because: (a) less bulk would need to be consumed to achieve the desired therapeutic effect and, (b) the pyrolysis products of unwanted bulk plant materials would not be inhaled.

g. Ingesting the resin compounds in the form of baked goods is, for some conditions, significantly more effective than other routes of administration.

h. Topical application of the compounds in the resin by way of salves or oils produces less or no psychoactive side effects while also being more effective for the appropriate conditions.

i. There is no realistic possibility of overdose death from cannabis consumption by humans, whether the consumption is oral, inhaled or topical. The lethal dose of THC in monkeys (as biologically similar to human as possible) has been estimated at 9g/kg meaning that an 80 kg person would need to ingest 720 grams of pure THC at one time to reach this level. That is, for all practical purposes, not possible.

j. There exists no scientific basis, either botanical or pharmaceutical, to differentiate between the whole dried plants and the glandular trichomes or contained resin in a manner that permits patient access to the whole dried plant, but not the glandular trichomes or contained resin harvested from that very same plant.

10. To the extent necessary, I also adopt all opinions set out in Schedule C as my opinion in this expert report.

(*f*) in the case of a report that is provided in response to another expert's report, an indication of the points of agreement and of disagreement with the other expert's opinions.

11. Not applicable.

(*g*) Reasons for each opinion expressed.

12. The reasons for the opinions expressed are my own professional experience as a biologist, chemist and professional researching, studying and working with cannabis, cannabinoids and the therapeutic application thereof.

(*h*) Literature or other materials specifically relied on in support of the opinions.

13. Not applicable.

(*i*) Summary of the methodology used, including any examinations, tests or other investigations on which the expert has relied, including details of the qualifications of the person who carried them out, and whether a representative of any other party was present.

14. Not applicable.

(*j*) Caveats or qualifications necessary to render the report complete and accurate, including those relating to any insufficiency of data or research and an indication of any matters that fall outside the expert's field of expertise.

15. The study of cannabis and cannabinoids is ongoing and new information about the medicinal value of these compounds, predominately positive, is being discovered regularly. I am reasonably confident that the information known about cannabis and cannabinoids at the present time and which support my opinions will not change in a way that undermines the factual or scientific basis for my opinions.

(*k*) Particulars of any aspect of the expert's relationship with a party to the proceeding or the subject matter of his or her proposed evidence that might affect his or her duty to the Court.

16. I have no relationship to any party in these proceedings. Nor do I have a relationship with the subject matter that might affect my duty to the Court.

CONSULATE GENERAL OF CANADA - CONSULAT GÉNÉRAL DU CANADA SAN FRANCISCO

SWORN BEFORE ME at the City of San Francisco, the State of California, USA, this ____ day of October, 2014

David W. Pate

DAVID W. PATE

SWORN / DECLARED / AFFIRMED BEFORE ME IN THE CITY OF SAN FRANCISCO IN THE STATE OF CALIFORNIA, UNITED STATES OF AMERICA THIS 29 DAY OF October A.D. 2014

OCT 29 2014

A Commissioner for Taking Affidavits for the State of California, USA

CONSUL

Julienne Gray

SCHEDULE "A" TO EXPERT REPORT OF DAVID W. PATE

July 15, 2011

LIST OF PUBLICATIONS

I. ORIGINAL PUBLICATIONS: **1a. Primary Research**

1. Juntunen, Juha, Juhani Huuskonen, Krista Laine, Ricku Niemi, Hannu Taipale, Tapio Nevalainen, David W. Pate, and Tomi Järvinen. Anandamide prodrugs 1. Water-soluble phosphate esters of arachidonylethanolamide and *R*-methanandamide. *European Journal of Pharmaceutical Sciences* 19: 37-43 (2003).

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3. Laine, Krista, Tomi Järvinen, Juha Savinainen, Jarmo T. Laitinen, David W. Pate and Kristiina Järvinen. Effects of topical anandamide uptake inhibitors, AM404 and olvanil, on intraocular pressure in normotensive rabbits. *Pharmaceutical Research* 18 (4): 494-499 (2001).

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6. Pate, David W., Kristiina Järvinen, Arto Urtti, Vaidyanath Mahadevan, Tomi Järvinen. Effects of topical *alpha*-substituted anandamides on intraocular pressure in normotensive rabbits. *Pharmaceutical Research* 14: 1738-1743 (1997).

7. Callaway, J.C., T. Tennilä and D.W. Pate. Occurrence of "*omega*-3" stearidonic acid (*cis*-6,9,12,15-octadecatetraenoic acid) in hemp (*Cannabis sativa* L.) seed. *Journal of the International Hemp Association* 3 (2): 61-63 (1996).

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9. Pate, David W., Kristiina Järvinen, Arto Urtti, Pekka Jarho, Mette Fich, Vaidyanath Mahadevan and Tomi Järvinen. Effects of topical anandamides on intraocular pressure in normotensive rabbits. *Life Sciences* 58 (21): 1849-1860 (1996).

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12. Laster, B.H., S.B. Kahl, D.W. Pate, E.A. Popenoe and R.G. Fairchild. Biological efficacy of boronated low density lipoproteins (LDL) for neutron capture therapy (NCT) as measured in cell culture. *Cancer Research* 51: 4588-4593 (1991).

13. Cashman, John R., John Proudfoot, David W. Pate and Thomas Högberg. Stereoselective *N*-oxygenation of zimeldine and homozimeldine by the flavin-containing mono-oxygenase. *Drug Metabolism and Disposition* 16 (4): 616-622 (1988).

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16 Järvinen,Tomi, David W. Pate and Krista Laine. Cannabinoids in the treatment of glaucoma. *Pharmacology & Therapeutics* 95: 203-220 (2002).

17. Deferne, Jean-Luc and David W. Pate. Hemp seed oil: A source of valuable essential fatty acids. *Journal of the International Hemp Association* 3 (1): 1, 4-7 (1996).

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20. Clarke, Robert C. and David W. Pate. Medical marijuana. *Journal of the International Hemp Association* 1 (1): 9-12 (1994).

I. ORIGINAL PUBLICATIONS: 2. Patents and patent publications

1. Whittle, Brian; Geoffrey Guy, David Downs and David Pate. Processes and apparatus for extraction of active substances and enriched extracts from natural products. International Patent Cooperation Treaty Document WO 02/89945 (November 14, 2002); Australian Patent 2002255150 (January 22, 2009); Canadian Patent 2446195 (July 22, 2008); China Patent 1,524,007 (March 28, 2007); European Patent (Pending); Israel Patent 158709 (February 1, 2008); New Zealand Patent 529,360 (December 8, 2005); U.S. Patent 7,622,140 (November 24, 2009);

Great Britain Patent 2,376,464 (September 9, 2004); Great Britain Patent (divisional) 2,400,319 (March 31, 2005); Great Britain Patent (divisional) 2,400,320 (March 31, 2005).

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5. Pate, David W.; Tomi Järvinen, Kristiina Järvinen and Arto Urtti. Anandamide analogue compositions and method of treating intraocular pressure using same. International Patent Cooperation Treaty Document WO 96/01558 (January 25, 1996); U.S. Patent 5,977,180 (November 2, 1999); Canadian Patent 2,192,965 (December 4, 2007).

6. Pate, David W.; Tomi Järvinen, Kristiina Järvinen and Arto Urtti. Anandamides useful for the treatment of intraocular hypertension, ophthalmic compositions containing the same and methods of use of the same. U.S. Patent 5,631,297 (May 20, 1997).

I. ORIGINAL PUBLICATIONS: 3a. M.Sc. Thesis

The phytochemical ecology of *Cannabis.* University of Missouri-St. Louis. April, 1979.

3b. Ph.D. Dissertation

Anandamide structure-activity relationships and mechanisms of action on intraocular pressure in the normotensive rabbit model. Kuopio University Publications A. Pharmaceutical Sciences 37, 1999.

I. ORIGINAL PUBLICATIONS: 4. Proceedings Publications

1. Pate, David W. Development of *Cannabis*-based therapeutics. Prospects for Cannabinoid Drug Development, February 23-24, 1998. "Medical Use of Marijuana: Assessment of the Science Base" Workshop Series. Institute of Medicine, National Academy of Sciences, Washington, D.C., *Journal of the International Hemp Association* 5 (1): 36-39 (1998).

2. Pate, David W. Anandamides: Alternative cannabinoids for glaucoma? In: Biorohstoff Hanf (Bioresource Hemp), Proceedings of the Symposium, February 27-March 2, 1997, Frankfurt am Main, Germany, nova-Institute, Büro Hürth, Cologne, p. 684.

3. Pate, David W. Hemp seed: A valuable potential food crop. *In ibid.*, p. 484.

4. Jarho, P., A. Urtti, D.W. Pate, P. Suhonen and T. Järvinen. The effects of HP-*beta*-CD on aqueous solubility, stability and *in vitro* corneal penetration of anandamide. In Proceedings of the Eighth International Symposium on Cyclodextrons, Szejtli, J. and L. Szente, Eds., p. 395-398, Kluwer Academic Publishers, The Netherlands, 1996.

5. Pate, David W., Some national policies and practices on *Cannabis*. Hamppu Kulttuurikasvina-Hankasalmen hamppuseminaari (Proceedings from the Hankasalmi Hemp Seminar), J.C. Callaway and A. Hemmilä, Eds., Hankasalmen kunnan monistamo (Hankasalmi County Press), September 9, 1995, Hankasalmi, Finland.

6. Pate, David W., Products and potentials: *Cannabis* hemp in Finland. *In ibid.*

7. Pate, David W. *Cannabis*: The chemistry of its ecology and evolution. In: Biorohstoff Hanf (Bioresource Hemp), Proceedings of the Symposium, March 2-3, 1995, Frankfurt am Main, Germany, 2nd Edition, nova-Institute, Büro Hürth, Cologne, pps. 164-169.

8. Kahl, Stephen B., David W. Pate, Brenda H. Laster, Edward A. Popenoe and Ralph G. Fairchild. *In vitro* biological efficacy of boronated low density lipoproteins for NCT. *In* Progress in Neutron Capture Therapy for Cancer, Barry J. Allen, Douglas E. Moore and Baiba V. Harrington, Eds., pp. 365-68, Plenum Press, NY, 1992.

II. BOOK CHAPTERS

1. Callaway, J.C. and David W. Pate. Hemp Seed Oil. Chapter 6 *in* Gourmet Oils and Health-Promoting Specialty Oils, A. Kamal-Eldin and R. Moreau, Eds., pp. 185-213, American Oil Chemists Society Press, Champaign, IL, 2009.

2. Pate, David W. Taxonomy of the Cannabinoids. Part I, Chapter 2 *in* Cannabis and Cannabinoids: Pharmacology, Toxicology and Therapeutic Potential, F. Grotenhermen and E. Russo, Eds., pp. 15-26, Haworth Press, Binghamton, NY, 2002. (German version: *Cannabis* und Cannabinoide: Pharmakologie, Toxikologie und therapeutisches Potenzial, F. Grotenhermen, Hrsg., Verlag Hans Huber, Bern, Schweis, 2001.)

3. Pate, David W. Glaucoma. Part II, Chapter 19 in *ibid*, pp. 215-224.

4. Pate, David W. Anandamides: Potential Glaucoma Medicine? Part VI, Chapter 34 in *ibid*, pp. 371-380.

5. Pate, David W. The Phytochemistry of *Cannabis*: Its Ecological and Evolutionary Implications. Chapter 2 *in* Advances in Hemp Research, P. Ranalli, Ed., pp. 21-42, Haworth Press, Binghamton, NY, 1999.

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7. Clarke, Robert C. and David W. Pate. The Economic and Environmental Value of *Cannabis*. Chapter 17 *in* *Cannabis* in Medical Practice M.L. Mathre, Ed., pp. 192-211, McFarland and Company, Jefferson, NC, 1997.

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III. BOOK REVIEWS

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2. Tomi Järvinen, Juha Juntunen, Juhani Huuskonen, Tapio Nevalainen, David W. Pate and Krista Laine. Water-soluble anandamide prodrugs. International Cannabinoid Research Society Meeting, June 28-30, 2001, Madrid, Spain, Symposium Program and Abstracts.

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Society Meeting, June 28-30, 2001, Madrid, Spain, Symposium Program and Abstracts.

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5. Laine, K., Järvinen, K., Pate, D.W., Urtti, A., Järvinen, T. Effects of phenylmethyl sulfonyl fluoride on the intraocular pressure profile of anandamide. Arch Pharm 333: S1,7 (2001).

6. Kristiina Järvinen, Krista Laine, David W. Pate, Arto Urtti and Tomi Järvinen. The effect of topical anandamide on intraocular pressure, with and without a topical transport inhibitor. Proceedings of the XIV International Congress of Eye Research. October 15-20, 2000, Santa Fe, New Mexico, USA, p. S.77.

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9. Pate, David W. *Cannabis* and human cannabinoids: Their potentials as medicines. The First National Clinical Conference on *Cannabis* Therapeutics, Medical Marijuana: Science-Based Clinical Applications. April 6-8, 2000, University of Iowa, Iowa City, Iowa, USA.

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11. Pate, David W. Development of *Cannabis*-based therapeutics. Pharmaciae Sacrum Symposium, *Cannabis:* het groene medicijn? De medicinale toepassingen van *Cannabis*, Dec. 9-11, 1998. University of Gronigen, The Netherlands, Abstracts booklet, pp. 31-32.

12. Pate, David W., Kristiina Järvinen, Arto Urtti, Vaidyanath Mahadevan and Tomi Järvinen. Effect of CB_1 receptor antagonist on cannabinoid-induced ocular hypotension in rabbits. International Cannabinoid Research Society Meeting, July 23-25, 1998, La Grand Motte, France. Symposium Program and Abstracts, p. 74.

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15. Jarho, P., D.W. Pate, P. Suhonen, A. Urtti and T. Järvinen. The Effects of HP-*beta*-CD on aqueous solubility, stability and *in vitro* corneal penetration of anandamide. The 8th International Cyclodextrin Symposium, March 30-April 2, 1996, Budapest, Hungary. Symposium Program and Abstracts, Section 3, p.14.

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18. Urtti, A., D. Pate, K. Järvinen, P. Jarho, T. Järvinen. Ophthalmic arachidonylethanolamide decreases intraocular pressure in rabbits. Association for Research in Vision and Ophthalmology Annual Meeting, May 14-19, 1995, Fort Lauderdale, Florida. Investigative Ophthalmology & Visual Science, Proceedings Abstracts 36 (4): S720.

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21. Cashman, John R., John Proudfoot, David W. Pate and Thomas Högberg. Unusual rearrangements in the oxidative metabolism of tertiary amines. Pacific Conference on Chemistry and Spectroscopy, October 26-28, 1988, San Francisco, California.

V. POPULAR MEDIA

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3. Interviewed by Lisa Nainggolan in "Marijuana-a missed market opportunity?" *Scrip (World Pharmaceutical News)*, pps. 22-26. December, 1997.

4. Interview of Dr. Yukihiro Shoyama. *Journal of the International Hemp Association* 4 (2): 95-96 (1997).

5. Interview of Dr. Rudolf Brenneisen. *Journal of the International Hemp Association* 4 (1): 22-25 (1997).

6. Appearance on the "Whatever Happened to Hemp" episode produced by Kate Howell for the "Omnibus" current-affairs series of BBC Radio, London, England. Presented by David Lodge on May 3-8, 1997.

7. Interview of Dr. Mahmoud A. ElSohly. *Journal of the International Hemp Association* 3 (1): 43-44 (1996).

8. Appearance on the "Hemp: Raw Material of the Future" program. Produced and presented by Helen Barrington for Radio Nederlands, Amsterdam, The Netherlands, February 28, 1996.

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10. Interview of Dr. Raphael Mechoulam. *Journal of the International Hemp Association* 1(1): 9-12 (1994).

/ DECLARED / AFFIRMED BEFORE ME IN THE CITY OF SAN
SCO IN THE STATE OF CALIFORNIA, UNITED STATES OF AMERICA
29 DAY OF October
2014

CONSULATE GENERAL OF CANADA - CONSULATE GENERAL DU CANADA SAN FRANCISCO

OCT 29 2014

CONSUL

Julienne Gray

David W. Pate

PAGES 14 THROUGH 16 HAVE BEEN REMOVED FOR PRIVACY REASONS.

SCHEDULE "C" TO EXPERT REPORT OF DAVID W. PATE

File No.149345-2
Victoria Registry

IN THE SUPREME COURT OF BRITISH COLUMBIA

REGINA

v.

OWEN EDWARD SMITH

EXPERT REPORT OF DR. DAVID W. PATE

Kirk Tousaw
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Law Office of Kirk Tousaw
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Counsel for Accused

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Vancouver, BC V6Z 2S0

1. My name is Dr. David W. Pate and I make this expert report on the basis of my own personal knowledge, study and experience.

2. I hold two advanced degrees; a Master of Science in Biology and a Doctor of Philosophy in Pharmaceutical Chemistry. My current professional emphasis is the study of cannabis products, including cannabinoids and other constituent components of the *Cannabis* plant, both from a botanical and pharmaceutical perspective.

3. Attached to and made part of this report as Exhibit A is my curriculum vitae.

4. The emphasis of my professional work is the medicinal aspects of phytocannabinoids (cannabinoids produced in the *Cannabis* plant) and endocannabinoids (cannabinoids endogenous to the human body).

5. Based on my professional expertise, knowledge and study, I am aware of the following facts and hold the following opinions.

6. The *Cannabis* plant (producing the crude drug, marijuana) is a dieocius plant in the family Cannabacae.

7. The female *Cannabis* plant produces flowers, referred to in slang vernacular as "buds", which themselves are composed of varying parts.

8. These parts include the pistil, bracteole (i.e., perigonal bract), and subtending leaflet.

9. The primary therapeutically active compounds found in *Cannabis* are secreted by the plant in the glandular trichomes that are found in their highest population concentration on the bracteole abaxial (i.e., outer) surface of unfertilized female flowers. These glandular trichomes are often referred to as "resin glands". This is scientifically inaccurate as the glandular trichomes manufacture, contain and surround the resin itself.

10. The two primary therapeutically active compounds found in the resin are tetrahydrocannabinol (THC) and cannabidiol (CBD), plus associated minor cannabinoids and terpenes. .

11. Within each category of compound there are several to many particular chemical species.

12. For example, there are at least dozens of terpenes and several cannabinoids found in the resin contained within the glandular trichomes of the *Cannabis* plant.

13. Cannabinoids are not found in any other plant species, although the human body produces fatty acid functional analogues (i.e., endocannabinoids) that also fit into cannabinoid receptors in the human body (e.g., brain). Terpenes are found broadly in the plant kingdom, including in mints, fruits, spices and flowers.

14. The medical effects of cannabinoids have been well documented and there is no reasonable dispute, in my opinion, that these compounds

are therapeutically active in humans. Terpenes may very well augment these effects.

15. *Cannabis* has a number of phenotypes, commonly referred to as strains. Various strains are created by breeding different varieties of the plant with each other. Different strains are reputed to produce differing effects on the patient, depending on the individual and condition..

16. A reason for the differing effects, which include varying levels of efficacy for a variety of medical symptoms and conditions, is probably due to varying amounts and ratios of the therapeutically active compounds.

17. It has been suggested, and in my opinion it is correct, that the various compounds can produce synergistic effects and that any one compound, in isolation, may not provide the full spectrum of medical benefits sought by the patient.

18. This is because the effects, both positive and negative, of the primary active ingredients may be enhanced or mitigated by secondary compounds. In this regard I attach and incorporate into my opinion the following studies: "Cannabis and Cannabis Extracts: Greater Than the Sum of Their Parts?" McPartland, John M., and Ethan B. Russo. Co-published simultaneously in Journal of Cannabis Therapeutics (The Haworth Integrative Healing Press, an

imprint of The Haworth Press, Inc.) Vol. 1, No. 3/4, 2001, pp. 103-132; and: Cannabis Therapeutics in HIV/AIDS (ed: Ethan Russo), and "Taming THC: Potential Cannabis Synergy and Phtyocannabinoid-Terpenoid Entrourage Effects." Ethan B. Russo, British Journal of Pharmacology (2011) 163 pages 1344-1364.

19. The glandular trichomes containing these chemical compounds can be isolated from the female flowers, thus eliminating most of the plant matter in the final product.

20. There are a variety of methods for isolating the glandular trichomes, including the use of micro-pore screens upon which dried flowers are agitated, causing the glandular trichomes to fall off and pass through the screen; and immersion of the plant matter in cold water followed by straining the water through fine mesh to capture the glandular trichomes. These processes result in removal of the glandular trichomes from most other plant matter, but leave the resin housed within the glandular trichomes.

21. Alternatively, it is possible to directly extract the resin contained within the glandular trichomes by rubbing the flowers by hand then scraping the sticky resin from the hands; by soaking the whole plant matter (or isolated trichomes) in fat (typically food-grade oils or butter) or alcohol and then straining out the plant debris (the glandular trichome contents are fat and/or alcohol soluble, but are

not water soluble); and with the use of petrochemical solvents (e.g., petroleum ether) that are then evaporated. These are extraction processes that result in the separation of the active compounds, such as THC, CBD and terpenes, from the plant matter, including from the glandular trichomes.

22. The resin-containing glandular trichomes remaining after the processes referred to in paragraph 20 are often referred to as "hash" (dry sieved) or "bubblehash" (wet sieved) when found in lump or brick form due to compression, or often referred to (erroneously) as "kif" or "pollen" when found in uncompressed powder form. The material remaining after cannabis extraction into fats is often called "cannabis cooking oil" or "cannabis butter" and the extract produced by solvent extraction is often called "hash oil."

23. All of these processes are designed to capture the glandular trichomes and/or their contents (i.e., the therapeutically active resin), while removing most or all of the plant matter and the various by-products that remain in the plant matter following harvest.

24. The plant matter itself is not a desired therapeutic component, except as a vehicle for carrying the resin prior to, and during, the act of pyrolysis and smoke inhalation.

25. This is because plant matter can contain a variety of harmful or unwanted compounds, which may include heavy metals, fertilizer residue, pesticides, molds and insect remnants.

26. In addition, plant matter is composed of non-digestible cellulose which, while not harmful, may be contra-indicated for persons with gastro-intestinal conditions.

27. Moreover, this plant matter contains silicified non-glandular trichomes that are not digestible and have no therapeutic value, but which, due to their micro-abrasive potential, may be contra-indicated for persons with gastro-intestinal sensitivities.

28. The glandular trichomes themselves itself are not a desired therapeutic component, except as a vehicle for carrying the resin prior to, and during, the act of extraction into fat, alcohol, solvents or fatty bodily fluids.

29. There are multiple ways to ingest the active compounds in cannabis. These include:

    a. Inhalation: This is either a high-temperature process by which the plant matter, and/or the glandular trichomes themselves, are heated to the point of ignition and the smoke is inhaled (using a cigarette/"joint" or a pipe) or a low-temperature process by which the plant matter is heated only to the point at which

the active ingredients vaporize and become an airborne aerosol which is then inhaled (commonly referred to as "vaporization.")

b. Oral ingestion: This is a process by which the active ingredients are ingested by eating or drinking. Typically, food products are prepared using cannabis-infused oil or butter. Essentially any food product that is made with fat and cannabis will be infused with cannabis resin extracted *in situ*. Common forms of these baked goods are cookies and brownies. In addition, cannabis capsules can be produced that contain an extract of the glandular trichomes which are swallowed in the same manner as over-the-counter remedies, prescription pharmaceuticals or natural health products.

c. Topicals: Oil-based preparations into which the resin has been extracted are either applied directly to the skin or are dispersed from patches which are applied to the skin.

d. Trans-mucosal: This method of ingestion is typically an alcohol extract of the resin that is sprayed under the tongue.

30. The modes of ingestion set out above carry with them different risks and benefits. Specifically, for purposes of this opinion, I focus on the relative benefits of oral ingestion or topical administration *vs.* the method of inhalation.

31. A primary benefit of orally ingesting cannabis-based medicines arises for people suffering from gastro-intestinal conditions such as Crohn's Disease or Irritable Bowel Syndrome. For these individuals, oral ingestion allows for the application of therapeutic compounds directly to the site of pathogenicity. Good pharmaceutical practice dictates the use of a minimum effective drug amount and a treatment as close to the site of pathogenicity as possible. This provides the benefit of direct therapeutic action that can be more effective and require lesser dosages, thus ameliorating potential unwanted side effects.

32. Another benefit of oral ingestion is that it produces longer lasting therapeutic effects than inhalation. Inhalation tends to produces spikes in the systemic load of the active compounds which quickly fall to low levels, resulting in elevating patient blood levels with more of the active compounds than necessary while making the effect of these compounds more transient. Oral ingestion, by contrast, provides a plateau of longer and more stable systemic load of the therapeutic agents. This eliminates the need to repeatedly ingest the medicine at short intervals in order to achieve continuous therapeutic benefits. It also allows for the treatment to continue during sleeping hours. This latter aspect is particularly of benefit to glaucoma patients.

33. Another benefit of oral ingestion is the elimination of any damage that may be caused by smoking the dried flowers, a practice discouraged within contemporary medicine. Oral ingestion also excludes possible damage that could be caused by the inhalation of unwanted substances found in or on the plant matter.

34. For certain chronic conditions, oral ingestion is often the more effective mode of ingestion for the reasons set out above.

35. For acute (and particularly crisis) conditions, inhalation may be preferred because of the rapid onset of symptom relief coupled with the transient nature of the condition itself.

36. By way of example, inhalation would be preferable to oral ingestion to treat the acute pain and other symptoms associated with migraine headaches.

37. For many of the same reasons that oral ingestion is preferable to inhalation, topical administration is preferable for certain conditions such as inflammatory skin conditions or some forms of chronic pain, particularly of the joints. The onset time of topical administration is quicker than oral administration, the drug is better targeted to the site of action, and a full systemic treatment to obtain a localized therapeutic benefit is not administered. An added benefit is the elimination of psychoactive side-effects.

38. In addition to the foregoing, I hold the following opinions:

a. The *Cannabis* plant is harvested for the medicinal resin compounds found inside the glandular trichomes of the plant.

b. There is no medical utility to the dried plant matter.

c. In essence, the plant is no more than a carrier for the glandular trichomes which are, themselves, a manufacturing site and reservoir for the resin which contains the cannabinoids and terpenes.

d. There are negative effects associated with ingesting whole *Cannabis* plant matter, either orally or by smoke inhalation, which can range from minor to serious.

e. Ingesting the resin by means of smoking would be less harmful to the patient than smoking the dried plant matter which bears the resin because: (a) less would need to be consumed to achieve the desired therapeutic effect and, (b) the pyrolysis products of unwanted bulk plant materials would not be inhaled.

f. Ingesting the resin compounds in the form of baked goods is, for some conditions, significantly more effective than other routes of administration.

g. Topical application of the compounds in the resin by way of salves or oils produces no psychoactive side effects while also being more effective for the appropriate conditions.

h. There exists no scientific basis, either botanical or pharmaceutical, to differentiate between the whole dried plants and the glandular trichomes or contained resin in a manner that permits patient access to the whole dried plant, but not the glandular trichomes or contained resin harvested from that very same plant.

Executed this 6th day of January, 2012 in Berkeley, State of California, United States of America.

David W. Pate

David W. Pate PhD, MSc

TO BE SWORN BEFORE FILING:

SWORN BEFORE ME at the City of Victoria)
in the Province of British Columbia,)
this _____ day of _____)
2011)
)
)
_____)
A Commissioner for Taking Affidavits in)
and for the Province of British Columbia)

David W. Pate

David W. Pate PhD, MSc

SWORN / DECLARED / AFFIRMED BEFORE ME IN THE CITY OF SAN FRANCISCO IN THE STATE OF CALIFORNIA, UNITED STATES OF AMERICA
THIS 29 DAY OF October
A.D. 2014

OCT 29 2014

CONSUL

CONSULATE GENERAL OF CANADA - CONSULAT GÉNÉRAL DU CANADA - SAN FRANCISCO

Julienne Gray