Oregon Medical Marijuana Act
Debilitating Medical Conditions Advisory Panel

Psychotic Disorders Research Review

NOTE: This research review evaluates two petitioners' written and oral comments. The two petitions are for Schizophrenia and Schizoaffective Disorder. The literature base relating to cannabis and Schizophrenia is large and consists mostly of research describing the various negative associations between cannabis and psychosis. As much of this research as possible has been reviewed considering panel time constraints. Expert testimony is included here due to the emphasis on psychotic disorders, which was relayed to the panel. It will not be included in other reviews. As well, research describing dependence issues associated with cannabis has been included here unless there is direct association with another psychiatric disorder.

1. CONSIDERATION OF EVIDENCE
Description of Evidence Considered:

1**. A retrospective study of symptom patterns of cannabis-induced psychosis [Imade et. al., Acta Psychiatr Scand 1991: 83: 134-136.]**
Medical records and case notes of 272 psychotic patients attempted to discover "whether there are any similarities between cannabis psychosis on the one hand and schizophrenia and mania on the other..." The researchers concluded, "It was not possible to demonstrate a consistent pattern of symptoms typical of cannabis psychosis."

GRADE: Good evidence that cannabis is not categorically contraindicated in psychosis, i.e. causes psychotic breaks.

2. **Letter to the editor, Journal of Clinical Psychiatry: Anti psychotic Effect of Cannabidiol [56:10, October 1995.]**
Single-case experimental study of cannabidiol (CBD) administration for 26 consecutive days to an acutely psychotic woman showed documented improvement as measured by a decrease in psychotic symptoms on the Brief Psychiatric Rating Scale (BPRS) as well as a decrease in Haldol administration.

GRADE: Good experimental basis for considering that cannabidiol may have anti-psychotic effects although study sample is small.

3**. Towards a Cannabinoid Hypothesis of Schizophrenia: Cognitive Impairments Due to Dysregulation of the Endogenous Cannabinoid System**

[Emrich et. al. Pharmacology Biochemistry and Behavior. Vol. 56, No. 4, pp803-807, 1997.]
Discusses neurochemistry of schizophrenia, historical overview of research into cannabinoid receptor system in humans. Presents results of experimental study of 40 subjects (13 schizophrenia patients) comparing visual projections before and after administration of cannabis resin. Cannabis resin was not administered to psychotic patients. This research concluded, "A subgroup of schizophrenic syndromes may pathogenetically be related to a functional disturbance of the endogenous cannabinoid/anandamide system."

GRADE: Good evidence that humans' endogenous cannabinoid receptor system ideally functions as a component of psychological homeostasis.

4. **Elevated endogenous cannabinoids in schizophrenia [Leweke et.al. Clinical Neuroscience; Vol. 10, No. 8, June 1999, pp1665-1669.]**
Excellent discussion of brain neurochemistry and research study where cerebrospinal fluid (CSF) is examined in 10 schizophrenic patients and 11 non-schizophrenic patients. Analysis showed that endogenous cannabinoid concentrations were significantly higher in schizophrenic patients than in controls. This lends support to a hypothesis that schizophrenia may in part be due to chemical signaling malfunctions involving the endogenous cannabinoid signaling system.

GRADE: Fair evidence that self-medicating behavior of schizophrenics may be an attempt to reestablish psychological homeostasis. Good evidence that receptor signaling malfunctions of the endogenous cannabinoid system may contribute to schizophrenia.

5. **Mesolimbic dopaminergic decline after cannabinoid withdrawal [Diana et. al., Proceedings of the National Acadamy of Science, Vol. 95, 1998, pp 10269-10273.]**
Research study where rats were chronically treated with THC followed by administration of cannabinoid antagonist SR 141716A. Administration of cannabinoid antagonist precipitated intense withdrawal symptoms. Abrupt termination of THC failed to produce a withdrawal syndrome. Results indicate that withdrawal from chronic cannabinoid administration is associated with reduced dopaminergic transmission in the limbic system. i.e. possible anti-psychotic effect due to increased dopamine.

GRADE: Good evidence that cannabinoids may modulate dopamine levels. Fair evidence that cannabinoids may act as an anti psychotic through D-2 receptor blockade.

6. **Toward a rational pharmacotherapy of comorbid substance abuse in schizophrenic patients [Krystal et. al. Schizophrenia research 35, 1999, s35-s39.]**

Review of factors contributing to comorbid substance use in schizophrenic patients. ETOH most common drug used followed by cannabis. The article compares "self-medication hypothesis" with "comorbid addiction vulnerability" hypothesis. Use of non-prescribed substances may increase extrapyramidal symptoms (EPS) or decrease them. Article indicates an association between cannabis use and psychotic symptoms in vulnerable populations.

GRADE: Good evidence that cannabis may contribute to worsening of psychotic symptoms in some patients (those using neuroleptics).

7. **DSM-4 Diagnoses associated with class of substances [Diagnostic and Statistical Manual of Mental Disorders, 4th ed., pp 177.]**
Indicates that cannabis use is associated with psychotic disorders.

GRADE: Excellent indication that there may be a diagnostic association between cannabis use and psychosis.

8. **Dual diagnosis of substance abuse in schizophrenia; prevalence and impact on outcomes [Dixon, et. al., Schizophrenia Research 35, 1999, s93-s100.]**
Discusses outcomes of psychotic disorders as they relate to cannabis use and states: "Comorbid substance disorders are associated with a variety of poorer outcomes, including increased psychotic symptoms..."

GRADE: Fair survey of evidence indicating that cannabis use may worsen the course of psychotic illness. Limitation is the continuous linkage of cannabis and alcohol with little consideration of neurochemical differences between the two.

9. **Effects of Clozapine on Substance Use in Patients With Schizophrenia and Schizoaffective Disorder: A Retrospective Study [Zimmet, et. al., Journal of Clinical Psychopharmacology, Vol. 20, No. 1, 2000, pp94-98.]**
"Substance use disorders, particularly those involving alcohol, marijuana, and cocaine, are highly prevalent among patients with schizophrenia and contribute markedly to its overall morbidity." Clozapine use is correlated with a decrease in the use of these substances.

GRADE: Poor evidence that cannabis use contributes to substance use disorders- only that there is a decrease in cannabis use by those on Clozeril therapy. No discussion regarding the relative risks of clozeril therapy- i.e. potentially lethal neutropenia.

10. **Cannabis and Schizophrenia: A Longitudinal Study of Swedish Conscripts [Andreasson et. al., The Lancet, 1987, pp 1483-1486.]**
Fifteen year study of 45,000 Swedish conscripts concluded that heavy cannabis use (>50 times) could be an independent risk factor for development of schizophrenia but admitted that cannabis use still accounts for a minority of

cases of schizophrenia- in other words, there are other more prevalent causes of schizophrenia.

GRADE: Good evidence that there is an association between cannabis use and psychosis however those using cannabis 2-4 times showed no increase above controls (non-users). Limitation is reliability of self-reports of substance use which may indicate an underreport of actual cases.

11. **Cannabis Abuse and the Course of Recent-Onset Schizophrenic Disorders [Linszen, et. al., Archives of general Psychiatry, Vol 51(4), 1994, pp 273-279.]**
A prospective cohort study over a year using monthly BPRS assessments concluded that: "Significantly more and earlier psychotic relapses occurred in the cannabis-abusing group. Interestingly, in "the mild cannabis-abusing group, symptoms of anxiety and depression tended to be less present than in the non-abusing and heavy cannabis-abusing group."

GRADE: Good evidence that moderate and heavy use may worsen positive symptoms of schizophrenia. Fair evidence that low-dose use may relieve negative symptoms.

12. **American Psychiatric Association Policy on the medical Use of Marijuana [1997.]**
Recommends further research, and compassion for the ill ; recommends FDA drug-approval process be followed

GRADE: Inconclusive

13. **Marijuana and Medicine:Assessing the Science Base; Institute of Medicine, 1999, pp105-109.]**
Research review states: "The association between marijuana and schizophrenia is not well understood." Also describes that schizophrenics prefer marijuana to cocaine for unknown reasons but "this raises the possibility that schizophrenics might obtain some symptomatic relief from moderate marijuana use" , "but compared with the general population, people with schizophrenia....are likely to be at greater risk for adverse psychiatric effects."

GRADE: Good evidence that cannabis may be beneficial in a sub-population of schizophrenics and good evidence that cannabis may be associated with greater morbidity in many schizophrenics.

14. **Ovid Technologies, Inc. Email Service Literature Search- 11 pages of research abstracts**
NOTE: The following abstracts are basic descriptions of these studies. I have not read these individual studies and therefore am constrained as to how much weight I can reliably assign to them.

A. Alcohol Dependence and Hospitalization in Schizophrenia [Gerding, et.al., Schizophrenia Research, 38(1): 1999, pp71-75.]
"Marijuana or cocaine dependence was slightly but not more statistically more common among admitted patients" . . . [than alcohol dependence.]

GRADE: Poor evidence that cannabis is contraindicated in psychiatric disorders. Little relevance to this inquiry

B. Carbamazapine as an adjunct in the treatment of schizophrenia-like psychosis related to cannabis abuse. [Leweke, et. al. International Clinical Psychopharmacology, 14(1): 1999, pp 37-39.]
Two patients were successfully treated for cannabis- related schizophrenia-like symptoms with carbamazapine and showed marked improvement.

GRADE: Inconclusive: Limited relevance to inquiry although indicates that there may be an association between heavy prolonged cannabis use and "schizophrenia-like psychosis."

C. Cannabinoid/anandamide system and schizophrenia: is there evidence for association? [Schneider, et.al. Pharmacopsychiatry, 31, Suppl 2: , 1998, pp 110-113.]
[SEE #3]

D. Effect of patient and family insight on compliance of schizophrenic patients [Smith, et. al., Journal of Clinical Pharmacology, 37(2),:1997, pp147-54.]
Marijuana use was associated with non-compliance of medication regimens of people who had greater awareness and insight into the importance of their treatments.

GRADE: Inconclusive. No information as to why persons with higher medication/treatment insight would use cannabis against medical advise. The issue was not explored in the abstract.

E. Chronic substance-induced psychotic disorders: state of the literature [Boutros, et. al., Journal of neuropsychiatry & Clinical Neurosciences. 8(3): 1996, pp262-9.]
Literature search concludes that a number of drugs of abuse in different classes...can cause or increase the susceptibility for a state of chronic psychosis.

GRADE: Fair evidence that there is a worsening of psychosis among many substance-using schizophrenics.

F. Substance use among schizophrenic outpatients; prevalence, course and relation to functional status. [Chouljian, et. al., Annals of Clinical Psychiatry. 7(1) 1995, pp 19-24.]
A retrospective study of 100 schizophrenics over 18 months . . .. Problem substance use (abuse and dependence) was not associated with differential attrition from out patient treatment.

GRADE: Fair to good evidence that substance use is not a causal factor with treatment non-compliance though the study did point out that the detrimental effect of substance use appeared to increase over time.

G. Substance use among the mentally ill: prevalence, reasons for use, and effects on illness. [Warner, et. al., American Journal of Orthopsychiatry, 64(1): 1994, pp30-9.]
A random sample of community-based mentally ill patients showed that "there was no association between heavy substance use and elevated psychopathology, hospitalization or medication non-compliance." "Hospital admissions and some symptoms were less prevalent among users preferring marijuana."

GRADE: Good evidence that some schizophrenics may be managing symptoms using cannabis without having a detrimental effect on course of disease or management.

H. Psychiatric symptoms in cannabis users. [Thomas, British Journal of Psychiatry, 163: 1993, pp141-9.]
Unknown research format concludes: "The evidence that cannabis has a causative role in chronic psychotic or affective disorders is not convincing, although the drug may modify the course of an already established illness."

GRADE: Fair evidence that cannabis use is not predictive of "cannabis psychosis."

I. Cannabis and schizophrenia: a longitudinal study of cases treated in Stockholm County[Allebeck, et. al. Acta Psychiatrica Scandinavica, 88(1): 1993, pp 21-4.]
A study of 229 medical records showed that 69% "had a record of heavy cannabis abuse at least 1 year before onset of...symptoms."

GRADE: Good evidence that cannabis use may be a risk factor for schizophrenia.

J. The human toxicity of marijuana [Nahas, et. al., Medical Journal of Australia, 156(7) 1992, pp495-7.]
Describes many harmful effects of marijuana including mutagenic harm, neurobehavioral toxicity, gonadal harm, fetotoxicity, airway obstruction signs,

squamous metaplasia, impairment of memory, impairment of psychomotor performance, six-fold increase in schizophrenia and cancer of the mouth.

GRADE: Inconclusive and limited evidence that cannabis causes schizophrenia Good evidence that marijuana can be harmful.

K. A history of substance abuse complicates remission from acute mania in bipolar disorder [Goldberg, et. al., Journal of Clinical Psychiatry, 60(11) : 1999, pp. 733-40.]
Retrospective review of hospital records concluded that: "...bipolar patients with past substance abuse have poorer naturalistic treatment outcomes, but may show a better response to anticonvulsant mood stabilizers than lithium."

GRADE: Good evidence that comorbid substance use increases morbidity.

L. Treatment of comorbid affective and substance use disorders. Therapeutic potential of anti-convulsants [Donovan, et.al., American Journal on Addicitions, 7(3), 1998, pp. 210-220.]
"The authors examine the use of anticonvulsant/mood stabilizers to treat patients with substance use disorders." They hypothesize that a new syndrome called "Explosive Mood Disorder" is connected to marijuana use.

GRADE: Poor evidence that cannabis use is contraindicated in psychosis and questionable relevance to the inquiry.

M. The use of cannabis as a mood stabilizer in bipolar disorder; anecdotal evidence and the need for clinical research. [Grinspoon, et. al., Journal of Psychoactive Drugs, 30(2), 1998, pp. 171-7.]
Case histories indicating a number of patients find cannabis useful in treatment of their bipolar disorder. "The potential for cannabis as a treatment for bipolar disorder unfortunately can not be fully explored in the present circumstances."

GRADE: Good evidence that a sub population of bipolar patients effectively use cannabis to treat both mania and depression.

N. Do patients use marijuana as an antidepressant? [Gruber, et. al., Depression, 4(2): 1996, pp. 77-80.]
The authors "present 5 cases in which the evidence seems particularly clear that marijuana produced a direct antidepressant effect. If true, these observations argue that many patients may use marijuana to "self-treat" depressive symptoms."

GRADE: Good case study evidence that some patients use cannabis to treat depressive symptoms.

O. Cannabis psychosis following bhang ingestion [Chaudry, et.al., British Journal of Addicition, 86(9): 1991, pp. 1075-81.]

A “preliminary investigation” concluded that: “ The presenting symptoms of bhang-induced psychosis are consistent with a brief mania-like disorder with paranoid psychotic features and cognitive dysfunction.”

GRADE: Fair evidence that ingestion of bhang among psychotic people could precipitate psychosis-like behaviors.

P: Chronic PTSD in Vietnam combat veterans: course of illness and substance abuse. [Bremner, et. al., American Journal of Psychiatry, 153(3): 1996, pp. 369-75.]
Sixty-one combat veterans were interviewed. Conclusion: “These findings suggest that symptoms of PTSD begin soon after exposure to trauma...that the natural course of alcohol and substance abuse parallels that of PTSD, and that specific substances have specific effects on PTSD symptoms.”

GRADE: Insufficient information to determine whether cannabis use is a treatment of consequence for combat veterans suffering from PTSD.

15. **Cannabis Abuse and the Course of Recent-Onset Schizophrenic Disorders. [Linzen, et. al., Archives of General Psychiatry, Vol. 51(4), 1994, pp. 273-279.]**
A retrospective cohort study of 106 people using monthly BPRS assessments concluded: “Cannabis abuse and particularly heavy abuse can be considered a stressor eliciting relapse in patients with schizophrenia and related disorders and possibly a premorbid precipitant.”

GRADE: Good evidence that heavy cannabis use (> once per day) may increase a schizophrenic patients’ relapse rate. Fair evidence that it may be a causative factor in the onset of schizophrenic symptoms

16. **Cannabis, A breed apart [Chapter from Handbook of psychotropic herbs. [Russo, Haworth Press, 2000.]**
A survey of the history and uses of cannabis states: “ CBD also improved symptoms of psychosis in one patient, without induction of Parkinsonian symptoms, as commonly occurs with standard anti-psychotic agents.”

GRADE: Fair evidence that a small number of psychotic people may benefit from using cannabis.

17. **Literature search on Ovid Technologies Inc. Email Service- 2 citations**

A. **Schizophrenia in users and nonusers of cannabis. A longitudinal study in Stockholm County. [Andreasson, Acta Psychiatrica Scandinavica, 79(5): 1989, pp. 505-10.]**
A small case study evaluating the symptom patterns in cannabis users concluded that:

"Although the number of cases... was small, the findings support the hypothesis that cannabis does play an aetiological role in schizophrenia."

GRADE: Good evidence that cannabis may contribute to the onset of schizophrenic symptoms.

B. **Cannabis and schizophrenia, a longitudinal study of Swedish conscripts [Andreasson, et.al., Lancet, 2(8574): 1987, pp. 1483-6.]**
[see # 10]

18. **Substance use among the mentally ill: Prevalence, Reasons for Use, and Effects on Illness [Warner, et. al., American Journal of Orthopsychiatry, 64(1): 1994, pp. 30-39.]**
Literature review and interview of 55 subjects conducted by an independent researcher. Researchers state: " The two-year admission rate was significantly lower among those whose drug of preference was marijuana ...compared to the remainder of the sample, including non-users." "...most subjects who preferred marijuana and reported anxiety, depression, insomnia, or physical discomfort...perceived the substance as relieving those symptoms."

GRADE: Good evidence that a significant number of patients in this study used cannabis to decrease agitation and that this use did not contribute to increased hospitalization rates.

19. **Psychiatric Illness and Comorbidity Among Adult Male Jail Detainees in Drug treatment. [Swartz, et. al., Psychiatric Services, Vol. 50, No. 12: 1999, pp. 1628-1630.]**
Two-hundred and four pretrial detainees were evaluated and interviewed. The results indicate:

" Detainees with comorbid disorders were more likely than others to have more than one co-occurring psychiatric disorder...and to be dependent on alcohol, marijuana, or PCP.

GRADE: Poor evidence that marijuana is contraindicated in schizophrenic patients and minimal relevance to the inquiry, although it does affirm that many offenders are likely to have serious comorbid conditions.

20. **Adverse effects of cannabis [Hall, et. al., Lancet, 352: 1998, pp. 1611-1615.]**
A review of the health effects of cannabis that states: "There is some evidence that heavy use has adverse effects on family formation, mental health, and involvement in drug-related crime."

GRADE: Poor evidence that cannabis is contraindicated in schizophrenia and of minimal relevance to the inquiry.

21. **Severe mental illness and substance misuse [Weaver, et. al., BMJ 318: 1999, pp. 137-8.]**
Editorial in the BMJ which emphasizes that "...use as well as dependency may be problematic among people with psychosis. Whether there is any causal relationship between substance misuse and psychotic disorders remains controversial."

GRADE: Poor evidence that cannabis is contraindicated in psychosis and of minimal relevance to the inquiry.

22. **Efforts begin to expand pot law [Cain, Klamath Co. Herald News: Feb. 9, 2000 editorial.]**

Editorial in Klamath Falls Herald and News describes task force meeting to discuss addition of new diseases to be covered under the OMMA.

GRADE: No relevance to inquiry

23. **Leave pot law alone [No author listed, Baker City, Or. Herald: Feb. 9, 2000 editorial.]**
Editorial in Baker City herald recommending no additions to the OMMA

GRADE: No relevance to inquiry

24. **Proceed with caution on medical marijuana [No author listed, Salem, OR. Statesman Journal, Feb. 17, 2000 editorial.]**
Salem Statesman Journal editorial recommending that advisory group and the OHD proceed with caution in expanding OMMA to include psychiatric conditions or symptoms.

GRADE: No relevance to inquiry

25. **Pot plan should be an easy call [No author listed, Bend OR Bulliten, Feb. 14, 2000.]**
Bend Bulletin editorial recommending against expansion of OMMA

GRADE: No relevance to the inquiry

26. **Testimony by William Wilson, MD, professor of psychiatry at OHSU.**

"I am opposed to expanding the list of conditions allowing medical use of marijuana..."
"My opposition stems from 3 sources...
1. There is no demonstrated efficacy or effectiveness of marijuana treatment for these conditions.
2. There is scientifically demonstrated risk of exacerbating many of these disorders by the use of marijuana, and
3. The [OMMA] does not provide for medical supervision..."

GRADE: Convincing evidence that all petitioned conditions should be refused admittance to the OMMA based on expert personal experience with some research citations

27. **Testimony by Rupert Goetz, MD Medical Director of the OMHS.**
Testifying against inclusion of any of the petitioned conditions : "There is currently no credible evidence that the benefits of using marijuana for the treatment of any of the psychiatric conditions listed ... outweigh the risks."

GRADE: Good evidence of an opinion in opposition to inclusion of any conditions.

28. **Testimony presented by Doris Cameron-Minard, President of NAMI Oregon. Board of Directors statement.**
Opposing addition of any of the petitioned conditions. " In the absence of compelling scientific evidence, NAMI Oregon stands opposed to the use of alcohol and illegal drugs, including marijuana by persons with major mental illness."

GRADE: Good evidence that NAMI opposes enlarging list of debilitating medical conditions to include psychiatric conditions.

29.**Testimony and position statement by NAMI of Multnomah County presented by Jason Renaud, Executive Director.**
Statement in opposition to adding any conditions to the list of Debilitating medical conditions:

" Typically, regular users of marijuana have an untreated mental illness."....
"Calling marijuana medicine for mental illness is pure newspeak, convincingly calling a thing it's opposite to baffle and confound."

GRADE: Good evidence that NAMI Oregon of Multnomah County opposes addition of any conditions. Mostly opinion-based.

30. **Testimony of Kevin Fitts, Office of Consumer Technical Assistance.**
Testified in favor of including affective disorders to the list and of not adding thought disorders to the list.

"I know hundreds of people using marijuana to treat anxiety and depression." "I don't think it should be a criminal act."

GRADE: Good evidence that he supports expanding the act to include psychiatric conditions and that he knows many people using cannabis for relief of affective symptoms- anxiety and depression.

31. Telephone testimony from Petitioner and caregiver regarding her use of cannabis.
Patient had great difficulty expressing herself and required frequent assistance form caregiver. They both repeatedly stated that cannabis is the only medicine, which decreases her irritable bowel symptoms, helps her relax and increases medication compliance. Additionally, they state that cannabis decreases the severity and frequency of negative schizophrenic symptoms by giving her the strength to go outside the house and socialize with others.

The petitioner's physician has written a note included with her packet which states:

"PT has been using marijuana to help control her schizophrenia and in fact it has been under control for the last 4-5 years."

GRADE: Good evidence that patient has been using cannabis to control the symptoms of schizophrenia based upon her, her caregiver, and her physician's report.

32. **Telephone testimony from Petitioner regarding his application to include Neural Transmitters Disorder/Negative Symptomatology to list of debilitating medical conditions**.
Petitioner states in his telephone testimony that he has not tried cannabis but desires to because of its ability too stimulate dopamine production and thus decrease negative symptoms of schizophrenia. His submitted documentation includes 6 lengthy letters to the Division as well as 1 page of physician notes indicating that:

'He may be able to benefit from THC + the cannabinoids in low doses."

GRADE: Since the petitioner does not use cannabis there is no evidence that it helps him. There is slim evidence that indeed he may benefit from it.

33. **Expert testimony from Barbara Cimaglio, Director of Oregon Office of Alcohol and Drug Abuse Programs.**
Ms. Cimaglio submitted a statement opposing the opening of the Marijuana Registry Program to people suffering from psychiatric problems.

GRADE: Good evidence that Oregon's Office of Alcohol and Drug Abuse Programs opposes including any psychiatric conditions.

34. **Expert testimony from Dr. Constance Powell, President of the Oregon Psychiatric Association.**
Dr. Powell stated that there is no evidence that marijuana is a treatment for mental disorders, and testified in opposition to including any psychiatric conditions into the legal exemption created by the OMMA.

GRADE: American Psychiatric Association opposes inclusion of psychiatric conditions into list of those covered under the OMMA.

Clinical Effectiveness (and comparison with established alternatives)
Petitioner number two has apparently not used cannabis and therefore there is no way to evaluate clinical effectiveness.

Petitioner number one has a long history of use of cannabis (12 years) under the guidance of her physician and caregiver. It is clear that they believe her medication compliance is increased through her cannabis use. She does not have as many "episodes" of panic. She has not tried atypical anti-psychotics like Risperdal due to lack of money to see a psychiatrist so there is no ability to evaluate whether these, in fact, would help her and preclude cannabis use. However, they relay that her cannabis use does not increase hallucinations, but makes her forgetful- not as intense, and increases her appetite. The extent to which this patient's experience reflects the schizophrenic population as a whole is completely unknown.

Health Benefits and Risks:
It appears that the petitioner is benefiting from her use of cannabis. As stated by her caregiver: "I am completely convinced that marijuana is a legitimate and necessary component in ___'s success at living a relatively happy and untroubled life in spite of a severely depressed and disoriented personality." Additionally, the petitioner benefits (and in fact has a registry card for symptoms associated with irritable bowel syndrome) because her use of cannabis relieves nausea, cramps and diarrhea, which may "last from all day to all week. Marijuana is very helpful at the outset of these episodes...." and "...is helpful in getting [petitioner] back on food after the episode."

Risks include respiratory problems associated with inhaling as a vehicle of administration. There is no indication that the petitioner is suffering from respiratory compromise as a result of using cannabis seven times per day over many years. These risks persist and may increase over time. Unknown whether petitioner concomitantly uses tobacco which significantly increases pulmonary risks

Factors Affecting Safety, Effectiveness, and Related Considerations for All patients and for Specific Patient Types.

There are primarily four issues relating to the petitioners and others with Schizophrenia and Schizoaffective disorders who use cannabis;

1. Legal status. The criminal penalties and associated contacts with police include arrest, search and seizure of assets, conviction and potentially, incarceration for the petitioners. In the case of petitioner #2 this is not a consideration since he does not use cannabis. For petitioner #1 the consequences with the legal system could be grave due to her isolation and relatively feeble ability to care for herself. Her condition would likely deteriorate and this poses probably the greatest risk to her safety and fragile internal security. As well, contacting the illegal cannabis market carries with it attendant risks which include ingestion of adulterated cannabis and contact with potentially-violent black market people.

2. Risks of exacerbation of illness. Petitioner #1 is at some risk that cannabis could at some point cease to be a stabilizing medication and instead become a contributing factor in her schizophrenic symptoms. She and her caregiver should be cognizant of the signs of worsening psychosis which may be attributable to cannabis. This would appear to be a remote possibility based upon the patients 12 years of apparently continuous use.

3. Cannabis dependence. The potential for cannabis dependence exists primarily in chronic heavy users of cannabis and petitioner #1 falls into this category. She and her caregiver and her physician should be aware of the signs of dependence. This would appear to be an insignificant issue at this point because of the severity of her symptoms and the benefit she clearly derives in her quality of life.

4. Respiratory complications. Long-term heavy cannabis smoking is associated with an increase of risk for pulmonary complications which some studies report exceeds that of tobacco use. The petitioner should attempt to minimize these risks by consuming high-potency cannabis in smaller amounts and considering alternative dosing arrangements such as vaporizers or eating.

Net Health and Overall Impact of Medical Marijuana Use for This Condition:

The net health impact and overall impact for petitioner is clearly that long-term cannabis use is benefiting her personally. The net health and overall impact of cannabis use to schizophrenics as a whole is less clear. There clearly is strong evidence, based upon many research reports, that the overall impact of cannabis use on most schizophrenic patients is negative. Cannabis use appears to substantially increase morbidity, and severity of psychosis (hallucinations, delusions and paranoia) in many patients as well as increasing the frequency of relapses. It appears this is due to the psychopharmacological receptor-mediated effects of cannabinoids on the brain, which result in confusing and sometimes profound alterations in cognitive processing.

There is a small but sound research base that indicates that a sub-population of schizophrenics who use cannabis obtain significant benefit from it through decreased hospitalizations as well as a significant decrease in affective symptoms (anxiety, agitation, depression) and negative symptoms of schizophrenia (anhedonia, loss of libido, social withdrawal and isolation.) This research seems to factor in the quality-of- life benefits derived from decreased anxiety and depression, which severely incapacitate many persons with schizophrenia and may lead to destructive self-medication.

Other Considerations

[None]

II. Performance On Assessment Criteria

1. Quality and Sufficiency of Available Evidence: *There is sufficient available evidence of sufficient quality to permit reaching a sound determination relating to the use of medical marijuana for the treatment of this condition.*
NO

Comments: There is an absence of clinical trials differentiating and exploring the research base, which would describe on a neurochemical level why certain schizophrenic patients appear to benefit from using cannabis.

2. [A] **Clinical Effectiveness**: *The use of medical marijuana for this condition is clinically effective.*
POSSIBLY

Comments: Cannabis is clinically effective for what appears a small but unknown percentage of schizophrenic persons who use it. It is clearly not effective for a larger percentage of schizophrenic persons.

[B] **Relative Clinical Effectiveness:** *The use of medical marijuana for this condition is clinically effective relative to established alternative treatments for this condition.*
POSSIBLY

Comments: It appears that in a small percentage of persons with schizophrenia, cannabis increases medication compliance and thus enhances the clinical effectiveness of treatments such as atypical anti-psychotic medications.

3. Health Benefit/ Risk Ratio: *The health benefits of medical marijuana use for this condition outweigh the health risks.*
POSSIBLY

Comments: For a small sub-population there is fair evidence that cannabis use creates a net health benefit. For the majority of schizophrenic persons who use cannabis the risks outweigh the benefits.

4. Net Health Impact: ***T****he use of medical marijuana for this condition improves net health outcomes (functional status and/or ability to perform activities of daily living) for those individuals with this condition who use medical marijuana.*
POSSIBLY

Comments: For a small sub-population of patients (including petitioner #1) cannabis use improves quality of life and functional ability. For the majority of schizophrenic persons who use cannabis functional status appears to be decreased.

5. Net Overall Impact: *The use of medical marijuana for this condition improves net overall outcomes (quality of life and/or perceived satisfaction with condition improvement) for those individuals with this condition who use medical marijuana.*
POSSIBLY, NAD

Comments: As with #4 above, some cannabis using schizophrenics report marked improvement in global quality of life as measured by a decrease in agitation anxiety and depression. Petitioner #1 falls into this category. For a significant percentage, possibly a majority of schizophrenic persons who use cannabis, overall function is negatively impacted.

6. Safety, Effectiveness, or Related Issues: *There are no such compelling or overriding issues that alter any of the determinations regarding the use of medical marijuana for the treatment of this condition that would have been reached absent these issues.*
YES

The issue of the legal status of chronically ill people alters these determinations in the following way: The United States government has followed a deliberate policy of hindering research into the potential therapeutic uses of cannabinoids for nearly 6 decades. This policy, which continues today, make serious clinical research extremely difficult to pursue, and has been called "Byzantine and demeaning " by Ethan Russo, one of America's preeminent researchers into the utility of cannabinoids. To date only one study protocol exploring cannabis' medical utility is ongoing a full year after the Institute of Medicine's Report calling for more research. A research protocol by Dr. Abrams of UCSF was only allowed to proceed after the focus was changed to a search for the drug interactions of cannabinoids and protease inhibitors, instead of a comparison of efficacy. The continuing Federal policy of overt and covert obstruction has created a situation where high-grade evidence of clear medical utility is nearly impossible to obtain or corroborate. Until this research is allowed to proceed it is indefensible on humanitarian grounds to forbid access to cannabis for patients who are under a physician's care and who suffer severe symptoms. These determinations may be altered in the future by development of new therapeutic cannabinoid delivery vehicles, and by a governmental policy, which does not cause more harm to ill people than their use of cannabis.

III. Overall Findings and Recommendations

Summary of Findings

This review included the following:
Five (5) research studies indicating either efficacy or a lack of harm to schizophrenic persons who use cannabis;
The Institute of Medicine report recommending more research and saying the evidence is inconclusive;
A position statement by the American Psychiatric Association calling for more research;
Testimony from five (5) witnesses opposing any enlargement of the OMMA to include psychiatric conditions;
Testimony from one (1) person recommending the allowance of affective or mood conditions on the list and opposing inclusion of thought disorders on the approved list;
Four (4) Oregon newspaper editorials of questionable relevance generally opposed to opening the OMMA to include psychiatric conditions;
Five (5) studies of little relevance except for passing references to cannabis as being an etiological factor in the development of psychosis;
Four (4) studies of good quality describing various harms associated with the use of cannabis in schizophrenic patients;
Two (2) abstracts totaling 18 studies two of which are included elsewhere in this survey.

Of the 16 studies, eleven indicate moderate to severe detrimental effects on schizophrenic persons who use cannabis and five studies indicate either minimal harm associated with the use of cannabis or benefit;
Two (2) petitioner testimonies and supporting documents, one of which has little relevance since the petitioner has no experience with cannabis and one testimony, which correlates with a moderate to high degree of improvement of various symptoms because of her use of cannabis.

Recommendation Regarding Adding this Condition to the list of "Debilitating Medical Conditions" for Purposes of the Oregon Medical Marijuana Act
Add disease to list of disease conditions pursuant to ORS 475.302(2)(a)

COMMENTS:
[PLEASE SEE COMMENTS ABOVE]

RATIONALE Re: this recommendation
Due to a deliberate policy on the part of the Federal government to obstruct clinical research into the apparent therapeutic uses of cannabis and the continuing criminalizing of ill people who use it for Schizophrenia the default position of the OHD should be to approve this condition with the following suggested provisions:

A. The patient should be refractory to more conventional treatments and should not be taking conventional anti-psychotics- i.e. Thorazine, Haldol;

B. The MD should conduct periodic reviews of use to determine presence of excessive use (i.e. increasing dosage and frequency, signs of decreasing effectiveness and decreasing function.);

C. The MD should periodically evaluate pulmonary function;

D. The MD should consider "N-of-1" research evaluations;

E. The MD should carefully evaluate hepatic and neurochemical interactions with initiation of any new pharmacotherapy.

***NOTE:* Listing severe anxiety/agitation may adequately cover many schizophrenics under the protections of the OMMA.**

Submitted by:
Edward Glick, RN
March 28, 2000