UNITED STATES COURT OF APPEAL

FOR THE NINTH CIRCUIT

NO. 98-16950

OAKLAND CANNABIS BUYERS' COOPERATIVE and JEFFREY JONES,

Appellants/Defendants,

v.

UNITED STATES OF AMERICA

Appellee/Plaintiff.

Appeal from Order Denying Motion to Modify Preliminary Injunction
Appeal From Order Modifying Injunction by the United States District Court
for the Northern District of California
Case No. C 98-0088 CRB
entered on October 13, 1998, by Judge Charles R. Breyer.

EXCERPTS OF RECORD
VOLUME VI

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EXCERPTS OF RECORD

VOLUME I

EXCERPTS OF RECORD

VOLUME II

EXCERPTS OF RECORD

VOLUME III

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VOLUME IV

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VOLUME V

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VOLUME VI

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VOLUME VII

EXCERPTS OF RECORD

VOLUME VIII

COPY

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JEFFREY JONES

IN THE UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

UNITED STATES OF AMERICA,

Plaintiff,

v.

CANNABIS CULTIVATOR'S CLUB, et al.,

Defendants.

AND RELATED ACTIONS.

No. C 98-0085 CRB
C 98-0086 CRB
C 98-0087 CRB
C 98-0088 CRB
C 98-0089 CRB
C 98-0245 CRB

DECLARATIONS IN SUPPORT OF DEFENDANTS' RESPONSE TO SHOW CAUSE ORDER

Date: September 28, 1998
Time: 2:30 p.m.
Courtroom: 8
Hon. Charles R. Breyer

IN THE UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

UNITED STATES OF AMERICA,

Plaintiff,

v.

CANNABIS CULTIVATOR'S CLUB, et al.,

Defendants.

AND RELATED ACTIONS.

No. C 98-00085 CRB
C 98-00086 CRB
C 98-00087 CRB
C 98-00088 CRB
C 98 00089 CRB
C 98 00245 CRB

DECLARATION OF ROBERT T. BONARDI

I, ROBERT T. BONARDI, declare:

1. I am a patient-member of the Oakland Cannabis Buyers' Cooperative ("OCBC"). I have personal knowledge of the facts stated herein, and if called as a witness, I could and would testify competently as to them.

2. I live in Hayward, California with my wife of 53 years. I am the father of three children, and I have four grandchildren. I have owned a vacuum cleaner store for the past 20 years. I am no longer able to go to my store to work because I have cancer and am undergoing chemotherapy.

3. I was first diagnosed with cancer of the throat ten years ago. I underwent radiation therapy as part of my treatment then. At that time the doctors removed my voicebox and performed a tracheotomy. I still have a hole in my throat.

4. Two years ago I lived through prostate cancer.

5. Earlier this year the doctors discovered a tumor on the side of my neck. They removed it, but later the doctors discovered more tumors on my shoulder, chest, and neck area. Since I have already had radiation treatments, I had to undergo intensive chemotherapy for these new cancers.

6. After they started the chemotherapy treatments this year, I got really sick. The nausea was so bad I would retch whenever I thought about food or whenever anyone tried to put food in front of me. The nausea made me particularly afraid to eat because my throat condition makes it especially unpleasant if I vomit. Not only would vomit come out of my mouth, but it would also come out of my nose.

7. Over a period of about six weeks, I lost forty pounds. My wife and children became very worried about my not eating and about my dramatic weight loss.

8. I tried some medicines the doctors prescribed for me to help me with the nausea and my lack of appetite, but none of them worked for me. I took them but still I could not bring myself to eat. I was still losing weight.

9. Eventually, my daughter Judy forced me to go with her to the Oakland Cannabis Buyers Cooperative. At first I did not want to go. It took my daughter a long time to convince me to go I am 74 years old and I had never used marijuana before in my life.

10. The OCBC gave me papers to take to my doctor to fill out. My E.N.T. doctor from Kaiser in Fremont signed the papers. My daughter took me back to the OCBC. I bought cannabis brownies, some cannabis pills, and some cannabis banana muffins. Because of my condition I cannot smoke.

11. The first day I ate half a cannabis brownie before breakfast and nothing much happened.

12. Later that same day, I ate another half brownie and for the first time in several weeks, I felt like eating. The brownie caused my nausea to go away. I asked my wife to cook me eggs and sausage. She was so happy because it had been so long since I had asked for food. I have since regained some of the weight I lost.

13. Cannabis is the best medicine for my conditions caused by the chemotherapy treatments. In fact, it is the only medicine that has worked for me. I believe that without cannabis I would have continued to starve.

14. The OCBC has provided a safe place where I can get this life-saving medicine. If cannabis were not available through OCBC, I would be forced to go without the only medicine that has worked for me to relieve my nausea and to give me my appetite back. I would refuse to get my medicine from criminal street dealers.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct.

Executed this 9/10/98 day of September at Oakland, California.

Robert T. Bonardi

Robert T. Bonardi

IN THE UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

UNITED STATES OF AMERICA,

Plaintiff,

v.

CANNABIS CULTIVATOR'S CLUB, et al.,

Defendants.

AND RELATED ACTIONS.

No. C 98-00085 CRB
C 98-00086 CRB
C 98-00087 CRB
C 98-00088 CRB
C 98 00089 CRB
C 98 00245 CRB

DECLARATION OF ALBERT DUNHAM

I, ALBERT DUNHAM, declare:

1. My name is Albert Dunham. I am 43 years of age, am of sound mind, and am competent to testify to the matters stated herein.

2. I am a member of the Oakland Cannabis Buyers' Cooperative. I was present at the Cooperative on May 21, 1998.

3. I was diagnosed as HIV-positive in June, 1996. As a result of my disease, I have suffered from constant nausea, fatigue, insomnia, lack of appetite, weight loss, and pain throughout my back, neck, and head. Due to these problems, I was unable to maintain my job as a warehouse shipping and receiving clerk and am currently unemployed.

4. I have tried medicine other than cannabis to combat these problems, but they always had adverse side effects on my body, primarily by inducing vomiting. My stomach is very sensitive and does not react well to ingesting pills. At the end of 1997, my doctor prescribed cannabis for my symptoms, especially to alleviate my steady weight loss. My appetite had deteriorated so badly by this point that there were occasions when I had only one meal every two days.

5. I have been using medicinal cannabis for the past ten months, and the improvement in my overall health has been dramatic. My appetite has returned, along with some of the weight I lost, leading me to believe that continued use would allow me to return to my normal weight. In addition to my increased appetite, regular use of cannabis has alleviated the pain I feel throughout my body and generally relaxed me by reducing the anxiety and stress associated with my disease and symptoms. My insomnia has also improved.

6. Unlike others drugs I have tried for my illness, cannabis has left no lingering side effects. Using cannabis allows me to live a normal life, something I was unable to achieve prior to my doctor's prescription.

7. I live with my daughter, 27, who is supportive of my use of cannabis to fight the medical problems I have described. I have a new doctor now, and he is also supportive of my continued use of cannabis to combat my weight loss and other symptoms.

8. If I was no longer able to obtain cannabis through the OCBC, I would be forced to the streets to obtain it, which is a situation that I am emotionally and financially unprepared for. I have

doubts that I would be able to obtain cannabis under those conditions. The OCBC's continued existence insures that I will have a safe, clean location that I can regularly visit to obtain the medicine I require.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct.

Executed this 13 day of September, in Oakland, California.

Albert Dunham

IN THE UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

UNITED STATES OF AMERICA, Plaintiff, v. CANNABIS CULTIVATOR'S CLUB, et al., Defendants. AND RELATED ACTIONS.	No. C 98-00085 CRB C 98-00086 CRB C 98-00087 CRB C 98-00088 CRB C 98 00089 CRB C 98 00245 CRB **DECLARATION OF KENNETH ESTES**

I, KENNETH ESTES, declare:

1. My name is Kenneth Wayne Estes. I am 40 years of age, am of sound mind, and am competent to testify to the matters stated herein.

2. I am a member of the Oakland Cannabis Buyers' Cooperative. I was present at the Cooperative during a press conference on May 21, 1998.

3. I am quadriplegic. I am either confined to a wheelchair or bedridden. I use cannabis for pain relief, appetite stimulation, and sleep.

4. I was injured in a motorcycle accident when I was 18 years old. I broke my neck at cervical five and six. At first, all four of my limbs were paralyzed, but about two years after the accident, I regained some use of my arms, hands, and fingers. True and correct copies from my medical record are attached as "Exhibit A."

5. I live with constant pain. Sometimes it is a "tingling" that will not stop, almost as if you hit your funnybone. Other times, such as when I get spasms or back problems, the pain becomes intense, powerful, and overwhelming. Without cannabis the pain would be excruciating. Even after I medicate with cannabis, the pain is still there—it never goes away—but cannabis makes the pain bearable. Cannabis makes it possible for me to function in society and to deal with other people because it alleviates the pain I experience.

6. Before I discovered medical cannabis, the pain in my back was so bad that it drove me insane, and I wanted to kill myself. Having to live with the constant pain made me suicidal. I wanted the pain to end at any cost.

7. I was wasting away. I could not eat and I could not sleep. I was dying.

8. In my suffering, a hospital orderly who held a marijuana pipe to my lips allowed me to medicate with cannabis for the first time. It worked.

9. The pain went down. I was able to sleep through the night. The next morning, I finished breakfast. The nurse even brought in the doctors to show them that I ate the whole meal.

10. I am thankful that there is an herb I can turn to to alleviate my pain, because now I want to live, not die. With the three ingredients of rest, food, and my spirits raised, I can conquer anything, including conquering this illness. Cannabis saved my life.

11. I have tried many prescription drugs, sometimes several medicines per day. For example, I have tried Valium, Motrin, codeine, Vicodin, Darvocet, and many others. They either did not work, or had side effects that made me not want to use them. The pharmaceutical pills gave me stomach pain, other stomach problems, and constipation. They also made me emotionally unstable. They made me want to cry, they made me angry at my condition, or they made me frustrated.

12. The pills made my cognitive thinking defective and my mind blurred. I couldn't hold thoughts together, couldn't have conversations, and couldn't communicate with other people. It is hard to deal with paralysis—all I have left are my words. When I couldn't communicate with other people through words, it only made my condition worse.

13. The pharmaceuticals merely added to my discomfort. They gave me new pain (stomach pain) and made me self-conscious about not being able to speak, which detrimentally affected my eating and sleeping. Cannabis, by comparison, gives me no pain, helps me eat, helps me sleep, and makes me more sociable with other people.

14. Some of the prescription sleeping pills I used to take lost their effectiveness after a while, making me need to take more and more of them. The next morning I would feel "hung over" and "cloudy," and I still had the stomach pain. If I use cannabis to help me sleep, I feel better the next morning, I feel refreshed after a good night's sleep, and I have no stomach pain.

15. Pills can take 60 to 90 minutes to take effect. In contrast, the immediate effect of smoked cannabis is one of its great attributes. Medicating with cannabis allows access to sleep or hunger when I need it, either because it is nighttime and time to sleep or because a meal is ready.

16. Pharmaceuticals may work for some people, but they do not work for me. I know, because I have tried them. Cannabis, however, does work for me. It actually relieves my pain, and it does not have the physical and emotional side effects of the prescription medications.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct.

Executed this 11 day of September, in Oakland, California.

Kenneth Estes

EXHIBIT A

Monica Ruiz-Durant, M.D.
THE PERMANENTE MEDICAL GROUP, INC.

3400 DELTA FAIR BLVD.
ANTIOCH, CA 94509-4098 PHONE: 778-5080

NAME Estes, Kenneth

ADDRESS

PHONE DATE 5/16/12

PLEASE ✓ BOX WHEN PATIENT IS ☐ INDUSTRIAL ☐ TPL

One (1) Prescription Per Blank for Refill Authorization Request

℞ Mr. Estes
Hydrocodone Microgram.
for pain relief from the
Neuropathy that he
experiences from
chronic pancreatitis.

REFILL 0 · 1 · 2 · 3 · 4 · 5 · 6 Monica A Ruiz, M.D.

☐ NURSE PRACTITIONER ☐ COVERING M.D.

☐ CHECK BOX FOR REFILL AUTHORIZATION REQUEST FORM (MINIMUM 2 REFILLS)

CAL. LIC. NO. G64187 DEA NO. BR2245567

RESOURCE NO. 4523059

☐ LABEL: MAY CAUSE DROWSINESS

UNLESS CHECKED BELOW AUTHORIZATION IS GIVEN TO:

☐ DISPENSE NON-PROPRIETARY (GENERIC) NAME ☐ DISPENSE BY NEAREST STANDARD SIZE

SPECIFY MAJOR DRUG ALLERGIES TO BE ENTERED INTO PHARMACY SYSTEM

4523059 (5-86)

ER1179

Exhibit A

IN THE UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

UNITED STATES OF AMERICA, Plaintiff, v. CANNABIS CULTIVATOR'S CLUB, et al., Defendants. AND RELATED ACTIONS.	No. C 98-00085 CRB C 98-00086 CRB C 98-00087 CRB C 98-00088 CRB C 98 00089 CRB C 98 00245 CRB **DECLARATION OF LAURA A. GALLI, R.N.**

I, LAURA A. GALLI, declare:

1. I am one of two registered nurses who work at the Oakland Cannabis Buyers' Cooperative (the "Cooperative" or "OCBC"). As a staff nurse I am familiar with the policies and procedures of the OCBC. I have personal knowledge of the facts stated herein, and if called as a witness, I could and would testify competently as to them.

2. From 1990 through 1992 I worked as a student nurse intern and unit secretary in the Rehabilitation Unit at Mills-Peninsula Hospitals. During that time I studied for my nursing degree at Cal-State Hayward, which degree I received in 1992. However, in July 1992 I was diagnosed with pleurisy and with lupus. This medical condition prevented me from being able to continue employment as a nurse. Currently I am an "inactive" registered nurse.

3. I work as a volunteer at the Cooperative as a staff nurse. The Intake Department of the Cooperative includes two staff nurses, one of whom is always on duty while the Cooperative is open on weekdays.

4. Before a patient is accepted for membership into the Cooperative, he or she must complete an extensive screening process. This process is described in detail in the Oakland Cannabis Buyers' Cooperative Protocols ("Protocols"), a copy of which is attached hereto as Exhibit 1. Before reaching my office, all applicants must satisfy the threshold requirement of providing authorization from a treating physician assenting to cannabis therapy for one or more medical conditions listed on the Medicinal Cannabis User Initial Questionnaire (Exhibit C to the Protocols).

5. If, upon screening by the Cooperative Intake staff member, the applicant cannot provide such authorization, he or she will be denied membership to the Cooperative.

6. Once the applicant provides a doctor's authorization for medical cannabis, it is my job to independently verify the physician's approval. No applicant is admitted to membership to the Cooperative unless and until I or the other staff nurse verify the applicant's physician's approval.

7. For each and every Cooperative applicant, either I or the other staff nurse telephone the applicant's doctor's office to verify the authenticity of the authorization submitted by the prospective member. I talk with the doctor (or in some instances a member of the doctor's staff) to confirm that the doctor did in fact authorize the use of cannabis for a medical condition. I also will

confirm the date of the authorization. If the doctor or his staff cannot provide satisfactory responses to my questions, then I screen out the Cooperative applicant and reject the applicant for membership. A copy of the Verification of Physician's Written Recommendation form that I use is attached hereto as Exhibit 2.

8. For each and every doctor who has authorized the use of medical cannabis to one of the Cooperative applicants, either I or the other staff nurse confirm that the doctor is licensed to practice medicine in the State of California. If the doctor's credentials cannot be confirmed, then I reject the applicant for membership.

9. Soon after an applicant is admitted to membership in the Cooperative, he or she is issued a laminated membership card. A copy of a membership card is attached as Exhibit J to the Protocols. Each time a patient-member comes to the Cooperative, he or she must present this membership card along with secondary valid photo identification in order to gain entry.

10. I am familiar with the range of medical conditions from which the Cooperative's patient-members suffer. Patient-members of the Cooperative suffer from debilitating and often deadly diseases, including HIV and/or AIDS, cancer, arthritis, multiple sclerosis, and glaucoma. I know that medical cannabis provides relief to patient-members as a pain reliever, an appetite stimulant, an anti-nauseant, and an anti-convulsant. Medical cannabis also relieves intraocular eye pressure in patient-members who suffer from glaucoma.

11. Although every patient's experience is unique, some general comments apply to many patients. For some Cooperative members, they have tried other legal medicines to alleviate their conditions but these other medicines do not work for them. For other members, other drugs have intolerable negative side effects which they have chosen not to endure. Some members' experiences with other legal medicines is that, while they are somewhat effective, they are not nearly as effective at relieving their symptoms as medical cannabis.

12. I have seen patient-members who suffer from AIDS-related "wasting syndrome" as well as those who have cancer and are undergoing chemotherapy and radiation therapy. Medical cannabis reduces nausea and increases appetite in these patients. Other medicines either do not work for some of these patients or they have serious adverse side effects that cannabis does not have.

Supplying medical cannabis to these patient-members is necessary to avert imminent and potentially life-threatening harm.

13. I have also seen patient-members who suffer from multiple sclerosis or quadriplegia. They experience debilitating spasticity and/or constant pain. Other medicines simply do not work for many of these patient-members. These patients can also experience intolerable adverse side effects from other medications—side effects that cannabis does not have.

14. I suffer from both lupus and fibromyalgia. Lupus is a disease of the immune system which, among other things, causes an arthritic-type condition and arthritis-type pain. Fibromyalgia is a pain syndrome which affects the ligaments and tendons in all of my joints. I live in nearly-constant pain.

15. There are many medications I must take to treat my conditions. These medications have many adverse side effects, including stomach upset, chronic nausea and vomiting, and they can be addictive.

16. The doctors are not sure why I experience chronic nausea and vomiting. Over the years I have tried many medications and treatments to try to alleviate my nausea symptoms, but nothing worked for me.

17. Eventually, my primary care physician—Dr. Richard Morgan—authorized medical cannabis for my nausea and reduced appetite. This medicine has worked wonders for me. It has relieved my nausea and increased my appetite when nothing else would. Medical cannabis has had the additional benefit of helping to reduce my pain.

18. If I were forced to go without cannabis now I would be a mess—I would again have no appetite and would lose weight, I would experience a dramatic increase in nausea and vomiting, and the pain in my joints would increase. If the OCBC were forced to close down, I would in turn be forced to obtain cannabis on the criminal market. But at this point I would not know where to begin to look for cannabis. Resorting to the criminal market would make me seriously nervous for my safety.

19. In fact, many other patient-members' lives may be endangered if they were forced to try to obtain cannabis from criminal street dealers. This is in part because impurities in marijuana

purchased on the street may be harmful to their health. It is also because it would be very dangerous for many of our patient-members to enter a high crime area which is where they would have to go to obtain cannabis. Some patient-members may choose to forego their medication if they have no choice but to turn to street dealers for cannabis.

20. The Cooperative, by contrast, provides a safe environment for patient-members to obtain their much needed medicine.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct.

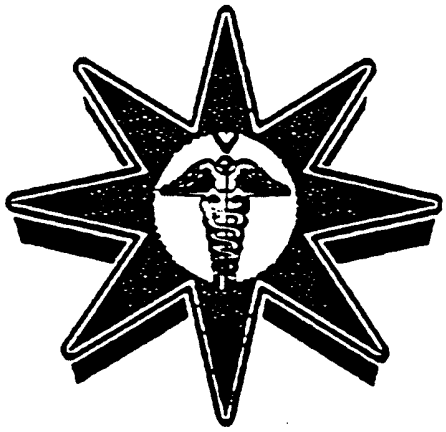
Executed this 12th day of September at Oakland, California.

Laura A. Galli, R.N.

EXHIBIT 1

Oakland Cannabis Buyers' Cooperative

Protocols



Compassion

Oakland Cannabis Buyers' Cooperative
Post Office Box 70401
Oakland, California 94612-0401
Tel. 510-832-5346
Fax 510-986-0534
Email ocbc@rxcbc.org
Web www.rxcbc.org

March, 30 1998

Oakland Cannabis Buyers' Cooperative

Protocols

The Oakland Cannabis Buyers' Cooperative operates pursuant to and in accordance with the statewide mandate of Proposition 215 (Exhibit A) and Resolutions passed unanimously by the Oakland City Council and an Administrative Memorandum promulgated by the Chief of Police (Exhibit B). Its operating procedures have been consolidated as these Protocols.

I. Admission and Membership Requirements

A person seeking membership of the Oakland Cannabis Buyers' Cooperative must at the threshold provide a note from a treating physician assenting to cannabis therapy for a medical condition listed on the Medicinal Cannabis User Initial Questionnaire (Exhibit C). Upon acceptance of the note by Intake staff, the prospective member will undergo an extensive screening and such questioning as shall establish that the candidate meets the Medical Admissions Criteria (Exhibit D) including, without being limited to, the Oakland Cannabis Buyers' Cooperative Information Form (Exhibit E). If, upon the screening by Cooperative staff the candidate does not appear to qualify for membership, he or she will be denied membership with a statement of reasons for his/her being screened out. If the candidate appears to qualify for membership, Intake staff will give the candidate the Authorization for Release of Patient Status form (Exhibit F) and the Physician Statement (Exhibit G), with a request that the candidate's treating physician sign it. When the form is returned, the Intake staff will verify the physician's approval by independent telephone verification. Medical cannabis cultivators and manufactures are issued cultivation and manufacturing Certificates (Exhibit H), which the City Council has approved to aid the Police in recognizing agents of the Cooperative.

No person under the age of eighteen shall be admitted to membership without the written consent of parents, in addition to meeting all other requirements.

II. Responsibilities of Membership

All members must sign a Membership Agreement (Exhibit I), whereupon they will receive a Membership Card (Exhibit J). Members agree to conduct themselves discreetly, in accordance with the Statement of Safe Use of Cannabis (Exhibit K) and the Principles of Responsible Cannabis Use (Exhibit L).

III. Other Provisions

A. Purpose. The purpose of the Oakland Cannabis Buyers' Cooperative is to help provide medicine for people who need it. Accordingly, it shall be operated as a not for profit organization.

B. Privacy of members. The staff of the Cooperative shall take steps to protect the privacy and identity of members. However, neither the Cooperative nor its staff shall be liable for any breach thereof

C. Changes. These Protocols, and all medical protocols, are subject to change without notice from time to time in the sole discretion of management.

D. Cooperative operation.

a. No smoking of anything on premises.
b. Members shall observe additional house rules as same maybe posted by management.
c. Management may eject any person at any time.

Exhibits

A. Proposition 215

B. Oakland City Council Resolutions and Police Memorandum

C. Medicinal Cannabis User Initial Questionnaire

D. Medical Admissions Criteria

E. Information Form

F. Authorization for Release of Patient Status

G. Physician Statement

H. Cultivation and Manufacturing Certificates

I. Membership Agreement

J. Membership Card

K. Statement of Safe Use of Cannabis

L. Principles of Responsible Cannabis Use

Ex. A

THE CALIFORNIA MEDICAL MARIJUANA INITIATIVE

This initiative to permit medical use of marijuana will appear on the ballot November 5, 1996. The Attorney General of California has prepared the following title and summary of the chief purpose and points of the initiative.

MEDICAL USE OF MARIJUANA. INITIATIVE STATUTE. Provides that patients or defined caregivers, who possess or cultivate marijuana for medical treatment recommended by a physician, are exempt from general provisions of law which otherwise prohibit possession or cultivation of marijuana. Provides physicians shall not be punished or denied any right or privilege for recommending marijuana to a patient for medical purposes. Declares that the measure not be construed to supersede prohibitions of conduct endangering others nor to condone diversion of marijuana for nonmedical purposes. Contains severability clause. Summary of estimate by Legislative Analyst and Director of Finance of fiscal impact on state and local government: Because this measure restricts the use of marijuana to only those persons for whom it is prescribed by a licensed physician, it would probably have no significant state or local fiscal impact.

Initiative text:

SECTION 1. Section 11362.5 is added to the Health and Safety Code, to read:

11362.5. (a) This section shall be known and may be cited as the Compassionate Use Act of 1996.

(b)(1) The people of the State of California hereby find and declare that the purposes of the Compassionate Use Act of 1996 are as follows:

(A) To ensure that seriously ill Californians have the right to obtain and use marijuana for medical purposes where that medical use is deemed appropriate and has been recommended by a physician who has determined that the person's health would benefit from the use of marijuana in the treatment of cancer, anorexia, AIDS, chronic pain, spasticity, glaucoma, arthritis, migraine, or any other illness for which marijuana provides relief.

(B) To ensure that patients and their primary caregivers who obtain and use marijuana for medical purposes upon the recommendation of a physician are not subject to criminal prosecution or sanction.

(C) To encourage the federal and state governments to implement a plan to provide for the safe and affordable distribution of marijuana to all patients in medical need of marijuana.

(2) Nothing in this act shall be construed to supersede legislation prohibiting persons from engaging in conduct that endangers others, nor to condone the diversion of marijuana for nonmedical purposes.

(c) Notwithstanding any other provision of law, no physician in this state shall be punished, or denied any right or privilege, for having recommended marijuana to a patient for medical purposes.

(d) Section 11357, relating to the possession of marijuana, and Section 11358, relating to the cultivation of marijuana, shall not apply to a patient, or to a patient's primary caregiver, who possesses or cultivates marijuana for the personal medical purposes of the patient upon the written or oral recommendation or approval of a physician.

(e) For the purposes of this section, "primary caregiver" means the individual designated by the person exempted under this act who has consistently assumed responsibility for the housing, health, or safety of that person.

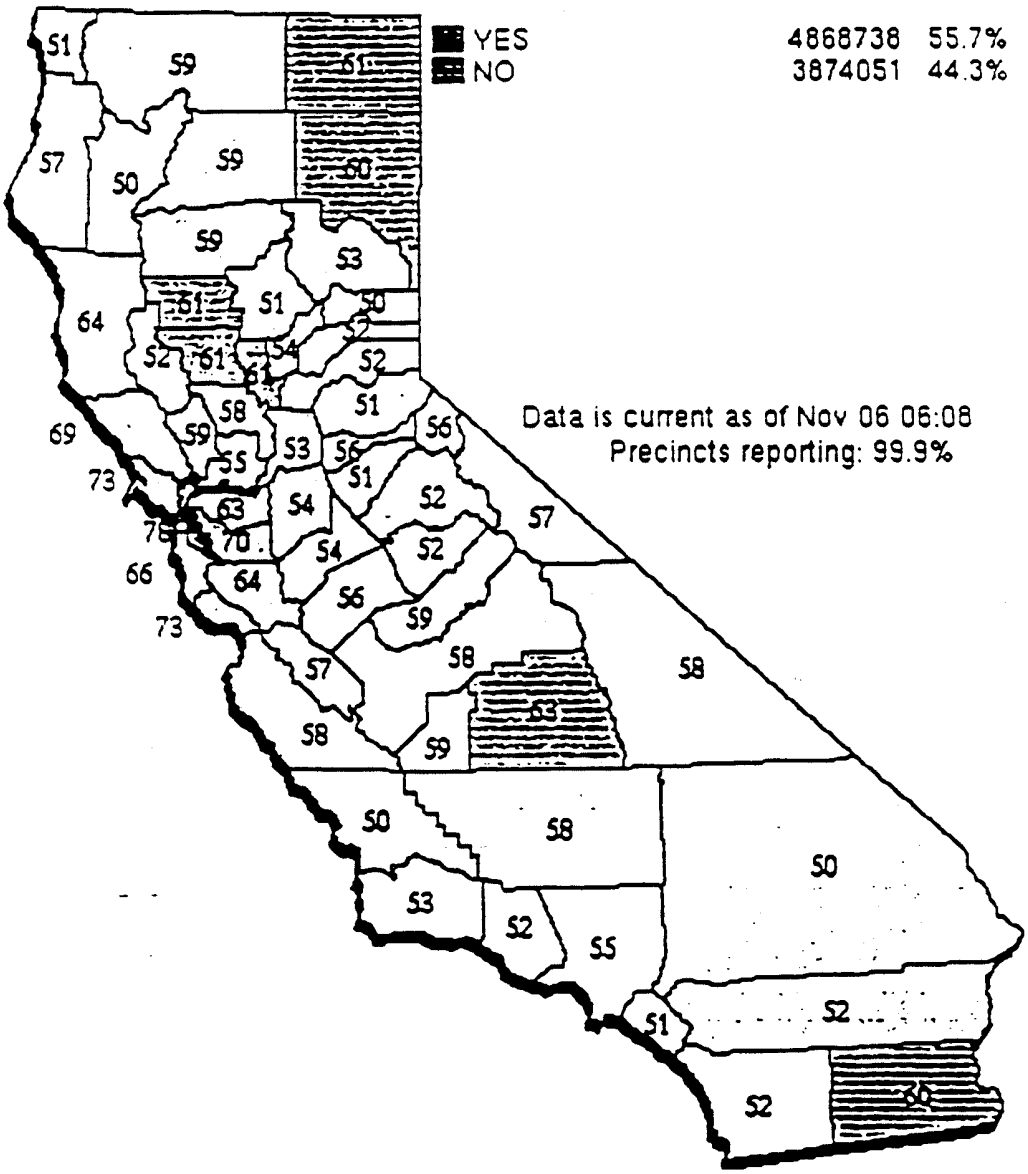
SECTION 2. If any provision of this measure or the application thereof to any person or circumstance is held invalid, that invalidity shall not affect other provisions or applications of the measure which can be given effect without the invalid provision or application, and to this end the provisions of this measure are severable.

For more information, contact: Californians for Medical Rights
1250 Sixth St., Suite 202, Santa Monica, CA 90401
(310) 394-2952 fax: (310) 451-7494

1996 General Election Returns for

Proposition 215 - Marijuana

The number in each county indicates the percentage of the vote cast as indicated by the color.



ER1190

OAKLAND CITY COUNCIL

RESOLUTION NO. 72379 C. M. S.

Ex. B

RESOLUTION ENDORSING AB - 1529, "THE MEDICAL MARIJUANA BILL" and the "COMPASSIONATE USE INITIATIVE OF 1996"

WHEREAS, marijuana has been shown to alleviate nausea and pain associated with cancer and;

WHEREAS, marijuana has been shown to helped people with AIDS to relieve stress and depression, eliminate nausea, reduce and manage pain and fight the "wasting away" syndrome by stimulating the appetite and;

WHEREAS, marijuana has been shown to control spasticity from multiple sclerosis and paralysis and;

WHEREAS, marijuana has been shown to arrest the advance of glaucoma and:

WHEREAS, marijuana has been shown to relieve the pain of arthritis and rheumatism and;

WHEREAS, marijuana has been shown to block epileptic seizures and help migraine headaches and;

WHEREAS, AB - 1529 and the "Compassionate Use Initiative of 1996" will not legalize the personal use of marijuana;

LET IT BE RESOLVED that the Oakland City Council endorses the passage of AB - 1529, "THE MEDICAL MARIJUANA BILL"; and let it be

FURTHER RESOLVED that the Oakland City Council endorses the "Compassionate Use Initiative of 1996".

I certify that the foregoing is a full, true and correct copy of a Resolution passed by the City Council of the City of Oakland, California on December 12, 1995

CEDA FLOYD
City Clerk and Clerk of the Council

Per Margie Sosa *Deputy*

C AKLAND CITY COUN IL

RESOLUTION NO. 72516 C. M. S.

INTRODUCED BY COUNCILMEMBER _____

RESOLUTION ENDORSING H.R. 2618, SUPPORTING THE ACTIVITIES OF THE OAKLAND CANNABIS BUYER'S CLUB AND DECLARING THAT THE INVESTIGATION AND ARREST OF INDIVIDUALS INVOLVED WITH THE MEDICAL USE OF MARIJUANA SHALL BE A LOW PRIORITY FOR THE CITY OF OAKLAND

WHEREAS, marijuana has been shown to help alleviate pain and discomfort in people suffering from a variety of illnesses including AIDS, cancer, glaucoma, and multiple sclerosis; and,

WHEREAS, marijuana has alleviated the suffering of people with chronic illnesses when no other medications have been effective; and,

WHEREAS, the use of marijuana is presently unlawful even under the supervision of physician; and

WHEREAS, the illegal purchase of marijuana by people already suffering with chronic illnesses subjects them to further suffering in the form of potential arrest and prosecution; and

WHEREAS, Representative Barney Frank (MA) and local co-sponsors Representative Ronald Dellums and Pete Stark have introduced H.R. 2618 which would allow physicians to prescribe marijuana for medical purposes and would insure the production of marijuana to meet the need for medical use; and

WHEREAS, the Oakland Cannabis Buyer's Club provides a way for patients needing to purchase marijuana for medical use to do so with greater ease and less risk of arrest and prosecution; and

WHEREAS, the City of Oakland wishes to declare its desire not to expend City resources in any investigation, detention, arrest or prosecution arising out of alleged violations of state and federal law regarding the distribution of marijuana for compassionate medical use; and

WHEREAS, the Oakland City Council passed Resolution 72379 C.M.S. endorsing state legislation AB 1529, "The Medical Marijuana Bill" and the "Compassionate Use Initiative of 1996;" now, therefore, be it

RESOLVED: That the Oakland City Council endorses of the passage of H.R. 2618; and be it further

RESOLVED: That the Oakland City Council authorizes the City Manager to instruct the City's federal lobbyists to work in support of H.R. 2618; and be it further

RESOLVED: That, the Mayor and City Council hereby declare that it shall be the policy of the City of Oakland that the investigation and arrest of members of the Oakland Cannabis Buyers' Club for purchasing, selling and distributing marijuana for medical purposes shall be a low priority; and be it further

RESOLVED: That, the Mayor and City Council hereby declare that it shall be the policy of the City of Oakland that the investigation and arrest of persons for planting, cultivating, purchasing, and/or possessing marijuana shall be a low priority for the City of Oakland if such persons have been medically diagnosed as suffering from an illness or injury, the symptoms of which may be alleviated by the medicinal use of marijuana; and be it further

RESOLVED: That, the Mayor and City Council hereby declare that it shall be the policy of the City of Oakland that the investigation and arrest of persons for cultivating, purchasing, possessing and/or distributing marijuana shall be a low priority for the City of Oakland if such persons purchase or possess marijuana for, and/or distribute marijuana to patients, whose physicians have determined that they are suffering physical pain that may be alleviated by the medicinal use of marijuana; and be it further

RESOLVED: That, the Mayor and City Council call upon the Alameda County District Attorney to cease prosecution of persons involved in the medical use of marijuana; and be it further

RESOLVED: That if any provision of this resolution is declared by a court of competent jurisdiction to be contrary to any statute, regulation or judicial decision, or its applicability to any agency, person or circumstances is held invalid, the validity of the remainder of this resolution and it applicability to any other agency, person or circumstance shall not be affected.

IN COUNCIL, OAKLAND, CALIFORNIA, MAR 12 1996 19 _____

PASSED BY THE FOLLOWING VOTE:

AYES- BAYTON, CHANG, DE LA FUENTE, ~~JORDAN~~, MILEY, RUSSO, SPEES, ~~WOODS-JONES~~, and PRESIDENT HARRIS — 7

NOES-NONE

ABSENT-NONE

ABSTENTION-NONE

Excused - Jordan/Woods-Jones - 2

ATTEST: Ceda Floyd
CEDA FLOYD
City Clerk and Clerk of the Council
of the City of Oakland, California

(CC-244 (1-95)

OAKLAND CITY COUNCIL

RESOLUTION NO. 72881 C. M. S.

INTRODUCED BY COUNCILMEMBER _____

BJP:trc

RESOLUTION ESTABLISHING A WORKING GROUP TO DISCUSS AND MAKE RECOMMENDATIONS TO THE CITY COUNCIL REGARDING THE MEDICAL MARIJUANA POLICY OF THE CITY OF OAKLAND

WHEREAS, marijuana has been shown to help alleviate pain and discomfort in people suffering from a variety of illnesses including AIDS, cancer, glaucoma, and multiple sclerosis; and

WHEREAS, marijuana has alleviated the suffering of people with chronic illnesses when no other medications have been effective; and

WHEREAS, the use of marijuana is currently unlawful even under the supervision of a physician, and

WHEREAS, the illegal purchase of marijuana by people already suffering chronic illnesses subjects them to further suffering in the form of potential arrest and prosecution; and

WHEREAS, the Oakland Cannabis Buyers Club provides a way for patients needing to purchase marijuana for medical use to do so with greater ease and less risk of arrest and prosecution; and

WHEREAS, the Oakland City Council passed Resolution 72516 C.M.S., supporting the activities of the Oakland Cannabis Buyers Club and declaring it to be the policy of the City of Oakland that the arrest of individuals involved with the medical use of marijuana shall be a "low priority" for the City of Oakland; and

WHEREAS, to the extent permitted by applicable law, the City of Oakland wishes not to expend any City resources, including but not limited to those of the Oakland Police Department, in any investigation, detention, arrest, and/or prosecution arising out of alleged violations of state or federal law regarding the cultivation, distribution, sale, purchase, and/or possession of marijuana for medicinal purposes; now therefore, be it

RESOLVED: that a Working Group be established to discuss and make recommendation to the City Council regarding refinement of the City's medical marijuana policy; and be it

FURTHER RESOLVED: that said Working Group shall consist of representatives designated by the City Manager and interested members of the public; and be it

FURTHER RESOLVED: that said Working Group shall consider legislative and administrative methods to insure enforcement of and compliance with the City's medical marijuana policy; and be it

FURTHER RESOLVED: that said Working Group shall consider the feasibility of any other matters pertaining to the City's medical marijuana policy; and be it

FURTHER RESOLVED: that said Working Group shall report to the Public Safety, Health, Human Services and the Family Committee no later than October 1, 1996, concerning the results of its discussions and any recommendations regarding the refinement of the City's medical marijuana policy.

I certify that the foregoing is a full, true and correct copy of a Resolution passed by the City Council of the City of Oakland, California on July 30, 1996.

CEDA FLOYD
City Clerk and Clerk of the Council

Per Margie Sosa *Deputy*

C .KLAND CITY COUNC

RESOLUTION NO. 73555 C.M.S.

RESOLUTION SUPPORTING MEDICAL MARIJUANA ACTIVITIES IN THE CITY OF OAKLAND AND DECLARING THAT THE INVESTIGATION AND/OR ARREST OF INDIVIDUALS INVOLVED WITH THE CULTIVATION, MANUFACTURE, AND/OR TRANSPORTATION OF MEDICAL MARIJUANA PRODUCTS SHALL BE A LOW PRIORITY FOR THE CITY OF OAKLAND

WHEREAS, on November 5, 1996, the voters of California passed Proposition 215, the Compassionate Use Act of 1996, by a YES vote of 55.7 percent, and the residents of Oakland voted YES for Proposition 215 by an overwhelming 79.3 percent; and

WHEREAS, marijuana had been shown to help alleviate pain and discomfort in people suffering from a variety of illnesses including AIDS, cancer, glaucoma, and multiple sclerosis when no other medications have been effective; and

WHEREAS, cultivation of medicinal strains of marijuana, the manufacture of medical cannabis products such as oral preparations, and the transportation of marijuana and cannabis products for medical purposes may remain illegal notwithstanding the passage of Proposition 215; and

WHEREAS, there is a need to ensure that patients have access to a safe and affordable supply of medical grade marijuana and cannabis products; and

WHEREAS, the Oakland City Council passed Resolution 72379 C.M.S. endorsing the Compassionate Use Act of 1996 and similar measures; and

WHEREAS, the Oakland City Council passed Resolution 72516 C.M.S. supporting the activities of the Oakland Cannabis Buyers Club and declaring it to be the policy of the City of Oakland that the investigation and arrest of certain individuals involved with the medical use of marijuana shall be a low priority for the City of Oakland; and

WHEREAS, the Oakland City Council passed Resolution 72881 C.M.S. establishing a Working Group to make recommendations regarding the City's medical marijuana policy; and

WHEREAS, to the extent permitted by applicable law, the City of Oakland wishes not to expend any City resources, including but not limited to those of the Oakland Police Department, in any investigation, detention, arrest, and/or prosecution arising out of alleged violations of state or federal law regarding the cultivation, manufacture, or transportation of marijuana or cannabis products for medical purposes; now therefore, be it

RESOLVED: that the Mayor and City Council hereby declare that it shall be the policy of the City of Oakland that the investigation, detention, arrest, or prosecution of a person and/or that person's primary caregiver for the cultivation, manufacture, or transportation of marijuana or cannabis products shall be a low priority for the City of Oakland if such person has been medically diagnosed as suffering from a serious illness or injury, the symptoms of which may be alleviated by the medicinal use of marijuana and such cultivation, manufacture and/or transportation of marijuana or cannabis products is for the personal medical use of such person upon the written or oral recommendation or approval of a physician; and, be it further

RESOLVED: that the Mayor and City Council hereby declare that it shall be the policy of the City of Oakland that investigation, detention, arrest, and/or prosecution of persons for the cultivation, manufacture or transportation of marijuana or cannabis products shall be a low priority for the City of Oakland if such persons cultivate, manufacture, or transport marijuana or cannabis products for patients whose physicians have determined that they are suffering from a serious illness or injury, the symptoms of which may be alleviated by the medicinal use of marijuana and have recommended or approved medical marijuana use for such patients; and be it further

RESOLVED: that the Mayor and City Council call upon the Alameda County District Attorney not to prosecute persons involved with the possession, purchase, distribution, cultivation, manufacture or transportation of marijuana or cannabis products for medical use; and be it further

RESOLVED: that if any provision of this Resolution is declared by a court of competent jurisdiction to be contrary to any statute, regulation, or judicial decision, or its applicability to any agency, person, or circumstance is held invalid, the validity of the remainder of this resolution and its applicability to any other agency, person, or circumstances shall not be affected.

IN COUNCIL, OAKLAND, CALIFORNIA, JUN 03 1997, 19___

PASSED BY THE FOLLOWING VOTE:

AYES- BRUNNER, CHANG, DE LA FUENTE, MILEY, NADEL, REID, RUSSO, SPEES, and PRESIDENT HARRIS — 9

NOES- None

ABSENT- None

ABSTENTION- None

ATTEST: Ceda Floyd
CEDA FLOYD
City Clerk and Clerk of the Council
of the City of Oakland, California

OAKLAND CITY COUNCIL

RESOLUTION NO. 74039 C.M.S.

RESOLUTION CALLING UPON FEDERAL AUTHORITIES TO DESIST THEIR EFFORTS TO TERMINATE THE OPERATIONS OF THE OAKLAND CANNABIS BUYERS' COOPERATIVE

WHEREAS, in November 1996 the voters of the State of California passed Proposition 215, the Compassionate Use Act of 1996, to "ensure that seriously ill Californians have the right to obtain and use marijuana for medical purposes" by a YES vote of 55.7 percent, and the residents of Oakland voted YES for Proposition 215 by an overwhelming 79.3 percent; and

WHEREAS, the City Council of the City of Oakland finds that many of its City residents are suffering from life-threatening or serious illnesses whose painful symptoms are alleviated by the ingestion of cannabis; and

WHEREAS, the City of Oakland has repeatedly expressed its support for access to a safe and affordable supply of marijuana for medicinal purposes and the operations of the Oakland Cannabis Buyers' Cooperative in Resolution Nos. 72379 C.M.S., 72516 C.M.S., 72881 C.M.S., and 73555 C.M.S.; and

WHEREAS, the City Council finds that the Oakland Cannabis Buyers' Cooperative has served the aforementioned residents with a well-organized, safe, and responsible opportunity to obtain cannabis in furtherance of a course of medical treatment; and

WHEREAS, federal law enforcement authorities have threatened to disrupt and prevent ill Oakland residents' access to cannabis by filing suit to enjoin the Oakland Cannabis Buyers' Cooperative from supplying medical marijuana and to shut down its operations; and

WHEREAS, the federal law enforcement policy impairs public safety by encouraging a market for street narcotic peddlers to sell cannabis to Oakland's ill citizens; now therefore be it

RESOLVED: the Mayor and the Oakland City Council urge the federal government to desist from any and all actions that pose obstacles to access to cannabis for Oakland residents whose physicians have determined that their health will benefit from the use of marijuana and recommended medical marijuana use for such residents; and be it

FURTHER RESOLVED: the Mayor and the Oakland City Council endorse Senator John Vasconcello's call for a statewide summit on the distribution of medical marijuana; and be it

FURTHER RESOLVED: the Mayor and the Oakland City Council urge the Alameda County Board of Supervisors to declare a state of medical emergency; and be it

FURTHER RESOLVED: the Mayor and the Oakland City Council express their support of the furtherance of medical marijuana research; and be it

FURTHER RESOLVED: copies of this resolution shall be forwarded to Senators Boxer and Feinstein and Congressman Ron Dellums urging the federal policy-makers to dismiss current lawsuits impacting California's cannabis buyers' clubs and cooperatives.

I certify that the foregoing is a full, true and correct copy of a Resolution passed by the City Council of the City of Oakland, California on January 27, 1998

CEDA FLOYD
City Clerk and Clerk of the Council

Per _____ *Deputy*

ADMINISTRATIVE MEMO
Oakland Police Department

TO	DATE	NUMBER	OUT DATE
BUREAU COMMANDERS (BFO)	11 Dec 96	-	-
SUBJECT: MEDICINAL USE OF MARIJUANA			

The City Council has adopted a resolution in support of the medicinal use of marijuana as a means of alleviating pain and discomfort for individuals suffering from medical illnesses.

In accordance with the subsequent directive of the City Manager to handle medicinal marijuana activity (in violation of Health and Safety Code 11357, relating to the possession of marijuana, and 11358, relating to the cultivation of marijuana) as a low priority, the following procedures will be implemented immediately:

- Citizen calls for service requesting police intervention at sites where such activity is occurring shall be assigned a "D" priority by Communications Division staff.

- At both field and dispatch levels, every effort shall be made to obtain and record the identity of the reporting citizen(s).

- Field units receiving a dispatched assignment or initiating a contact with persons purportedly involved in the use of marijuana for medicinal purposes shall summon a command-level officer to the scene if an enforcement action (citation or arrest) for the 11357 H&S or 11358 H&S violation is intended.

- The command officer shall evaluate the facts and exercise the discretion and decision-making required to resolve the incident, in accordance with the low-priority policy.

- If an enforcement action is to be taken, the command officer shall promptly notify his/her Bureau Commander and provide him with a written summary of the incident and a copy of all pertinent documents.

- Incidents involving persons who wish to make citizen arrests for the law violation shall be handled in the normal manner.

- Discretion to arrest will be left with the officer and commander at the scene, based upon the facts presented to them at the time. The marijuana should be turned in as evidence for follow-up investigation by the Vice/Narcotics Section.

There are varied and opposing views--professional, legal and medical in nature--regarding the practice of medicinal use of marijuana as a means of alleviating symptoms and controlling chronic pain of patients with specific medical conditions.

Nevertheless, the recent passage of Proposition 215 by California voters has now created law. Federal and state officials are reviewing the initiative and may issue guidelines in the near future. In the interim, the Department will continue its participation on a City working group to identify and resolve local implementation issues. As agreements are reached or decisions made, additional procedural guidelines will be set forth in Departmental publications or communications.

Interim training to all commanders in general and BFO commanders in particular shall be provided over the next 3-4 weeks by Lieutenant Peterson.

Joseph Samuels, Jr.
Chief of Police

CITY OF OAKLAND

Memorandum

TO: Bureau of Field Operations
ATTN: Command Staff
FROM: Vice/Narcotics Section
DATE: 12 Dec 96

RE: Medicinal Marijuana Enforcement

Attached is a copy of an administrative memorandum you will be receiving shortly outlining Chief's Samuels' guidelines for the enforcement of Proposition 215. It is similar to the guidelines dealing with the needle exchange issue. The primary people you will come into contact with will be members of the Oakland Cannabis Buyer's Club (CBC) who are working with us (to the extent they can) to find a way to make this thing work until the issue is settled in the courts.

Clients of the CBC are being issued new photo identification cards with a 24-hour number to contact to verify they are medicinal members. The City's working group has agreed to accept these new cards as a legitimate means of verifying identification if the person has no driver's license, etc. You may come into contact with older ID cards until the transition is complete; these more than likely will be valid.. I would assume non-CBC members will claim in some fashion to be medicinal marijuana users; they may, or may not, have some form of doctor verification.

In evaluating whether an arrest should be made, you should consider the intent of Proposition 215 and the City Council's resolution supporting it and setting a low priority on enforcement. Each case should be decided on its own merits.

It is requested the identification cards not be seized without a valid need. All information on the card should be listed on the report. The marijuana should be seized and turned into criminalistics. All such incidents require a report in addition to any citation which may be issued. Follow-up responsibility for verifying the medicinal use will rest with the Vice/Narcotics charging officers. The DA will make charging decisions. Ultimately, a court order will have to be initiated by the patient/suspect if no charges are filed.

I realize this is confusing; feel free to call me anytime, day or night. I will try to provide some guidance based upon what I know about the issue.

Peter A. Peterson
Lieutenant of Police
Vice/Narcotics Section

Ex. C

Medicinal Cannabis User Initial Questionnaire

Today's Date _____

Identifying Data

Last name_____, First name _____ Middle Initial __
Address _____ City _____ State ____ Zip _____
Res Ph _____-_____-_____ Work Ph _____-_____-_____ ext____ Fax _____-_____-____
Birthdate (MMDDYY)_____ SS#___-__-____ Sex M_ F_ Ethnic Wh_B_Hisp_Or_ NatAm_
Other _____ Education _____Occupation(s)_____ Unemployed_ Disabled_
Marital Status: Single_ Mar_ Sep_ Div_ W_ Living situation:_ Alone _ Couple_ Group_ Apartment_ House_ Institution_ Homeless_
Health Insurance None_ Medicaid_ Medicare_ Workers Compensation_ Other health plan._
(specify)_____ ID Number _____ GroupNumber_____
Address _____ City _____ State ___ Zip _____ Phone ___-___-____x _____
Referred by: Self _ Name_____ Institution _____
Address _____ City _____ State __ Zip_____
Phone ___-___-____x _____ Fax ___-___-____ Pager ___-___-____

Chief Complaint(s) circle and rank in importance: example: AIDS related illness 1 anorexia 2

1. Alcoholism
2. Alcohol Abuse
3. Sedative/Opiate Habit
4. Cocaine or Speed Habit
5. Nicotine Habit
6. AIDS related illness
7. Cancer & cancer Rx
8. Anorexia
9. Nausea
10. Vomiting
11. Diarrhea
12. Irritable bowel
13. Colitis
14. Cron's disease
15. Gastritis
16. Pancreatitis
17. Hepatitis
18. Peptic Ulcer
19. Antibiotic
20. Asthma
21. Sinusitis
22. Cough
23. Anxiety
24. Panic attacks
25. Insomnia
26. Mania
27. Depression
28. Lethargy
29. Weakness
30. Chronic Fatigue Syndrome
31. Epilepsy
32. Delirium Tremens
33. Dementia
34. Multiple Sclerosis
35. Huntington's Chorea
36. Cerebral Palsy
37. Brain Trauma
38. Spinal Cord Injury
39. Muscle spasm
40. Parkinson's disease
41. Tremor
42. Peripheal neuropathy
43. Tic doloroux
44. Tourette's syndrome
45. Glaucoma
46. Menstrual cramps
47. Labor pains
48. Migraine
49. Meniere's Disease
50. Hypertension
51. Itching
52. Hiccough
53. Arthritis
54. Carpal Tunnel Syndrome
55. Lupus, scleroderma
56. Amyloidosis
57. Conjunctivitis
58. Other Pain (specify source)_____
59. External Use ____
60. Drug Side Effect control (specify)____
61. Decrease Use of Other Drugs (specify)_____
62. Substitute for Other Drugs (specify) _____
63. Other _____

Chief Complaint _____ ICD9-CM Diagnoses _____ _____ _____
History ofPresent Illness: (date of onset, course) _____
PastMedicalHistory: (Allergies & adverse drug reactions):_____
Family Medical History:_____
Social History: _____ Drug law arrests/convictions: None_ Yes (specify) _____
Cannabis type preferred: Sinsemilla_ Mexican_ Hashish_ No preference Other_____
Age or date Use Begun:_____ Marinol ®(dronabinol) 2.5 mg _ 5 mg _ 10 mg _ result (+)_ (0)_ (-)_
Route: Oral_ Inhaled: Joint_ Pipe_ Water Pipe_ Vaporizer_ Other (specify):_____
Frequency: Monthly_ Weekly_ Semiweekly_ Daily_ Twice a day_ 3 x a day _ 4 x a day _more _
Other drugs using- Rx and Over the Counter_____
Has your physician discussed your use of cannabis with you? Yes _ No _ Discussed any non prescribed psychoactive drugs? (including alcohol and tobacco) Yes _ No _ Remarks _____
Completed by:_____

Ex. D

Medical Admissions Criteria
to Cannabis Buyers' Cooperative
Tod H. Mikuriya, M.D.
Medical Coordinator

Because of the vacuum of clinical knowledge about the therapeutic applications of cannabis caused by cannabis prohibition a widespread condition of ignorance exists. While it is acknowledged that there exists a range of illnesses on the dimension of seriousness objectively, there is none to the person afflicted who is seeking relief. Exclusion because the condition does not appear on a list developed by a group of non-medical politicians or bureaucrats merely perpetuate this clinical ignorance. Therefore the medical criteria are to be inclusive limited only by contemporary classifications of illness.

Medical Criteria
Persons shall have a verified specific diagnosis by a licensed physician that is included within the latest revision of the International Classification of Diseases ICD-9. Or the Diagnostic Statistical Manual DSM-IV vague statements about conditions, disorders, or syndromes without specific information or not recognized by either ICD-9 or DSM-IV are not acceptable.

Mental Disorders Admissions Protocol

Since the inception of Cannabis Buyers' Cooperatives some have expressed concern about the possibility of adverse effects on individuals suffering from emotional or mental disorders.

In clinical interviews I have conducted with members and patients in my psychiatric practice it is my impression that while many definitely benefit from cannabis there are others for whom use of cannabis is contraindicated.

The Cannabis Buyers' Cooperative Protocols seek to both address these concerns and study more fully the effects of cannabis on emotional and mental disorders.

All persons seeking membership in the Cooperative for treatment of conditions listed in DSM-IV or emotional or mental conditions listed in ICD-9 shall be reviewed by mental health professional after verification by intake staff.

Individuals in whom the use of cannabis is or has been problematic shall be excluded. This group includes persons suffering from cannabis related disorders.

Additionally, other emotional and mental conditions may be worsened by the use of cannabis. Some persons are involved in treatment requiring abstinence from cannabis especially those involved in twelve step recovery programs.

Cases where verification or suitability for the program is in dispute shall be reviewed by a panel of volunteer psychiatrists who will make final determination.

Adverse Effects of Cannabis

As with any drug, cannabis is a tool. There will always be individuals that experience adverse consequences from any drug use. The abuse of cannabis had been recognized for millennia. These problems were described by O'Shaughnessey during his observations in India in 1839 which included references in the Persian medical literature. With widespread non medical use of the drug for the past thirty years, psychiatrists have developed classifications of cannabis presented in the latest Diagnostic and Statistical Manual, Revision IV (DSM-IV).

Intoxication/Overdose

Overdose is most common by the oral route since the time from taking the drug until the experience of effects begin is from one to three or more hours. Inexperienced and ignorant first time users will have an unforgettable experience.

The effects of overdose have been numerously described in general, clinical, and scientific literature. Cannabis overdose comprises the majority of listings in the Surgeon General's list, 19th century precursor of the Indicus Medicus. American literary accounts in books: FizHugh Ludlows Hashish Eater and an essay on Hashish by Victor Robinson M.D are expressly devoted to cannabis. Descriptions of experience with the drug as part of travel to areas of indigenous use may be found in English and European literature over the past three centuries. Scientific and medical descriptions of effects of cannabis overdose have been numerous extensive. Before and after its removal in 1937.
The effects of overdose are from the stimulation and sedation of the central nervous system. Stimulation with a flooding of ideas and images that are vivid and rapidly changing. Attention and concentration are markedly impaired. Time perception is significantly altered with minutes seeming like hours. There may be distortion of spatial perception. Secondary physical effects, aside from a speeding up of the heart rate is generally no more than that associated with mild to moderate exercise.

Cannabis-Induced Disorders
292.89 Cannabis Intoxication

A. Recent use of cannabis.
B. Clinically significant maladaptive behavior or psychological changes (e.g. impaired motor coordination, euphoria, anxiety, sensation of slowed time, impaired judgment, social withdrawal) that developed during, or shortly after, cannabis use.
C. Two (or more) of the following signs, developing within 2 hours of cannabis use: (1) conjunctivae injection (2) increased appetite (3) dry mouth (4) tachycardia.
D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.

E. Specify if:
With Perceptual Disturbances: This specifier may be noted when hallucinations with intact reality testing or auditory, visual, or tactile illusions occur in the absence of delirium. Intact reality testing means that the person knows that the hallucinations are induced by the substance and do not represent external reality. When hallucinations occur in the absence of intact reality testing, a diagnosis of Substance-Induced Psychotic Disorder, with Hallucinations should be considered.

292.81 Cannabis Intoxication Delirium
292.11 Cannabis-Induced Psychotic Disorder, With Delusions Specify if with onset during intoxication.
292.89 Cannabis-Induced Anxiety Disorder, Specify if: with onset during Intoxication.

Continuing or chronic use.
Use or abuse? Cannabis, like any other drug, is a tool. Properly utilized with realistic expectations and awareness of its properties, cannabis is a safe and effective medicine. Improperly used with unrealistic expectations and ignorance, adverse effects may result. The onset of unwanted effects may be obvious or insidious. The general etiology is some emotional discomfort for which cannabis is taken to relieve producing undesirable consequences from using the drug itself.
Paranoia and delusional thinking are not uncommon effects of cannabis both acute and chronically. In the acute experience it appears to be from the perceptual distortions of space, time and feelings of detachment.
In chronic use paranoid and delusional thinking appear to be the consequences of the suppression of feelings, the dulling of feelings may alienate the cannabis users from others by diminishing empathetic capabilities. This emotional insensitivity then results in conflict through misperception. Misperception results from the dulling of affect that is important contextual collateral information source. An effective relief of emotional distress then becomes an impediment to relationships with the cannabis user. Feelings are an integral dimension of social perception that convey important contextual information. Cannabis, as an effective sedative and antidepressant, has this undesirable side effect when misused. The relief afforded by the drug may be paid for by complications caused by avoiding dealing with the causes of the emotional pain as well as diminished functioning while under its influence.
Cognitive impairment by continuing or overuse of cannabis creates a form of mild dementia that may persist for up to several weeks after discontinuing the drug.

Individuals sensitive to the drug report a persistent " hangover" that diminishes the ability to pay attention and concentrate. The onset may be insidious, subtle, and gradual. This condition is reversible with abstinence from cannabis.

304.30 Cannabis Dependence

A maladaptive pattern of cannabis use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the same 12 month period:

(1) tolerance, as defined by either of the following;
   (a) a need for markedly increased amounts of the substance to achieve intoxication or desired effect.
   (b) markedly diminished by either of the following;
(2) withdrawal, as manifested by either of the following:
   (a) the characteristic withdrawal syndrome for the substance.
   (b) the same (or a closely related) substance is take to relieve or avoid withdrawal symptoms.
(3) cannabis is often taken in larger amounts or over a longer period than was intended.
(4) there is a persistent desire or unsuccessful efforts to cut down or control cannabis use.
(5) a great deal of time is spent in activities necessary to obtain cannabis (e.g. visiting multiple dealers or driving long distances), use the substance (e.g. chain smoking) or recover from its effects
(6) important social, occupational, or recreational activities are given up or reduced because of cannabis use
(7) cannabis use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been cause or exacerbated by the substance.

305.20 Cannabis Abuse

A. Maladaptive pattern of cannabis use leading to clinically significant impairment or distress, as manifested by one (or more) of the following, occurring within a 12 month period:

1) recurrent cannabis use resulting in a failure to fulfill major role obligations at work, school, or home (e.g. repeated absences or poor work performance related to substance use; cannabis related absences, suspensions, or expulsions from school; neglect of children or household)
2) recurrent cannabis use in situations in which it is physically hazardous (e.g. driving an automobile or operating a machine when impaired by cannabis use)
3) recurrent cannabis related legal problems (e.g. arrests for cannabis relate disorderly conduct)

4) continued cannabis use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance (e.g. arguments with spouse about consequences of intoxication, forgotten promises)

B. The symptoms have never met the criteria for Cannabis Dependence for this class of substance.

232.9 Cannabis Related Disorder not Otherwise Specified

The Cannabis Related not Otherwise Specified category is for disorders associated with the use of cannabis that are not classifiable as one of the disorders listed above.

Ex. E

OAKLAND CANNABIS BUYERS' COOPERATIVE

INFORMATION FORM
(Please print clearly)

Name_____

Street Address _____Apt. Number_____

City _____, State_____ Zip Code_____

Phone Number (_____)_____Date of Birth_____

Driver License #_____State_____ Gender (M or F)____

Caregiver_____DL#_____DOB_____

Physician's Name _____DX #_____

Address, City, State _____PHD#_____

Phone (_____)_____

Specific Diagnosis _____

_____ ICD9 CODE_____

Medication(s)_____

_____

How do you use cannabis? Smoke hi grade___smoke lo grade___edibles___tinture__

Are you politically active?_____

_____ _____
Member Signature Date

_____ _____
Intake By Member #

OAKLAND CANNABIS BUYERS' COOPERATIVE, P.O. Box 70401 Oakland, CA 94612-0401
Phone (510) 832-5346 Fax (510) 986-0534 Email ocbc@ocbc.org Web www.ocbc.org

Ex. F

OAKLAND CANNABIS BUYERS' COOPERATIVE

Authorization for Release of Patient Status
(Please print clearly)

I,_____ hereby authorize my treating physician,
print patient name

Dr._____ to release to the Oakland Cannabis
print physician name
Buyers' Cooperative, my current patient status.

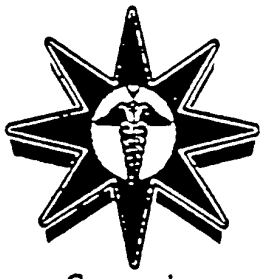
_____ Date _____
Member/ patient signature

Membership number_____

OAKLAND CANNABIS BUYERS' COOPERATIVE, P.O. Box 70401 Oakland, CA 94612-0401
Phone (510) 832-5346 Fax (510) 986-0534 Email ocbc@rocbc.org Web www.rocbc.org

Ex. G

Health and Safety Code 11362.5
PHYSICIAN'S STATEMENT



This certifies that _____ is a patient under my
print patient's name

medical care and supervision for the treatment of _____.
Diagnosis

I have discussed the medical benefits and risks of cannabis use with the patient as a treatment for these medical conditions. I recommend cannabis use for my patient.

If my patient chooses to use cannabis therapeutically, I will continue to monitor his/her medical condition and to provide advice on his/her progress.

I understand that I may be contacted to verify the information in this letter. My patient authorizes me to discuss their medical condition and the contents of this letter, for verification purposes only. I am a physician licensed to practice medicine in the state of California.

_____
Patient's Signature

_____ _____
Physician's Signature Date

_____ _____
Physician's Name (print) N.P./P.A. Signature (optional)

_____ _____
Physician CA License No. N.P./P.A. Name (optional-print)

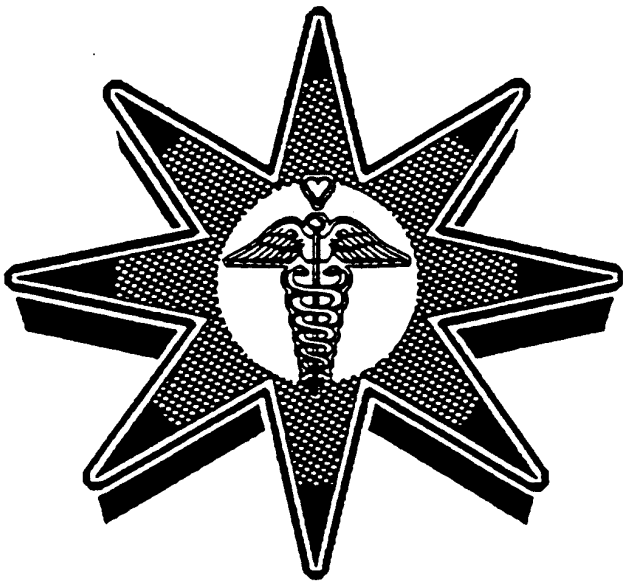
_____
(street)

_____
(City)

(___)_____
Phone Number

Oakland Cannabis Buyers' Cooperative

Ex. H



Compassion

Officer- This crop of medical herb is being grown in its entirety for my personal medical use, and is intended to be free of toxic chemical, fungus, and mold contamination. This crop is safe for use by people with HIV/AIDS and other patients. Any excess will be given to the Oakland Cannabis Buyers' Cooperative. Thank you for your courage and care. If there are any questions regarding this garden please call 1-888-304-1260 (law enforcement use only).

_____

Name, Grower
Oakland Cannabis Buyers' Cooperative

_____

Jeffrey W. Jones
Agent of Oakland Cannabis Buyers' Cooperative

OAKLAND CANNABIS BUYERS' COOPERATIVE, P.O. Box 70401 Oakland, CA 94612-0401
Phone (510) 832-5346 Fax (510) 986-0534 Email ocbc@ocbc.org Web www.ocbc.org

Ex. I

OAKLAND CANNABIS BUYERS' COOPERATIVE

Membership and Informed Consent

Compassion

I, (print clearly)_____, hereby consent to the benefits provided by the Oakland Cannabis Buyers' Co-op (OCBC).

I understand that the OCBC has made no efforts in encouraging me to produce or use any substances for my medical condition. I have been informed by an authorized representative of OCBC that I should continue to seek professional medical advice prior to and during my use of any cannabis product I may acquire through OCBC.

I understand that the OCBC was organized to fill the necessity of medical cannabis. Prompting the passing of the Oakland City Council Resolution Number 72516 C.M.S. which supports the OCBC operations. I further understand that circumstances may require defense of authorization in a court of law and agree to participate in such defense to the extent necessary and practicable.

I understand that the OCBC reserves the right to refuse service(s) to members.

I affirm that I am above eighteen (18) years of age or have the consent of my parent/guardian, and that I have a medical condition(s) as attested to on my information form.

I understand that my contributions to OCBC, through products I may acquire from the organization, are used to insure continued operation of the OCBC and that this transaction, in no way, constitutes commercial promotion.

I understand that medical marijuana, while being a well-known effective therapeutic agent, is still illegal in this country. Therefore, by signing this form, all members of OCBC are committing an act of collective Federal civil resistance.

I authorize the OCBC to acknowledge the fact of my membership, when needed, for the preservation of my medical rights under the Oakland Resolution # 72516 and the Compassionate use Act of 1996.

_____ _____

Member Signature Date

_____ _____

Intake By Member #

OAKLAND CANNABIS BUYERS' COOPERATIVE, P.O. Box 70401 Oakland, CA 94612-0401
Phone (510) 832-5346 Fax (510) 986-0534 Email ocbc@ocbc.org Web www.ocbc.org

Ex. J

Oakland Cannabis Buyers' Cooperative

Compassion

Shawn Malvo
222 Anyplace
Oakland CA 94612
CDL: XXXXXXXXXXX
DOB: 12/05/65
ISSUE DATE:10/24/97

Member # 167

Certificate of Membership

This is to certify that on file with the undersigned officer of the Oakland Cannabis Buyers' Cooperative is a signed statement of a licensed Physician ackowledging and assenting to cannabis therapy for the patient identified on the reverse hereof, who, having satisfied all conditions of membership, is recognized as a Member in good standing of the

Oakland Cannabis Buyers' Cooperative

with all benefits and subject to all conditions as same shall from time to time be established by the Oakland CBC in accordance with its rules and Protocols. Presentation of this card shall be evidence that said patient's Physician would consider prescribing cannabis if he/she were legally able to do so, assents to the theraputic use, and has agreed to monitor and provide medical advice on the patient's progress.

Hours: M & F 11am - 7pm T, W, TH 11am - 1pm, 5pm - 7pm

Office # (510) 832-5346

24 hr Emergency voicemail/pager service (for Law Enforcement use only) 1-888-340-1260.

[redacted]

Jeffrey W. Jones
Executive Director

Ex. K

Safe Use of Cannabis
1996 Tod H. Mikuriya, M.D.

Dosage and Route of Administration

Starting with a small amount and gradually increasing the dose is the key to avoiding unwanted mental side effects. This is called titration- self-titration if adjusted by the user.

Mental Effect Impatience and overdosing with oral cannabis is the most frequent mention of the drug in medical literature of the 1800's. Oral cannabis over-dosage is much more intense and longer lasting than from the inhaled route. Because of the two to three hours before onset of effects, a common mistake of the inexperienced is to repeat the oral dose with the consequence of overdosing.

Over-dosage

Should you take too much cannabis you may expect the mental effects of time distortion, racing thoughts, disorientation, speeding heart rate, dry mouth, and reddened eyes. The greater the dose, the greater intensity and longer these stimulant effects will last before sinking into a deep sleep. No lasting harm will result but the experience will not be forgotten.

Other Adverse Effects

Other adverse mental effects are a prolonged dullness after use of paranoia and a fear of loss of control. Cannabis, an effective relaxant, can cause an alienation or detachment. The price of relief of tension may be a dulling or suppression of feelings. Insensitivity to feelings of other or situations may result.

Set and Setting

The result of the drug is a combination of set (expectations), setting, personality, and the drug.

Best case: Enjoying a puff or two sitting at home with a friend at the end of the day.
Worst case: Taking a puff driving down the freeway, then looking sideways into the eyes of a cop.

Personality and Individual Difference

Individuals with personalities that are prone to substance abuse, allergy, sensitivity, or adverse reactions to other medicines should exert greater caution and try the drug only if absolutely necessary

Dependence and Withdrawal

Because cannabis is such an effective medicine for the relief of many uncomfortable conditions, using the
drug on a continuing basis is not uncommon. One must decide issues of personal risks/benefits of continuing using cannabis.

Withdrawal from chronic cannabis use produces several nights of more intense dreaming and possibly some slightly increased nervousness during the day. Some increased nervousness during the day. Some increase in exercise, if possible, and/or small amounts of other sedatives will ease the transition from cannabis dependence.

Ex. L

Principals of Responsible Cannabis Use

I. No Driving
The responsible consumer of cannabis does not operate a motor vehicle or other dangerous machinery while impaired by cannabis or - like other responsible citizens-any other substance or condition, including some medicines and fatigue. Although cannabis is said by most experts to be safer than many prescription drugs, responsible cannabis users never operate motor vehicles in an impaired condition. Public safety demands not only that impaired drivers be taken off the road, but also that objective measures of impairment other than chemical testing be developed and used.

II. Set and Setting
The responsible cannabis user will carefully consider his or her set and setting, regulating use accordingly. "Set" refers to the consumer's values, attitudes, experience and personality. "Setting" means the consumer's physical and social circumstances. The responsible cannabis consumer will be vigilant as to conditions-time, place, mood, etc- and should not hesitate to say no when those conditions are not conducive to a safe, pleasant and/or productive experience.

III. Resist Abuse
Use of cannabis to the extent that it impairs health, personal development or achievement is abuse, is resisted by responsible cannabis users. Abuse means harm. Some cannabis use is harmful; most is not. That which is harmful should be discouraged; that which is not, need not be. Wars have been waged in the name of eradicating "drug abuse," but instead of focusing on abuse, enforcement measures have been diluted by targeting all drug use, whether abusive or not. If Marijuana abuse is to be targeted, it is essential that clear standards be developed to identify it.

IV. Respect Other's Rights
The responsible cannabis user does not violate the rights of others, observes accepted standards of courtesy and propriety and respects the preferences of those who wish to avoid cannabis entirely. No one may violate the rights of others, and no substance use excuses any such violation. Regardless of the cannabis' legal status, responsible users will adhere to emerging tobacco smoking protocols in public and private places.

EXHIBIT 2

Oakland Cannabis
Buyers' Cooperative

OAKLAND CANNABIS BUYERS' COOPERATIVE

Health and Safety Code 11362.5

VERIFICATION OF PHYSICIAN'S WRITTEN RECOMMENDATION

_____ _____

Patient's Name (printed) Membership Number

I have documents stating the physician indicated below attests that:

___ He/She is aware of this patient's use of medical cannabis.
___ He/She has discussed the risks and benefits of cannabis use with this patient.
___ He/She will monitor the use of medical cannabis for this patient.
___ He/She recommends or approves the use of medical cannabis for this patient.

OR

___ He/She recommends <u>against</u> medical cannabis for this patient.

Verification Information was provided by _____ on _____ at _____

_____Office staff at physician's phone number
_____ Direct discussion with physician
_____ Nurse at physician's phone number
_____ Nurse practitioner or physician's assistant at physician's phone number

---

_____ _____

Physician's Name Date seen by Physician

_____ _____

Address M.D. Specified Expiration Date (optional)

_____ _____

CA License No. (obtain by phone)

(_____)_____ _____

Phone License Expiration Date

_____

ICD9 Code

I have verified this physician's California license as current and valid by checking with the California Board of Medical Quality Assurance. Date verified: _____

_____ _____

Employee's Name Employee's Signature

OAKLAND CANNABIS BUYERS' COOPERATIVE, P.O. Box 70401 Oakland, CA 94612-0401
Phone (510) 832-5346 Fax (510) 986-0534 Email ocbc@rxcbc.org Web www.rxcbc.org

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JAMES J. BROSNAHAN (State Bar No. 34555)
ANNETTE P. CARNEGIE (State Bar No. 118624)
ANDREW A. STECKLER (State Bar No. 163390)
CHRISTINA KIRK-KAZHE(State Bar No. 192158)
MORRISON & FOERSTER LLP
425 Market Street
San Francisco, California 94105-2482
Telephone: (415) 268-7000

Attorneys for Defendants
OAKLAND CANNABIS BUYERS'
COOPERATIVE AND JEFFREY JONES

IN THE UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

UNITED STATES OF AMERICA,

Plaintiff,

v.

CANNABIS CULTIVATOR'S CLUB, et al.,

Defendants.

AND RELATED ACTIONS.

No. C 98-00085 CRB
C 98-00086 CRB
C 98-00087 CRB
C 98-00088 CRB
C 98 00089 CRB
C 98 00245 CRB

DECLARATION OF LESTER GRINSPOON, M.D., IN SUPPORT OF DEFENDANTS' RESPONSE TO SHOW CAUSE ORDER

Date: September 28, 1998
Time: 10:00 a.m.
Courtroom: 8

Hon. Charles R. Breyer

I, LESTER GRINSPOON, M.D., declare:

1. I am an Associate Professor of Psychiatry, at Harvard Medical School in Boston, Massachusetts, where I have taught for more than 35 years. I am also Editor of The Harvard Mental Health Letter. My area of research is psychoactive drugs. I am particularly interested in the medicinal properties of cannabis. If called as a witness, I could and would testify competently to the facts set forth below. I have attached a copy of my *Curriculum Vitae* as Exhibit A. For the Court's convenience, where appropriate I have provided footnotes referencing the sources upon which I have relied.

2. I received a bachelor's degree in 1951 from Tufts College. I received a doctorate in 1955 from Harvard Medical School. I subsequently completed an internship in Medicine at Beth Israel Hospital in Boston, Massachusetts (1955-1956), and a residency in psychiatry at Massachusetts Mental Health Center (1958-1961). I received further training as a field instructor for the National Cancer Institute in Los Angeles, California (1956-1958).

3. Since joining the Harvard Medical School faculty in 1973, I have held numerous positions, including Associate Clinical Professor, Assistant Clinical Professor, and Senior Psychiatrist for the Massachusetts Mental Health Center. My other research and teaching appointments include, Assistant in Medicine for University of Southern California School of Medicine (1956-1958), Director of the Clinical Research Center for Massachusetts Mental Health Center (1961-1968), Consultant in Psychiatry and Research for Boston State Hospital (1963-1970) and an Examiner for the American Board of Psychiatry and Neurology (1969-present). I have also held several positions for the American Psychiatric Association such as Vice-Chairperson (1975-1977) and Chairperson for the Council on Research (1977-1979), Vice-Chairperson (1979-1980) and Chairperson for Scientific Program Committee (1980-1984).

4. I serve on several professional and community boards. These include many years as a member of the Beneficial Plant Research Association (1980-1984), the Drug Policy Foundation (1987-present), Physicians for Human Rights (1986-present), the Drug Research Group (1995-present), and Scientific and Policy Advisors of the American Council on Science and Health (1997 -

present). I recently served as Chairperson for the Board of Directors for the National Organization for the Reform of Marihuana Laws (1993-1995). I was also a faculty member for the Zinberg Center for Addiction Studies in Cambridge, Massachusetts (1993-1996). I am currently on several Editorial Boards, including editor for the Harvard Mental Health Letter (1984-present), the Journal of Social Pharmacology (1985-present), and Addiction Research (1991-present).

5. I have testified before the National Marijuana Commission Subcommittee of the Senate Small Business Committee in 1972, the House Select Committee on Narcotics in 1977, 1979 and 1989, the Controlled Substances Advisory Committee, the Drug Abuse Research Advisory Committee in 1978, the Senate Judiciary Committee in 1980, and the House Judiciary Committee, Sub-Committee on Crime in 1997. I am also a frequent presenter at national and international conferences.

6. I have authored and co-authored some 154 articles in scholarly and professional journals, most of which deal with clinical comparisons of drug therapies. I have contributed chapters of medical textbooks, research publications, clinical protocols and conference reports. My work has been published in the *Journal of Clinical Endocrinology and Metabolism*, *New England Journal of Medicine*, *Journal of the National Cancer Institute*, *Mental Patients in Transition*, *Science Digest*, *Archives of General Psychiatry*, *Comprehensive Psychiatry*, *Clinical Medicine*, *Journal of Psychiatric Research*, *Psychosomatic Medicine*, *Diseases of the Nervous System*, *American Journal of Psychiatry*, *Scientific America*, *Psychopharmacologia*, *International Journal of Psychiatry*, *Encyclopedia of Science and Technology*, *International Narcotic Report*, *New York Law Journal*, *Journal of Consulting and Clinical Psychology*, *Drug Therapy*, *World Journal of Psychosynthesis*, *Medical Tribune*, *Contemporary Drug Problems*, *Social Science and Medicine*, *Villanova Law Review*, *Congressional Digest*, *Biological Psychiatry*, *The Sciences*, *Journal of Ethnopharmacology*, *Handbook on Drug Abuse*, *The Hastings Center Report*, *Harvard Mental Health Letter*, *Harper's*, *Nova Law Review*, *New Harvard Guide to Psychiatry*, *Journal of State Government*, *Cancer Treatment & Marijuana Therapy*, *Journal of Drug Issues*, *North Carolina Journal of International Law & Commercial Regulation*, *Encyclopedia of Human Biology*, *Drugs, Society and Behavior*,

Journal of American Medical Association, *University of West Los Angeles Law Review*, and *Journal of Psychoactive Drugs*.

7. I have authored and co-authored some 13 books, several of which deal with the history and medical use of cannabis. These books include *Marihuana Reconsidered* (Harvard University Press, 2d ed. 1977), *Psychedelic Drugs Reconsidered* (Basic Books, 2d ed. 1981), *Psychedelic Reflections* (Human Sciences Press, 1982), *The Long Darkness: Psychological and Moral Perspectives on Nuclear Winter* (Yale University Press, 1986), and *Marihuana, The Forbidden Medicine* (Yale University Press, Revised Edition 1997).

8. Based on my research, I have found that cannabis is remarkably safe. Although not harmless, it is surely less toxic than most of the conventional medicines it could replace if it were legally available. Despite its use by millions of people over thousands of years, cannabis has never caused an overdose death. The most serious concern is respiratory system damage from smoking, but that can easily be addressed by increasing the potency of cannabis and by developing the technology to separate the particulate matter in marijuana smoke from its active ingredients, the cannabinoids (prohibition, incidentally, has prevented this technology from flourishing). Once cannabis regains the place in the U.S. Pharmacopoeia that it lost in 1941 after the passage of the Marihuana Tax Act (1937), it will be among the least toxic substances in that compendium. Right now the greatest danger in using cannabis medically is the illegality that imposes a great deal of anxiety and expense on people who are already suffering.

9. I have done extensive research on the history of the use of cannabis for medical purposes, as well as its legal regulation in the United States. The marijuana, cannabis, or hemp plant is one of the oldest psychoactive plants known to humanity. A native plant of central Asia, cannabis may have been cultivated as much as ten thousand years ago. It was certainly cultivated in China by 4000 B.C. and in Turkestan by 3000 B.C. It has long been used as a medicine in India, China, the Middle East, Southeast Asia, South Africa, and South America. The first evidence of the medicinal use of cannabis was published during the reign of the Chinese Emperor Chen Nun five thousand years ago. Cannabis was recommended for, among other things, malaria and rheumatic pains.

Another Chinese herbalist recommended a mixture of hemp, resin, and wine as an analgesic during surgery. Hemp was also noted as a remedy by Galen and other physicians of the classical and Hellenistic eras, and it was highly valued in medieval Europe.

10. Between 1840 and 1900, more than one hundred papers on the therapeutic uses of cannabis were published in American and European medical journals. It was recommended as an appetite stimulant, muscle relaxant, analgesic, sedative, anticonvulsant, and as a treatment for opium addiction. A professor at the Medical College of Calcutta, W.B. O'Shaughnessy, was the first Western physician to observe the use of cannabis as a medicine. He gave cannabis to animals, satisfied himself that it was safe, and began to use it with patients suffering from rabies, rheumatism, epilepsy, and tetanus. In a report published in 1839, he wrote that he had found tincture of hemp (a solution of cannabis in alcohol, taken orally) to be an effective analgesic. He was also impressed with its muscle relaxant properties and called it "an anticonvulsive remedy of the greatest value." In 1890, J.R. Reynolds, a British physician, summarized thirty years of experience with *Cannabis indica*, finding it valuable in the treatment of various forms of neuralgia, including tic douloureux (a painful facial neurological disorder), and added that it was useful in preventing migraine attacks. He also found it useful for certain kinds of epilepsy, for depression, and sometimes for asthma and dysmenorrhea.

11. The medical use of cannabis was in decline by 1890. It was believed that the potency of cannabis preparations was too variable, and that individual responses to orally ingested cannabis seemed erratic and unpredictable. Another reason for the neglect of research on the analgesic properties of cannabis was that the greatly increased use of opiates after the invention of the hypodermic syringe in the 1850s allowed soluble drugs to be injected for faster pain relief; hemp products are insoluble in water and so cannot easily be administered by injection. Toward the end of the nineteenth century, the development of such synthetic drugs as aspirin, chloral hydrate, and barbiturates, also contributed to the decline of cannabis as a medicine. But these new drugs had, and still have today, striking disadvantages. More than a thousand people die from aspirin-induced bleeding each year in the United States, and barbiturates are, or course, far more dangerous.

12. Cannabis use in the United States was particularly a matter of state or federal regulation until 1915, when the first state, California, prohibited marijuana possession or sale. In 1930, the year in which the Federal Bureau of Narcotics was founded, only sixteen states had laws prohibiting the use of cannabis. In contrast, by 1937, nearly every state had adopted legislation outlawing cannabis. Sociologists have speculated that pressure from the liquor lobby figured among the more subtle factors in this sudden legal onslaught. More important, lack of scientific understanding concerning the effects of cannabis enabled the unsubstantiated statements of the Federal Bureau of Narcotics to go substantially unchallenged. The Marihuana Tax Act of 1937 was the culmination of a series of efforts on the part of the Federal Bureau of Narcotics to generate anti-marijuana legislation.

13. One might have expected physicians looking for better analgesics and hypnotics to turn to cannabinoid substances, but the Marihuana Tax Act of 1937 undermined any such experimentation. The Marihuana Tax Act of 1937 imposed a transfer tax upon certain dealings in marijuana. The Marihuana Tax Act of 1937 provided that anyone who imports, manufactures, produces, compounds, sells, deals in, dispenses, prescribes, administers, or gives away marijuana was required to register, record transactions and pay special taxes depending on the defined purposes. Those who failed to comply were subject to large fines or prison for tax evasion. Although, it was ostensibly designed to prevent nonmedical use of cannabis, the Marihuana Tax Act of 1937 made cannabis so difficult to obtain, that cannabis was removed from the United States Pharmacopoeia and National Formulary in 1941. The Boggs Act of 1951 established mandatory prison terms and large fines for violation of any federal drug law, and the Narcotic Control Act of 1956 strengthened those penalties.

14. In the 1960s, however, the public began to rediscover the medical value of cannabis, as letters appeared in lay publications from people who had learned that it could relieve their asthma, nausea, muscle spasms, or pain and wanted to share that knowledge with readers who were familiar with the drug. Meanwhile, legislative concern about recreational use of cannabis increased, and in 1970 Congress passed the Comprehensive Drug Abuse Prevention and Control Act (also called the

Controlled Substances Act), which assigned psychoactive drugs to five schedules and placed cannabis in Schedule I, the most restrictive.

15. A few patients have been able to obtain medical cannabis legally in the last twenty years. Beginning in the 1970s, thirty-five states passed legislation that would have permitted medical use of cannabis but for the federal law. Several of those states actually established special research programs, with the permission of the federal government, under which patients who were receiving cancer chemotherapy would be allowed to use cannabis. These projects demonstrated the value of both smoked marijuana and oral THC (tetrahydrocannabinol). The FDA approved oral THC (Marinol) as a prescription medicine in 1986. In 1976, the federal government introduced the Individual Treatment Investigational New Drug program (commonly referred to as the Compassionate IND), which provided cannabis to a few patients whose doctors were willing to undergo the paperwork-burdened and time-consuming application process. About three dozen patients eventually received cannabis before the program was discontinued in 1992, and eight survivors are still receiving it — the only persons in the country for whom it is not a forbidden medicine.

16. The most effective spur to the movement for medical marijuana came from the discovery that it could prevent the AIDS wasting syndrome. It is not surprising that the Physicians Association for AIDS Care was one of the medical organizations that endorsed the California initiative prohibiting criminal prosecution of medical marijuana users.

17. I have conducted an extensive review of the literature concerning medical uses of cannabis and I am familiar with studies on the topic. Review of medical literature is a commonly used research tool. I have also studied clinically many patients who have used cannabis for the relief of a variety of symptoms; this clinical experience forms the basis of my book, *Marihuana, The Forbidden Medicine*. In my book I provide first-person accounts of the ways that cannabis alleviates symptoms of cancer chemotherapy, multiple sclerosis, osteoarthritis, glaucoma, AIDS and depressions, as well as symptoms of such less common disorders as Crohn's disease, diabetic gastroparesis, and post-traumatic stress disorder. The patient narratives illustrate not only cannabis's

therapeutic properties but also the unnecessary further pain and anxiety imposed on sick people who must obtain cannabis illegally.

18. Cannabis has several uses in the treatment of cancer. As an appetite stimulant, it can help to slow weight loss in cancer patients. It may also act as a mood elevator. But the most common use is the prevention of nausea and vomiting associated with cancer chemotherapy. About half of patients treated with anticancer drugs suffer from severe nausea and vomiting, which are not only unpleasant and painful but a threat to the effectiveness of the therapy. Retching can cause tears of the esophagus and rib fractures, prevent adequate nutrition, and lead to fluid loss. Some patients find the nausea so intolerable they say they would rather die than go on. The antiemetics most commonly used in chemotherapy are metoclopramide (Reglan), the relatively new ondansetron (Zofran), and the newer granisetron (Kytril). Unfortunately, for many cancer patients these conventional antiemetics do not work at all or provide little relief.

19. The suggestion that cannabis might be used in the treatment of cancer arose in the early 1970s when some young patients receiving cancer chemotherapy found that marijuana smoking reduced their nausea and vomiting. In one study of 56 patients who got no relief from standard antiemetic agents, 78% became symptom-free when they smoked marijuana.[1] Oral tetrahydrocannabinol (THC) has proved effective where the standard drugs were not,[2] but smoking generates faster and more predictable results because it raises THC concentration in the blood more easily to the needed level. Also, it may be hard for a nauseated patient to take oral medicine. In fact, there is strong evidence that most patients suffering from nausea and vomiting prefer smoked marijuana to oral THC.

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[1] Vinciguerra, V., et al. Inhalation Marihuana as an antiemetic for cancer chemotherapy. *New York State Journal of Medicine* 1988; 88:525-527. (Attached as Exhibit B).

[2] Sallan, S.E., et al. Antiemetic effect of delta-9-tetrahydrocannabinol in patients receiving cancer chemotherapy. *New England Journal of Medicine* 1975; 293:795-797. (Attached as Exhibit C).

20. Oncologists may be ahead of other physicians in recognizing the therapeutic potential of cannabis. In the spring of 1990, two investigators randomly selected more than 2,000 members of the American Society of Clinical Oncology (one-third of the membership and mailed them an anonymous questionnaire to learn their views on the use of cannabis in cancer chemotherapy. Almost half of the recipients responded. Although the investigators acknowledged that this group was self-selected and that there might be a response bias, their results provide a rough estimate of the views of specialists on the use of Marinol (dronabinol, oral synthetic THC) and smoked marijuana. Only 43% said the available legal antiemetic drugs (including Marinol) provided adequate relief to all or most of their patients, and only 46% said the side effects of these drugs were rarely a serious problem. Forty-four percent had recommended the illegal use of cannabis to at least one patient, and half would prescribe it to some patients if it were legal. On average, they considered smoked marijuana more effective than Marinol and roughly as safe.[3]

21. Cannabis is also useful in the treatment of glaucoma, the second leading cause of blindness in the United States. In this disease, fluid pressure within the eyeball increases until it damages the optic nerve. About a million Americans suffer from the form of glaucoma (open angle) treatable with cannabis. Glaucoma is treated chiefly with eyedrops containing betablockers such as timolol (Timoptic), which inhibit the activity of epinephrine (adrenaline). They are effective but may have serious side effects such as inducing depression, aggravating asthma, slowing the heart rate, and increasing the risk of heart failure. Cannabis causes a dose-related, clinically significant drop in intraocular pressure that lasts several hours in both normal subjects and those with the abnormally high ocular tension produced by glaucoma. Oral or intravenous THC has the same effect, which seems to be specific to cannabis derivatives rather than simply a result of sedation. Cannabis does

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[3] Doblin R. Kleiman M. Marihuana as anti-emetic medicine: a survey of oncologists' attitudes and experiences. *Journal of Clinical Oncology* 1991; 9:1275-80. (Attached as Exhibit D).

not cure the disease, but it can retard the progressive loss of sight when conventional medication fails and surgery is too dangerous.[4]

22. About 20% of epileptic patients do not get much relief from conventional anticonvulsant medications. Cannabis has been explored as an alternative at least since 1975 when a case was reported in which marijuana smoking, together with the standard anticonvulsants Phenobarbital and diphenylhydantoin, was apparently necessary to control seizures in a young epileptic man.[5] The cannabis derivative that is most promising as an anticonvulsant is cannabidiol. In one controlled study, cannabidiol in addition to prescribed anticonvulsants produced improvement in seven patients with grand mal convulsions; three showed great improvement. Of eight patients who received a placebo instead, only one improved.[6] There are patients suffering from both grand mal and partial seizure disorders who find that smoked marijuana allows them to lower the doses of conventional anticonvulsant medications or dispense with them altogether. Furthermore, anticonvulsants have many potentially serious side effects, including bone softening, anemia, swelling of the gums, double vision, hair loss, headaches, nausea, decreased libido, impotence, depression, and psychosis. Overdoses or idiosyncratic reactions may lead to loss of motor coordination, coma or even death.

23. There are many case reports of cannabis smokers using the drug to reduce pain: post-surgery pain, headache, migraine, menstrual cramps, and so on. Ironically, the best alternative analgesics are the potentially addictive and lethal opioids. In particular, cannabis is becoming increasingly recognized as the most effective treatment for the pain that accompanies muscle spasm, which is often chronic and debilitating, especially in paraplegics, quadriplegics, other victims of

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[4] Hepler, R.S., et al. Ocular Effects of Marihuana Smoking. M.C. Braude, S. Szara (eds.). *The Pharmacology of Marihuana*. New York: Raven Press, 1976.

[5] Consroe, Paul F., et al. Anticonvulsant nature of Marihuana smoking. *Journal of the American Medical Association* 1975; 234-306-307. (Attached as Exhibit E).

[6] Cunha, J.M., et al. Chronic administration of cannabidiol to healthy volunteers and epileptic patients. *Pharmacology* 1980; 21:175-185. (Attached as Exhibit F).

traumatic nerve injury, and people suffering from multiple sclerosis or cerebral palsy. Many of them have discovered that cannabis not only allows them to avoid the risks of other drugs, but also reduces muscle spasms and tremors; sometimes they are even able to leave their wheelchairs.[7]

24. One of the most common causes of chronic pain is osteoarthritis, which is usually treated with synthetic analgesics. The most widely used of these drugs — aspirin, acetaminophen (Tylenol), and nonsteroidal anti-inflammatory drugs (NSAIDs) like ibuprofen and naproxen — are not addictive, but they are often insufficiently powerful. Furthermore, they have serious side effects. Stomach bleeding and ulcer induced by aspirin and NSAIDs are the most common serious adverse drug reactions reported in the United States, causing an estimated 7,000 deaths each year. Acetaminophen can cause liver damage or kidney failure when used regularly for long periods of time; a recent study suggests it may account for 10% of all cases of end-stage renal disease, a condition that requires dialysis or a kidney transplant.[8] Cannabis, as I pointed out earlier, has never been shown to cause death or serious illness. The University of Iowa conducted a study of cannabis for the relief of pain. Researchers gave oral THC or placebo at random to hospitalized cancer patients who were in severe pain. The THC relieved pain for several hours in doses as low as 5-10 mg, and for even longer at 20 mg. At this dose and in this setting, THC proved to be a sedative as well. It had few physical side effects than other commonly used analgesics.[9]

25. Oncologists are legally permitted to administer the synthetic THC (Marinol) orally in capsule form. But inhaled cannabis may be necessary for several reasons. For one thing, oral THC is

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[7] Petro, D. J., Ellenberger, C., Treatment of human spasticity with delta-9-tetrahydrocannabinol. *Journal of Clinical Pharmacology* 1981; 21:413-416. (Attached as Exhibit G).

[8] Perneger, T.V., Whelton, P., Klag, M.J. Risk of kidney failure associated with the use of acetaminophen, aspirin, and nonsteroidal anti-inflammatory drugs. *New England Journal of Medicine* 1994; 331:25:1675-1679. (Attached as Exhibit H).

[9] R. Noyes, S. F. Brunk, D. A. Baram, and A. Canter, "Analgesic Effect of Delta-9-tetrahydrocannabinol," *Journal of Clinical Pharmacology* 15 (February-March 1975): 139-143. (Attached as Exhibit I).

subject to the variances of bioavailability. This means that two patients who take the same amount may absorb different proportions of the dose, and a given patient may respond differently on different days, depending on the condition of the intestinal tract and other factors. Furthermore, the effects of smoked cannabis are perceived almost immediately, so patients can smoke slowly and take only what they need for a therapeutic effect. Patients who swallow Marinol may discover after an hour or so that they have taken too much for comfort or not enough to relieve their symptoms. In any case, a patient who is severely nauseated and constantly vomiting may find it almost impossible to the capsule down. Furthermore, Marinol makes some patients anxious and uncomfortable. Smoked cannabis, unlike Marinol, contains other substances which reduces anxiety caused by the THC.

26. In theory, all the therapeutic properties of cannabis could be used if individual cannabinoids in addition to THC were isolated and made available separately as medicines. But this would be an enormously complicated procedure. Research sponsors would have to determine the therapeutic potential and evaluate the safety of sixty or more substances, synthesize each one found to be useful, and package it as a pill or aerosol. As some of these substances probably act synergistically, it would also be necessary to look at various combination of them. However no drug company would provide the resources needed for such a project because cannabis can not be patented, it is a plant material containing many chemicals rather than a single one and no drug in the present pharmacopoeia is delivered by smoking.

27. More than 300,000 Americans have died of AIDS. Nearly a million are infected with HIV, and at least a quarter of a million have AIDS. Although the spread of AIDS has slowed among homosexual men, the reservoir is so huge that the number of cases is sure to grow. Women and children as well as both heterosexual and homosexual men are now being affected; the disease is spreading most rapidly among intravenous drug abusers and their sexual partners. The disease can be attacked with anti-viral drugs, of which the best known are zidovudine (AZT) and protease inhibitors. Unfortunately, these drugs sometimes cause severe nausea that heightens the danger of semi-starvation for patients who are already suffering from nausea and losing weight because of the illness — a condition sometimes called the AIDS wasting syndrome.

28. Cannabis is particularly useful for patients who suffer from AIDS because it not only relieves the nausea but retards weight loss by enhancing appetite. In one study the body weight and caloric intake of twenty-seven marijuana users and ten control subjects were compared for twenty-one days on a hospital research ward. The marijuana smokers ate more than the controls and gained weight; the controls did not. When they stopped smoking marijuana, they immediately started to eat less.[10] When it helps patients regain lost weight, it can prolong life. Although Marinol has been shown to relieve nausea and retard or reverse weight loss in patients with HIV infection, most patients prefer smoked cannabis for the same reasons that cancer chemotherapy patients prefer smoked cannabis. Cannabis is more effective and has fewer unpleasant side effects, and the dosage is easier to adjust. Many patients report that cannabis provides an appetite and pain relief without the semi-comatose effect of narcotics.

29. Opponents of medical cannabis often object that the evidence of its usefulness, although strong, comes only from case reports and clinical experience. It is true that there are no double-blind controlled studies meeting the standards of the Food and Drug Administration, chiefly because legal, bureaucratic, and financial obstacles have been constantly put in the way. However, we know more about cannabis than about most prescription drugs. Furthermore, individual therapeutic responses are often obscured in group experiments, and case reports and clinical experience are the source of much of our knowledge of drugs. As Dr. Louis Lasagna has pointed out, controlled experiments were not needed to recognize the therapeutic potential of chloral hydrate, barbiturates, aspirin, insulin, or penicillin.[11] Nor was that the way we learned about the use of

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[10] I. Greenberg, J. Kuehnle, J. H. Mendelson, and J. G. Bernstein, "Effects of Marijuana Use of Body Weight and Caloric Intake in Humans," *Journal of Psychopharmacology* (Berlin) 49 (1976): 79-84. (Attached as Exhibit J).

[11] Lasagne, L. Clinical trials in the natural environment. C. Stiechele, W. Abshagan, J. Kich-Weser (eds.). *In Drugs Between Research and Regulations*. New York: Springer-Verlag, 1985: 45-49. (Attached as Exhibit K).

propranolol for hypertension, diazepam for status epilepticus, and imipramine for enuresis. All these drugs had originally been approved for other purposes.

30. In the experimental method known as the single patient randomized trial, active and placebo treatments are administered randomly in alternation or succession. The method is often used when large-scale controlled studies are inappropriate because the disorder is rare, the patient is atypical, or the response to treatment is idiosyncratic.[12] Several patients have told me that they assured themselves of cannabis's effectiveness by carrying out such experiments on themselves, alternating periods of cannabis use with periods of abstention. I am convinced that the medical reputation of cannabis is derived partly from similar experiments conducted by many other patients.

31. Some physicians may regard it as irresponsible to advocate use of a medicine on the basis of case reports, which are sometimes disparaged as merely "anecdotal" evidence which counts apparent successes and ignores apparent failures. That would be a serious problem only if cannabis were a dangerous drug. The years of effort devoted to showing that cannabis is exceedingly dangerous have proved the opposite. It is safer, with fewer serious side effects, than most prescription medicines, and far less addictive or subject to abuse than many drugs now used as muscle relaxants, hypnotics, and analgesics.

32. Based on the best available medical information, it is evident that cannabis should be made available even if only a few patients could get relief from it, because the risks are so small. For example, as I mentioned, many patients with multiple sclerosis find that cannabis reduces their muscle spasma and pain. A physician may not be sure that such a patient will get more relief from cannabis than from the standard drugs baclofen, dantrolene, and diazepam — all of which are potentially dangerous or addictive — but it is almost certain that a serious toxic reaction to cannabis will not occur. Therefore the potential benefit is much greater than any potential risk.

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[12] Larson, E.B. N-of-1 clinical trials: A technique for improving medical therapeutics. *Western Journal of Medicine* 1990; 152:52-56; Guyatt, G.H., Keller, J.L., Jaeschke, R., et al. The N-of-1 randomized controlled trial: Clinical usefulness. *Annals of Internal Medicine* 1990; 112:293-299. (Attached as Exhibit L).

33. During the past few years, the medical uses of cannabis have become increasingly clear to many physicians and patients, and the number of people with direct experience of these uses has been growing. Therefore, the discussion is now turning from whether cannabis is an effective medicine to how it should be made available.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct.

Executed this 11 th day of September, 1998, at Boston, Massachusetts.

LESTER GRINSPOON, M.D.

EXHIBIT A

LESTER GRINSPOON, M.D.

Date of birth: June 24, 1928, Newton, Massachusetts

Marital status: married, three children

EDUCATION:

1951	B.S., Tufts College, Medford, Massachusetts, magna cum laude.
1955	M.D., Harvard Medical School, Boston, cum laude.

POSTGRADUATE TRAINING AND EXPERIENCE:

1955-1956	Intern in Medicine, Beth Israel Hospital, Boston, Massachusetts.
1956-1958	Field Investigator for the National Cancer Institute, Los Angeles, California.
1958-1961	Resident in Psychiatry, Massachusetts Mental Health Center, (Chief of Drug Unit 1959-1960; Chief of Service 1960-1961).

RESEARCH AND TEACHING APPOINTMENTS:

1950-1951	Olmstead Fellow in Biology, Tufts College, Medford, Massachusetts
1956-1958	Assistant in Medicine, University of Southern California School of Medicine, Los Angeles, California
1958-1959	Teaching Fellow in Psychiatry, Harvard Medical School, Boston, Massachusetts
1961-1962	Assistant in Psychiatry, Harvard Medical School, Boston, Massachusetts
1961-1963	Lecturer on Social Relations, Harvard University, Cambridge, Massachusetts
1962-1964 1962-1965	Instructor in Psychiatry, Harvard Medical School, Boston, Massachusetts
1961-1991	Senior Psychiatrist, Massachusetts Mental Health Center, Boston, Massachusetts
1964-1965	Clinical Associate in Psychiatry, Harvard Medical School, Boston, Massachusetts

1965-1968	Assistant Clinical Professor of Psychiatry, Harvard Medical School, Boston, Massachusetts
1968-1973	Associate Clinical Professor of Psychiatry, Harvard Medical School, Boston, Massachusetts
1973-	Associate Professor of Psychiatry, Harvard Medical School, Boston, Massachusetts.

OTHER APPOINTMENTS:

1961-1968	Director, Clinical Research Center, Massachusetts Mental Health Center
1962	Director, Summer Institute on Alternative Ways of Handling Conflict: Behavioral Science Research Toward Peace, Sponsored by the American Academy of Arts and Sciences
1963-1970	Consultant in Psychiatry and Research, Boston State Hospital
1969-	Examiner, American Board of Psychiatry and Neurology
1972-1988	Advisory Board, National Organization for the Reform of Marijuana Laws
1973-1974	Budget Committee, American Psychiatric Association
1973-	Executive Director, Massachusetts Mental Health Research Corporation
1974-1979	Consultant, Task Force on Interface between Psychiatry and Industry, American Psychiatric Association
1974-1979	Council on Research, American Psychiatric Association
1975-1977	Vice-Chairperson, Council on Research, American Psychiatric Association
1976-1981	Advisory Board, The Center for the Study of Non-Medical Drug Use
1977-1979	American Psychiatric Association Representative to the American Association for the Advancement of Science
1977-1979	Chairperson, Council on Research, American Psychiatric Association

1979-1980	Vice-Chairperson, Scientific Program Committee, American Psychiatric Association
1979-1980	Chairperson, Subcommittee on Awards for Scientific Exhibits, American Psychiatric Association
1979-	Council on Marihuana and Health, National Organization for the Reform of Marijuana Laws
1980-1984	Chairperson, Scientific Program Committee, American Psychiatric Association
1980-1984	Scientific Advisory Board, Beneficial Plant Research Association
1984-1985	Chairperson, Task Force on Soviet/American Relations, American Psychiatric Association
1986-1990	Founding Board of Directors, Physicians for Human Rights
1987-	Advisory Board, The Drug Policy Foundation
1987-	Board of Advisors, The Albert Hofmann Foundation
1989-	Vice President, International Antiprohibitionist League
1989-1991	Advisory Board, Civil Liberties Union of Massachusetts/ACLU
1989-1991	Board of Directors, Center for Psychological Studies in the Nuclear Age
1990-	Advisory Board, Physicians for Human Rights
1990-1992	Board of Directors, Drug Policy Foundation
1991-1993	Board of Directors, Civil Liberties Union of Massachusetts
1993-1996	Faculty Member, Zinberg Center for Addiction Studies, Cambridge, Massachusetts
1994-1995	Chairperson, Board of Directors, National Organization for the Reform of Marihuana Laws
1995-	Advisory Board, The Drug Research Group
1997-	Board of Scientific and Policy Advisors of the American Council on Science and Health

1997- Honorary Member, Arbeitsgemeinschaft Cannabis als Medizin (Alliance for Cannabis as Medicine), Germany

1997- International Advisory Committee, Physicians for Human Rights

EDITORIAL BOARDS:

1982-1984 Editor, Psychiatry Update: The American Psychiatric Association Annual Review; Volumes I-III

1982-1993 Journal of Psychiatric Research

1984- Editor, The Harvard Mental Health Letter

1985- Journal of Social Pharmacology

1985- The Harvard Health Letter

1991- Addiction Research

OTHER PROFESSIONAL ACTIVITIES:

Testified before legislative committees in the states of Massachusetts, Colorado, New Jersey, Washington, Vermont, and New York. Also testified before the National Marijuana Commission (1972), the House Armed Services Committee (1962), the Monopoly Subcommittee of the Senate Small Business Committee (1976), the House Select Committee on Narcotics (1977, 1979, 1989), the Controlled Substances Advisory Committee, the Drug Abuse Research Advisory Committee (1978), and the Senate Judiciary Committee (1980), etc.

HONORARY SOCIETIES:

Phi Beta Kappa
Alpha Omega Alpha
Boylston Society, Harvard Medical School
Columbia University Seminar Associate

PROFESSIONAL ORGANIZATIONS:

Massachusetts Medical Society
American Psychiatric Association (Fellow)
American Association for the Advancement of Science (Fellow)
Group for the Advancement of Psychiatry
Society of Biological Psychiatry
World Federation of Mental Health

MEDICAL LICENSING AND CERTIFICATION:

Diplomate, National Board of Medical Examiners
Licensed, State of Massachusetts
Diplomate, American Board of Psychiatry

PSYCHOANALYTIC TRAINING:

Graduate, Boston Psychoanalytic Institute, Boston, Massachusetts, April 1967

Member, Boston Psychoanalytic Society, Boston, Massachusetts, 1967-1985

AWARDS:

Mencken Award: Honorable Mention Winner for contribution to Dealing with Drugs, 1988

Alfred R. Lindesmith Award for Achievement in the Field of Scholarship, a $10,000 award of the Drug Policy Foundation, Washington, D.C., 1990*

Norman E. Zinberg Award for Marihuana Research, an award of The National Organization for the Reform of Marijuana Laws, Washington, D.C., 1990

*see citation, page 23

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Citation for
The Alfred R. Lindesmith Award for Achievement
in the Field of Scholarship

Presented to Dr. Lester Grinspoon
1990

Dr. Lester Grinspoon of Harvard Medical School is the complete medical scholar. His research and writing have covered a broad spectrum but perhaps his most important work has been his pursuit of truth about the nature of certain illegal drugs. In the course of that work, like Alfred R. Lindesmith, he upset many powerful people, including some in the medical establishment, who viewed impartial research on feared drugs as tantamount to heresy. Yet, in the face of that criticism, Dr. Grinspoon has persisted in his heretical pursuit of truth.

Although his earlier medical education had convinced him that the drug was dangerous, upon reviewing all of the available scientific and clinical evidence, he found marijuana to be relatively benign and to have several helpful applications for human beings.

Dr. Grinspoon was one of the most important witnesses in the suit which won a ruling from the chief administrative law judge of the DEA that marijuana was one of the safest therapeutically active drugs known to the human race.

Lester Grinspoon represents all those scholars who report the results of their research truthfully, despite the political consequences of this unwelcomed honesty.

EXHIBIT B

Vincent Vinciguerra, MD; Terry Moore, MSW; Eileen Brennan, RN

October 1988/ New York State Journal of Medicine pp. 525-527

ABSTRACT: A prospective pilot study of the use of inhalation marijuana as an antiemetic for cancer chemotherapy was conducted. Fifty-six patients who had no improvement with standart antiemetic agents were treated and 78% demonstrated a positive response to marijuana. Younger age and prior marijuana exposure were factors that predicted response to treatment. Toxicity was mild and consisted primarily of sedation and xerostomia. This preliminary trial suggests the usefulness of inhalation marijuana as an antiemetic agent. Because of the lack of a randomized placebo control group, the precise role of this agent is unclear. Further studies should include derivatives of this substance in combination with standard effective drugs to control chemotherapy-induced nausea and vomiting.

(NY State J Med
1988; 88: 525-527)

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Supported in part by the Don Monti Memorial Research Foundation, Community Clinical Oncology Program (CCOP) grant #CA-53579, and the New York State Department of Health.

A great deal of clinical information has recently been generated concerning the efficacy of various antiemetic agents for patients treated with cancer chemotherapy. (1-3). Without effective control of nausea and vomiting, patient compliance with potentially curative chemotherapy programs diminishes, compromising not only quality but quantity of life. Effective new chemotherapeutic agents could never be successfully tested in clinical trials if they possessed potent emetic side-effects.
Although a number of agents have recently been found to be active, including metoclopramide, (4,5) haloperidol, (6) dexamethasone, (7) and lorazepam, (8) the need to introduce newer agensts and combination antiemetic therapy may be necessary for continued control of symptoms. Also, complete control of nausea and vomiting during anticancer treatment must take into account not only the physical effects but also the psychological ones. Control of anxiety through behavior modification and relaxation is an effective antiemetic treatment of anticipatory nausea and vomiting. (9)

Natural and synthetic cannabinoids are known to be effective antiemetic agents. (10-12) Delta-9-tetrahydrocannabinol (THC) has been found to be superior to prochlorperazine. (13) Also, patients who are refractory to standart antiemetic agents have significant reduction in nausea and vomiting with oral THC. (14) There is little information on the efficacy of inhalation marijuana aside from anecdotal reports from patients who obtained the drug privately.
As a part of a New York State Department of Health program, North Shore University Hospital conducted a preliminary study of the use of inhalation marijuana as an antiemetic agent for cancer chemotherapy. The purpose of this study was to evaluate the efficacy of inhalation marijuana for patients refractory to standard agents, to identify patient characteristics to predict response, and to evaluate toxicity and patient acceptance of this form of treatment.

METHODS

Patients with histologically confirmed malignancies who were actively receiving chemotherapy were entered into the protocol. Eligibility criteria included: 18 years of age or older, refractoriness to conventional antiemetic agents, and absence of severe cardiac or psychiatric disease. Patients had to agree not to drive or operate heavy machinery or a motor vehicle for at least 12 hours after the last dose of marijuana. Central nervous system depressants including alcohol were prohibited during the administration of marijuana.

Marijuana cigarettes were supplied by the National Institute on Drug Abuse (NIDA) to the New York State Department of Health. All patients were instructed on standard smoking procedures. The patient inhales deeply, holds the inhalation for ten seconds, and then exhales. After waiting 10 to 15 seconds, the cycle is repeated. The total dose is completed within five minutes. A flame-proof holder was available to permit delivery of nearly all of the cigarette appropriate to the patient's dosage. The dose schedule, which was calculated to the nearest one-fourth cigarette; was 5 mg THC/m2, starting 6-8 hours prior to chemotherapy and every 4-6 hours thereafter, for a total dose of four doses per day on each day of chemotherapy (one cigarette= 10.8 mg THC). In order to prevent cigarettes from drying out and causing harsh smoke, patients were instructed to keep the cigarettes in the refrigerator or humidified.
This was a nonrandomized study where patients served as their own controls. Patients were asked to self-rate their status by completing a patient evaluation form after each therapeutic episode. Nausea was graded on a scale from 1 (none) to 4 (severe), vomiting was graded from 1 (none) to 5 (10+ times), appetite was graded from 1(none) to 5 (above normal), and physical state was graded from 1 (very weak) to 4 (above normal), and mood was graded from 1 (very depressed to 5 (very happy). Based on the degree of nausea, vomiting, food intake, physical state, and over-all mood, patients rated the overall effectiveness of marijuana as none, moderately effective, and very effective.
Physician investigators were approved by the Hospital's Patient Qualification Review Board. Physicians utilized the official New York State triplicate prescription form as their research order for medication. Informed consent was obtained from all patients and the procedures followed were approved by an institutional research committee.

RESULTS

Seventy-four patients entered the study and 56 were evaluable. Eighteen patients who had initially agreed to be treated with marijuana later decided not to participate. Eighteen patients rated the marijuana very effective (34%) and 26 patients rated it moderately effective (44%) for an overall response rate of 78% (44/56). Twelve patients (22%) noted no benefit.

TABLE I. Patient Characteristics (Percent)

	Responders (N=44)	Nonresponders (N=12)	P Value
Female	64	75	NS*
Mean age (yr) (median)	41 (40)	51 (54)	
Breast cancer	36	33	NS
Lymphoma	34	25	NS
Prior radiation therapy	30	8	NS
Prior THC	29	20	NS
Prior Marijuana	52	17	0.06
Euphoria (high)	60	36	NS
Smoker	53	38	NS

*NS= not significant
Standard deviation= 11.9
Standard deviation= 15.6

Characteristics of responding and nonresponding patients are listed in Table I. While no statistically significant differences were noted between responders and nonresponders with regard to sex, type of diagnosis, prior radiation therapy, prior oral THC treatment, incidence of euphoria, or

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smoking history, it is important to remember that the sample sizes were small, making interpretation of differences difficult. Patients who responded to marijuana cigarettes were more likely to be younger, median age 40 vs 54 for nonresponders, and had prior marijuana exposure, 52% vs 17% ($p = 0.06$).
The most common diagnoses for this group of patients were breast cancer, lymphoma, lung cancer, colon cancer, ovarian cancer, testicular cancer, sarcoma, acute leukemia, and myeloma. The most common emetic chemotherapeutic agents were cyclophosphamide, doxorubicin, cis-platinum, procarbazine, methotrexate, dacartazine, and streptozocin, given either singly or in combination. Four of seven patients treated with cis-platinum responded favorably to marijuana cigarettes.
Toxic side effects included sedation in 88%, dry mouth in 77%, dizziness in 39%, and confusion in 13%. Anxiety, headache, and fantasizing were also seen but were less common. There was no toxicity in 13% of patients (Table II).

TABLE II. Percent Toxicity

Sedation	88
Dry Mouth	77
Dizziness	39
Confusion	13
Anxiety	11
Headache	11
Fantasizing	11
None	13

DISCUSSION

The results of this prospective study suggest that inhalation marijuana is active in controlling nausea and vomiting resulting from chemotherapy. Marijuana benefited patients who were treated with a wide range of chemotherapeutic agents including drugs which have considerable emetogenic potential. A prior report by Chang et al (15) documented effectiveness of oral THC and inhaled marijuana against high-dose methotrexate, which normally has mild gastrointestinal toxicity. While most experience indicates that THC is generally ineffective against cis-platinum-induced emesis, benefit was seen in a small number of patients treated in our program with this agent.
Since this was a single arm, nonrandomized, outpatient program, this study lacks a controlled placebo group. Nevertheless, the patients acted as their own controls, having previously failed standard antinausea medications. They evaluated marijuana based on their subjective rating of the severity of nausea, vomiting, appetite and food intake, mood, and physical state after chemotherapy treatment. A placebo-controlled, randomized inpatient study which quantitates all emetic episodes would obviously provide objective and precise information. (16)
Failure to respond to oral THC does not preclude benefit from inhaled marijuana. Twenty-nine percent of patients who failed oral THC responded to the cigarette form. This is not unexpected, since only 5-10% of orally administered THC is absorbed, whereas inhaled marijuana has a five-to tenfold greater bioavailability. (17) Clearly, oral THC is an effective treatment for chemotherapy-induced emesis. Most studies have demonstrated THC to be better than placebo and comparable to prochlorperazine. (18)
The major obstacle related to the oral and inhaled cannabinoids is the route of administration. Patients with anticipatory vomiting do not retain the oral THC. Because of its poor water solubility, parenteral adminstration of cannabinoids has been difficult. The only cannabinoid available for parenteral use, levonantradol, is currently being investigated and has documented activity comparable to THC. (19) Perhaps intranasal or transdermal forms of THC will be developed and found to be clinically useful.
Patient characteristcs were evaluated to identify factors which would predict response to marijuana. There were no significant differences between responders and nonresponders with regard to sex, diagnosis, prior radiation therapy, prior THC ingestion, induced euphoria, and history of cigarette smoking. The only factors that approached significance were young age and prior marijuana intake. Unlike the experience with oral THC, experiencing a euphoric high was not a prerequisite to obtaining the antiemetic effect with marijuana. (20)
The mechanism of the antiemetic action of cannabinoids is unknown. Inhibition of prostaglandin and cyclic adenosine monophosphate has been

suggested. Its major action is more likely related to its effect on the brain, as marijuana causes central nervous system depression and impairment of brain function. At the cellular level, cannabinoids interfere with the synthesis of nucleic acids and chromosome proteins. (21)
Some of the problems encountered in this study which could influence interpretation of the results were the low patient accrual and the fact that nearly 25% of patients who initially consented refused to receive treatment. Reasons for patients' refusal to participate included physician and patient bias against smoking, harshness of smoke from the cigarettes, and preference for oral THC capsules. The major objection was related to the social stigma attached to the use of marijuana. Many patients rejected the idea of "smoking pot" at home and exposing their children to the implications of this type of medication. Should this therapy become available in a different vehicle of administration, patient acceptance would significantly improve.
Our results demonstrate that inhalation marijuana is an effective therapy for the treatment of nausea and vomiting due to cancer chemotherapy. A randomized, controlled trial would, however, be necessary to accurately define the exact role of this drug. Toxic effects are well tolerated and the availability of a parenteral form would improve patient utilization of this agent. Future antiemetic protocols should include the active ingredient of marijuana in combination with current effective agents.

Acknowledgments. The authors thank Rosemarie Galderisi and Annie Middleton for their assistance.

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EXHIBIT C

Antiemetic Effect of Delta-9-Tetrahydrocannabinol in Patients Receiving Cancer Chemotherapy

Sallan, Stephen E., Norman E. Zinberg, and Emil Frei. "Antiemetic Effect of Delta-9-Tetrahydrocannabinol in Patients Receiving Cancer Chemotherapy." The New England Journal of Medicine. Vol. 293(16) (1975): 795-797.

Contents

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i. Abstract

Anecdotal accounts suggested that smoking marihuana decreases the nausea and vomiting associated with cancer chemotherapeutic agents. Oral delta-9-tetrahydrocannabinol was compared with placebo in a controlled, randomized, "double-blind" experiment. All patients were receiving chemotherapeutic drugs known to cause nausea and vomiting of central origin. Each patient was to serve as his own control to determine whether tetrahydrocannabinol had an antiemetic effect. Twenty- two patients entered the study, 20 of whom were evaluable. For all patients an antiemetic effect was observed in 14 of 20 tetrahydrocannabinol courses and in none of 22 placebo courses. For patients completing the study, response occurred in 12 of 15 courses of tetrahydrocannabinol and in none of 14 courses of placebo ($P < 0.001$). No patient vomited while experiencing a subjective "high." Oral tetrahydrocannabinol has antiemetic properties and is significantly better than a placebo in reducing vomiting caused by chemotherapeutic agents.

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I. Introduction

Nausea and vomiting of central origin occur after the administration of a variety of cancer chemotherapeutic agents and frequently constitute the major morbidity associated with such treatment. Control with classic antiemetics is incomplete and variable.

Anecdotal accounts from patients suggested that smoking marihuana before receiving intravenous anti- tumor drugs resulted in diminution of nausea and vomiting, and, in contradistinction to the usual post- therapeutic anorexia, some were able to take food shortly after therapy. Effects of marijuana on nausea and vomiting in human beings deserve to be reported. It has been demonstrated that oral delta-9- tetrahydrocannabinol (THC) causes the same physiologic effects as smoking marijuana (1,2).

The purpose of this study was to determine the effects of orally administered THC on

nausea and vomiting in patients receiving cancer chemotherapy.

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I. Patients, Materials and Methods

Twenty-two patients known to have a variety of neoplasms were enrolled in the study. Ten males and 12 females ranging in age from 18 to 76 years (median of 29.5) participated. Twenty patients had previously received cancer chemotherapeutic agents known to cause nausea and vomiting (adriamycin, 5-azacytidine, nitrogen mustard, imidazole carboxamide, procarbazine, high-dose cyclophosphamide or high-dose methotrexate, or combinations thereof). Twenty of the 22 were known to be refractory to conventional antiemetics. The other two patients had never been treated with chemotherapy before entering the study. Pregnant women and patients with a past history of emotional instability or untoward reactions to psychoactive drugs were not eligible.

The study was thoroughly explained to the patients. They were told that they would receive a placebo or a "marihuana-like drug for the purpose of controlling nausea and vomiting." Subjects agreed not to smoke marihuana during the course of the study.

THC was supplied by the National Institute on Drug Abuse. The drug was suspended in 0.12 ml of sesame oil and supplied in gelatin capsules. Identical-appearing placebo capsules contained only sesame oil. Initially, THC dosage was 15 mg given every four hours for three doses. Because of some variability in responses, the dose was changed to 10 mg per square meter body-surface area per dose. Nineteen patients received 15-mg doses, and three 20-mg doses.

A randomized, "double-blind," crossover experiment was employed, each patient t being used as his own control. Optimally, patients received three one-day courses of drug (either THC or placebo). Each course consisted of three doses of drug, the first taken two hours before and the other two and six hours after chemotherapy. Patients were randomized to receive courses in one of four sequences: THC-placebo-THC; THC-placebo-placebo; placebo-THC-placebo; or placebo-THC-THC.

Nausea, vomiting, and food intake were assessed by the patient on the day after treatment through the use of self-administered questionnaires. In addition, the patient, nurses, and other personnel in contact with the patient were interviewed by one of us (S.E.S.), who also reviewed the questionnaires and nurses' notes.

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II. Results

Definitions of responses are based upon a comparison of THC and placebo courses.

Complete response to THC means that there was no vomiting in patients for whom the same antitumor drugs caused unequivocal moderate to severe vomiting after placebo. Conversely, a complete response to placebo theoretically is possible, but never occurred.

Partial response to THC means that there was at least a 50 per cent reduction in vomiting as compared to placebo after the same chemotherapy. Included in this group are the patients whose vomiting, which occurred shortly after chemotherapy during a placebo course, was delayed until escape from control of THC. These patients attained a "high" that wore off before the next dose, or after the last dose of THC, and during this time vomiting "broke

through." A partial response to placebo is also a theoretical possibility but never occurred.

No response to the THC means that there was either no decrease or less than a 50 per cent reduction in vomiting as compared with placebo after the same antitumor drugs. No response to placebo means that the patients vomited after chemotherapy as often or more often than after THC.

Absence of vomiting after both THC and placebo makes the response unevaluable because there was neither demonstrable emetic effect of chemotherapy nor antiemetic effect of THC or placebo. One patient who had no prior chemotherapy before entering the study, was excluded from analysis for this reason.

Eleven patients completed three courses of treatment, two completed two courses, and nine completed one course.

One of the 11 never vomited and was excluded from evaluation as noted above. The remaining 10 patients received 30 courses of drug, but a single course was excluded from analysis because the dose of cancer chemotherapeutic agent was reduced by 50 per cent. Therefore, 29 courses were evaluated: 14 placebo and 15 THC. All courses of placebo resulted in no response. Of the THC courses, there were five complete responses, seven partial responses, and three no responses. The therapeutic response derived from the THC was independent of the sequence of THC or placebo courses administered. Accepting complete and partial responses as positive responses, the difference between THC and placebo is highly significant (chi-square with Yates's correction $P<0.001$).

Of the two patients who completed two courses in the study, one died of disease, and the other decided to smoke marihuana, thus becoming ineligible to continue. Both these patients had no response after placebo; after THC, both had partial responses.

Nine patients received one course of treatment. Six had placebo only, and five of them vomited after chemotherapy. The patient who did not vomit after placebo had no prior chemotherapy. His response to placebo, therefore, is unevaluable because of the impossibility of differentiating an antiemetic effect of placebo from the emetic effect of chemotherapy. Of the six, two voluntarily withdrew from the study because they did not want to risk another placebo course, one had chemotherapy discontinued, one died of disease, and two are still in the study. Three had THC only. Of these, two vomited and left the study, and the third went off study because of THC toxicity.

In summary, 20 courses of THC were administered, resulting in five complete responses, nine partial responses, three no responses, and three unevaluable responses. Twenty-two courses of placebo resulted in no complete responses, no partial responses, 16 no responses, and six unevaluable responses.

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III. Side Effects

Of 16 patients receiving THC, 13 (81 per cent) experienced a "high." This effect was characterized by mood changes, which varied and consisted of one or more of the following: easy laughing; elation; heightened awareness; mild aberrations of fine motor co-ordination; and minimal distortion of their activities and interactions with others. There were no hangovers or delayed effects.

The next most common side effect was somnolence. For one third of the patients,

somnolence curtailed activities for two to six hours, but the patients were easily aroused. Another third had somnolence which did not curtail activities; the remainder experienced no somnolence.

Toxicity characterized by paranoid ideation, apprehension, fear, panic, and frightening visual hallucinations has been reported after single THC doses of 35 mg (2). Only two of our patients (9 per cent) experienced THC toxicity, both after three doses of 20 mg. One had visual distortions lasting for a few seconds, and the other reported visual hallucinations of 10 minutes' duration and depression of several hours.

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IV. Discussion

The results of this placebo-controlled "double-blind" study demonstrate that THC has antiemetic effects.

The study was designed to compare THC with placebo. It was not designed to evaluate placebo effect. No comparisons were made between placebo and absence of placebo, or between placebo and retrospective emesis control. If a placebo effect exists in this clinical and investigative setting, THC cannot be evaluated.

No patient vomited while experiencing a subjective "high." No "highs" were reported after placebo. In some patients, the "high" wore off before the next THC dose, and during this interval, nausea and vomiting frequently occurred. After this study, patients taking THC received their next dose as soon as the "high" began wearing off. Preliminary results indicate that this dose-scheduling adjustment sustains the antiemetic effect of THC.

Variability in gastrointestinal absorption of orally administered THC between, but not within, individual subjects has been reported (2). Three of our patients (19 per cent) reported the absence of a "high" after THC. The lack of THC effect ("high" and antiemesis) in at least some patients may be related to failure of absorption. Some patients who did not attain a "high" after the initial dose were able to do so with subsequent doses. This effect may be analogous to the experience of Weil et al (3) with smoked marihuana: failure to respond to an initial dose of marihuana, and then response to subsequent doses. This phenomenon may also be related to induction of hepatic microsomal enzymes necessary for drug metabolism as suggested by Lemberger er al (4).

Patients became "high" 20 to 60 minutes after ingestion of drug. The duration of the "high" varied from one to five hours, but was usually two to three hours, suggesting that the rigid four-hourly schedule between doses was probably too long for some patients, and possibly explaining some partial responses. When dosage was based on body-surface area, less variability in onset and duration of effects was noted.

Time of onset, duration of effect, and intensity of "high" were unrelated to previous marihuana use. Six patients admitted prior use of marihuana, but only one was considered more than an occasional user (defined here as smoking less than once a week).

It has been demonstrated that orally administered THC results in the same physiologic effects as inhaled marihuana (1,2). The previous studies showing inhaled marihuana to be more potent than oral THC (1) were probably in error because the THC was delivered in poorly absorbed vehicles (2). Inhalation appears to be more suitable for patients with suboptimal gastrointestinal absorption.

Hollister has shown that the effects of smoked THC clearly resemble those of marihuana (5). We have made preliminary observations comparing the antiemetic effect of smoked marihuana and oral THC. The marihuana belonged to individual patients and, therefore, was neither qualitatively nor quantitatively controlled. For most patients, both smoked and oral routes had identical effects. Theoretically, smoking might be the preferable route since it may result in less variability of absorption than the gastrointestinal route. Moreover, smoking provides greater opportunity for individual patient control by permitting the patient to regulate and maintain the "high."

THC has been reported to have a biphasic clinical effect, with initial stimulation and elation followed by sleepiness and tranquillity (6). With other antiemetics, such as the phenothiazine derivatives, sedative effect seems to parallel antiemetic effect (7). Although somnolence occurred in about two thirds of out patients, in the dosage used, THC prevented or reduced vomiting in most patients without appreciable curtailment of activities.

Appetite stimulation follows the smoking of marihuana (8). Four of our patients reported food intake "more than usual" after chemotherapy when taking THC. No patient reported this effect after placebo.

These data demonstrate that THC is an effective antiemetic for patients receiving cancer chemotherapy. Failure of response in 19 per cent of patients receiving THC perhaps is explicable on the basis of pharmacologic factors. THC can be used safely in the dosage of 10 mg per square meter per dose every four hours for at least three doses. Lack of effectiveness for some patients might be correctable by shortening the interval between doses to maintain a "high." The safety of such a dose-schedule adjustment is still to be determined.

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V. References

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We are indebted to Drs. Lester Grinspoon and Yvonne Bishop for assistance in this investigation.

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EXHIBIT D

Marijuana as Antiemetic Medicine: A Survey of Oncologists' Experiences and Attitudes

Doblin, Richard E. and Mark A. R. Kleiman. "Marijuana as Antiemetic Medicine: A Survey of Oncologists' Experiences and Attitudes." Journal of Clinical Oncology. Vol. 9(7) (1991): 1314-1319.

Contents

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i. Abstract

A random-sample, anonymous survey of the members of the American Society of Clinical Oncology (ASCO) was conducted in spring 1990 measuring the attitudes and experiences of American oncologists concerning the antiemetic use of marijuana in cancer chemotherapy patients. The survey was mailed to about one third (N = 2,430) of all United States-based ASCO members and yielded a response rate of 43% (1,035). More, than 44% of the respondents report recommending the (illegal) use of marijuana for the control of emesis to at least one cancer chemotherapy patient. Almost one half (48%) would prescribe marijuana to some of their patients if it were legal. As a group, respondents considered smoked marijuana to be somewhat more effective than the legally available oral synthetic dronabinol [THC] Marinol; Unimed, Somerville, NJ) and roughly as safe. Of the respondents who expressed an opinion, a majority (54%) thought marijuana should be available by prescription. These results bear on the question of whether marijuana has a "currently accepted medical use," at issue in an ongoing administrative ad legal dispute concerning whether marijuana in smoked form should be available by prescription along with synthetic THC in oral form. This survey demonstrates that oncologists' experience with the medical use of marijuana is more extensive, and their opinions of it are more favorable, than the regulatory authorities appear to have believed.

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i. Introduction

Marijuana (smoked) has been reported to be effective in treating emesis associated with cancer chemotherapy (1-4), but its use is currently prohibited by law (5). The main psychoactive ingredient in marijuana, tetrahydrocannabinol (THC; dronabinol), was approved in 1985 by the Food and Drug Administration (FDA) for use in the treatment of emesis. As marketed under the trade name Marinol (Unimed, Somerville, NJ) and synthetically formulated in sesame oil in gelatin capsules to be taken orally, almost 100,000 doses were prescribed in 1989 (6).

Litigation concerning the rescheduling of marijuana to permit its medical use has been making its way through the courts since 1972 (7). The central issue in the longstanding administrative and legal dispute, argued before the United States Court of Appeals (DC Circuit) on March 4, 1991 (8), is whether or not marijuana has a "currently accepted medical use in treatment in the United States." This is the standard for rescheduling required by the Uniform Controlled Substances Act of 1970 (5), which created the current system of drug scheduling. The Act does not further specify the standard.

In September 1988, after 2 years of Drug Enforcement Administration (DEA) administrative hearings, DEA Administrative Law Judge Francis Young issued a recommendation in favor of rescheduling marijuana. He ruled that the appropriate standard for current acceptance is identical to the one established for a successful defense in medical malpractice cases, which requires only that the medical practice at issue be accepted by a "respectable minority" of physicians (9). Ironically, the 1955 medical malpractice case that established this standard involved a lawsuit against an oncologist for the unsuccessful use of chemotherapy, which was then new and did not have the approval of the American Medical Association. The court stated that as long as there was no infallible cure and the doctor "did not engage in quackery by representing that he had one," the support of a respectable minority of peers would be sufficient to avoid malpractice liability. The court remarked "We [the court] are not physicians and we have no light on the subject except such as is shed by the testimony of physicians..." (10).

On December 29, 1989, the Administrator of DEA rejected Judge Young's recommendation and refused to reschedule marijuana on the grounds that medical use of marijuana was not currently accepted. The Administrator used an eight-part standard for determining current acceptance similar to the "safety and efficacy" standard used by the FDA to approve the marketing of new drugs by pharmaceutical companies (11). The DEA first articulated this standard in another rescheduling case in 1987, after the United States Court of Appeals (1st Circuit 1987) rejected its contention that FDA new drug approval itself was the appropriate standard (12). On April 26, 1991, the United States Court of Appeals (DC Circuit) (13) ruled that DEA's standard was impossible to meet, and was therefore invalid. The court remanded to the DEA its ruling rejecting Judge Young's recommendation in favor of the rescheduling of marijuana.

The extent of oncologists' acceptance of medical use of marijuana remains a disputed issue. Dr Ivan Silverberg, an oncologist and witness in the DEA hearings, testified, "There has evolved an unwritten but accepted standard of treatment within the oncologic community which readily accepts marijuana's use" (14). On the other hand, the DEA characterized the medical use of marijuana as a "cruel and dangerous hoax" (15). In a newspaper interview, DEA Associate Chief Counsel Steven Stone suggested that only a fringe group of oncologists accepted marijuana as an antiemetic. Stone remarked, "The Judge seems to hang his hat on what he calls a 'respectable minority of physicians.' What percent are you talking about? One half of one percent? One quarter of one percent?" (16). This report of oncologists experiences with and attitudes about marijuana as an antiemetic is based on a survey of these specialists conducted in the spring of 1990.

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I. Subjects and Methods

A random sample of the United States-based members of the American Society of Clinical Oncology (ASCO) was surveyed. The membership of ASCO, the only formal association of clinical oncologists in the United States, comprises about 80% of the approximately 5,000 board-certified oncologists and almost 60% of the approximately 11,700 oncologists

in the United States, including academic and research-oriented oncologists as well as clinicians in private practice. The survey was conducted independently of ASCO sponsorship.

The survey, responses to which were anonymous, was sent to about 35% (N = 2,430) of the total United States-based ASCO 1989 membership (N = 6,830). The 1,035 surveys returned resulted in a response rate of 43%, representing 15% of United States-based ASCO members and 9% of all oncologists in the United States. Of the respondents, 57 (6%) returned the survey unanswered, indicating that they did not treat patients. Other respondents did not answer every question. The data analysis is based on the total number of respondents answering each particular question.

The survey initially elicited personal information about the oncologist's year of graduation from medical school and size of practice. Oncologists were then asked to estimate the proportion of their cancer chemotherapy patients for whom the currently available antiemetics provided adequate relief or caused significant problems with side effects.

Respondents were asked how frequently they prescribed Marinol, whether any of their patients had used marijuana as an antiemetic, whether they had directly observed or discussed marijuana's medical use with patients, and whether they had ever recommended that a patient try marijuana.

Oncologists were also asked to estimate the proportion of their patients who reported effective emetic control or negative side effects from using marijuana or Marinol, to directly compare the safety and efficacy of marijuana and Marinol, and to estimate what proportion of their patients experienced net benefits from their use of marijuana.

Oncologists were further asked to respond to the statements "Marijuana can be effective in the control of emesis," "Marijuana can be used safely in the control of emesis," 'Marijuana should be given an accepted place in the antiemetic armamentarium," and "I find the use of Marinol in the control of emesis to be a legitimate, currently acceptable medical practice" by indicating strong agreement, agreement, strong disagreement, disagreement, or no opinion. Oncologists were also asked, if marijuana were legal, whether they would prescribe it to "many," "few," or "none" of their patients or if they needed more information.

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II. Results

Ten percent of the respondents graduated from medical school in the 1980s; almost one half (48%) of the respondents graduated from medical school in the 1970s; almost one third (31%) in the 1960s; 9% in the 1950s; and 2% in the 1940s. In 1989, almost one half (49%) of the respondents had an annual patient population of more than 225; almost one quarter (24%) treated between 150 and 225 patients; 18% treated between 75 and 150 patients; and 9% treated 75 or fewer patients.

Two hundred nine (21%) of oncologists reported that the available medicines provided inadequate relief to half or more of their patients (Fig 1). More than half (520, 54%) of the respondents reported that the available antiemetics caused significant problems with side effects in more than a "few" of their patients (Fig 1).

Slightly more than 70% (686) of respondents reported that at least one of their patients had used marijuana as an antiemetic and that they had directly observed or discussed marijuana's medical use with that patient(s). Marinol had been prescribed by 557

respondents (57%).

A surprising proportion of respondents (432, 44%) said they had recommended marijuana to at least one patient. Only six respondents noted that they did so as part of a legally authorized research protocol. Not surprisingly, respondents who treated more than 150 patients per year were more likely to have recommended marijuana than respondents treating fewer than 150 patients (46% v 34%, $P < .05$). Respondents who graduated from medical school in the 1950s, the 1960s, or the 1970s had statistically similar rates of recommending marijuana (1950s, 46%; 1960s, 44%; 1970s, 44%). However, those who graduated during the 1980s had a significantly lower rate (30%. $P < .05$).

Efficacy of Marijuana and Marinol

Three hundred eighty-five respondents (64%) stated that marijuana was effective in 50% or more of their patients, and 266 (56%) reported the same of Marinol (Fig 2). The difference is statistically significant ($P = .008$).

Of the 277 respondents (28%) who felt they had sufficient information to compare marijuana directly with Marinol in terms of efficacy, 44% believed marijuana to be more effective, 13% believed Marinol to be more effective, and 43% thought they were about equally effective. Of those who reported a preference (N = 157), 121 (77%) thought marijuana was more effective than Marinol. The difference between 77% and 50% (the null hypothesis) is statistically significant below the .0001 level.

Six hundred eight respondents (63%) agreed with the statement affirming the efficacy of marijuana in the treatment of emesis (9% "strongly agreed" and 54% "agreed"), and 77 respondents (8%) disagreed (2% "strongly disagreed" and 6% "disagreed"). Two hundred eighty-three (29%) had no opinion. Of the respondents with opinions (N = 685), 89% believed marijuana to be effective in the control of emesis. Of respondents to a question concerning net benefits (N = 644), 409 (64%) reported that 50% or more of their patients experienced net benefits from marijuana. Only 15 (2%) reported that none of their patients experienced net benefits from marijuana.

Safety of Marijuana and Marinol

Two hundred twenty-four respondents (47%) stated that the use of Marinol caused negative side effects in 50% or more of their patients, and 235 (40%) reported the same about marijuana (Fig 3). The difference is statistically significant ($P = .018$).

Of the 288 respondents (29%) who felt they had sufficient information to compare marijuana with Marinol in terms of side effects, 20% believed marijuana to cause fewer problems with side effects, 23% believed Marinol to cause fewer problems, and 57% thought they were equal. Slightly more than half, 52% (65), of those who reported a preference (124) reported Marinol to cause fewer problems with side effects. The difference between 52% and 50% is not statistically significant ($P = .596$).

Four hundred seventy-eight respondents (49%) agreed with the statement affirming that marijuana could be safely used in the treatment of emesis (6% "strongly agreed" and 43% "agreed"), and 131 (14%) disagreed (4% "strongly disagreed" and 10% "disagreed"). Three hundred sixty-one (37%) had no opinion. Of the respondents with opinions (N = 609), almost four fifths (79%) believed that marijuana could be safely used to control emesis.

Almost half (423, 44%) of the respondents reported that they believe marijuana to be both safe and efficacious. Of respondents with opinions on both safety and efficacy (N = 577), 73% believe marijuana to be both safe and efficacious. There were no significant

differences in positive opinions of marijuana's safety and efficacy between respondents who treated 150 patients or fewer annually and those who treated more than 150 patients annually, or among respondents who graduated in different decades.

Three hundred twenty respondents (33% of all respondents) stated that marijuana should be accepted (50% "strongly agreed" and 28% "agreed") and 279 (29%) felt that it should not (7% "strongly disagreed" and 22% "disagreed"); 364 (38%) expressed no opinion. Of the 599 respondents with opinions, 53% favored making marijuana available by prescription. The surplus of positive over negative opinions is within the bounds of sampling error ($P = .092$). There were no significant differences in rate of acceptance by size of patient population. However, respondents who graduated in the 1950s were significantly less likely to accept the medical use of marijuana (22%) than respondents who graduated in the 1960s (35%), the 1970s (34%), or the 1980s (39%) ($P < .05$).

When asked whether Marinol should be accepted, 705 respondents (73%) agreed (20% "strongly agreed" and 53% "agreed") and 83 (9%) disagreed (2% "strongly disagreed" and 7% "disagreed"); 177 (18%) had no opinion. Of the 788 respondents with opinions, 89% accept the medical use of synthetic THC.

Almost half of the respondents (440, 48%) would prescribe marijuana to at least a few patients (4% to "many," 44% to "few") if it were legal; 200 (22%) would not prescribe it; and 274 (30%) said they would need more information. The 48% who would prescribe marijuana if it were legal is only slightly less than the 54% who have prescribed Marinol, which is legally available. Of those oncologists who had previously recommended marijuana to at least one patient ($N = 432$), 279 (65%) would prescribe marijuana to at least a few patients if it were legally available. Of those oncologists who had not recommended marijuana to at least one patient ($N = 550$), 161 (29%) report that they would prescribe marijuana to at least a few patients if it were legally available.

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III. Discussion

Although substantial, the response rate of 43% makes it difficult to determine precisely the views of the entire ASCO membership. The views of the sample who returned the survey may differ significantly from the views of those who did not. Since ASCO itself does not compile membership statistics for age, year of graduation from medical school, or patient population size, respondents cannot be compared with the full membership in these respects. However, no obvious anomalies in their characteristics were observed. Furthermore, the distribution of postmarks by state on the returned surveys - the main information available with which to evaluate response bias - very closely matched the geographic distribution of the survey forms mailed. Although there is nothing specific to suggest the presence of response bias, it cannot be ruled out. Therefore, all reported statistics should be considered indications of the general range of support for various propositions, rather than precise determinations.

The central empirical question the survey was designed to answer was whether a significant minority of the members of the ASCO supported the rescheduling of marijuana to permit its use in the treatment of nausea associated with cancer chemotherapy. The response rate is sufficiently large to resolve that question conclusively.

Of all oncologists with opinions responding to our survey, 54% supported rescheduling. Possible response bias makes it impossible to determine precisely whether a majority of the population with opinions actually holds that view. Ascertaining whether a significant minority of the population supports rescheduling is much simpler. A sensitivity analysis

varying the degree of acceptance of the medical use of marijuana by nonrespondents to the survey suggests that support for rescheduling marijuana is indeed present in at least a significant minority of our population. In the hypothetical event that all nonrespondents and all respondents without opinions were actually opposed to rescheduling, 13% of oncologists would remain in favor of rescheduling. If all nonrespondents and respondents without opinions were actually for rescheduling, 85% would support prescription availability of marijuana.

The survey data suggest that adding marijuana to the existing armamentarium of antiemetic agents would result in substantial benefits to patients. Oncologists believe smoked marijuana to be roughly as safe as legally available, oral synthetic THC (Marinol) and somewhat more effective. Of the oncologists responding to our survey, 44% - 73% of those with opinions - consider marijuana both safe and efficacious.

Oncologists may prefer to prescribe smoked marijuana over oral THC for several reasons. The bioavailability of THC absorbed through the lungs has been shown to be more reliable than that of THC absorbed through the gastrointestinal tract (17-18), smoking offers patients the opportunity to self-titrate dosages to realize therapeutic levels with a minimum of side effects, and there are active agents in the crude marijuana that are absent from the pure synthetic THC.

Although the survey did not ask whether marijuana or Marinol might be safer or more effective when used with specific patient groups, in space set aside for comments, 42 oncologists mentioned either that older patients had more problems with side effects from both Marinol and marijuana or that patients who had side effects tended to be inexperienced with marijuana. The increased prevalence of side effects in older patients may be a cohort effect and not an age effect. Marijuana and Marinol may be most useful in younger or marijuana-experienced patients.

More than four in 10 respondents (44%) report that they have recommended the (illegal) use of marijuana to control emesis to at least one cancer chemotherapy patient. The fact that so many physicians have advised patients to commit an illegal act to obtain marijuana suggests a substantial discrepancy between clinical and regulatory opinions. Almost half (48%) would prescribe it to some of their patients if it were legal.

The survey reported here of the opinions and experiences of clinicians is not a controlled clinical study of the use of marijuana as an antiemetic. Nevertheless, this survey demonstrates that oncologists' experience with the medical use of marijuana is more extensive, and their opinions of it are more favorable, than the regulatory authorities appear to have believed. It appears that current regulations create the somewhat anomalous situation that a substantial fraction of all practicing oncologists at least occasionally commit an act - ie, counseling a patient to acquire and use a controlled substance - that constitutes a crime and that at least in principle could lead to the revocation of their license.

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Acknowledgment

Joseph P. Newhouse, of the Kennedy School, reviewed both the survey instrument and this report and suggested several important improvements. Dr Jerome Jaffe, Director of the Addiction Research Center of the National Institute on Drug Abuse, also offered constructive suggestions.

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EXHIBIT E

Consroe/Epilepsy/1975

ANTICONVULSANT NATURE OF MARIHUANA SMOKING

Journal of the American Medical Association Oct 20, 1975---Vol 234, No 3: 306-307

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Marihuana smoking, in conjunction with therapeutic doses of pheno-barbital and diphenylhydantoin, was apparently necessary for controlling seizures in one 24-year-old epileptic patient.

ANECDOTAL accounts of beneficial therapeutic effects of Cannabis sativa have been known throughout recorded history. (1) The classic description by O'Shaughnessy (2) in 1842 of the ameliorative effects of marihuana extract on "infantile convulsions," "hydrophobia," and "lockjaw" invite speculation as to the anticonvulsant effect of the drug. Other 19th century physicians reported that marihuana preparations were of benefit in controlling various spastic and seizure states, (3,4) although entirely useless in states of "true chronic epilepsy" such as petit mal. (4) Synthetic derivatives of delta-9-tetrahydrocannabinol, the main psychoactive ingredient of marihuana, have been reported to be of val;ue in the treatment of human epilepsy, although explicit details are absent in the abstract-report. (3) Finally, there is also a published report in which grand mal convulsions in a 20-year-old man were exacerbated by smoking marihuana. (4)

These references are essentially the only available literature on the relationship between marihuana and human convulsions, which obviously indicates a paucity as well as a contradiction of information. The following case report describes the possible beneficial effect of marihuana in human epilepsy.

Report of a Case

A 24-year-old man has been seen in a neurology outpatient clinic for a period of eight years for control of his epileptic seizures. His history included febrile convulsions at 3 years of age and epileptic seizures since the age of 16. Since that age, the patient has been taking diphenylhydantoin sodium, 100 mg four times a day, and phenobarbital, 30 mg four times a day. Control seizures with this regimen was incomplete, and the patient complained of attacks about once every two months. From the age of 16 to 22, the incidence of seizures increased to one attack per month to one per week.

At 22 years of age, the patient began smoking marihuana (two to five joints per night) while continuing the prescribed anticonvulsant drug therapy. During this period, attack did not occur as long as the patient continued to take the combination of all three drugs. The patient's condition could not be maintained on marihuana alone, because on two occasions he experienced an attack three to four days after running out of his prescribed medication.

Neurological work-up has recently been done on the patient and he has been thoroughtly interviewed, because of the possible association between marihuana and epileptsy. The patient was found to have abnormal paroxysmal bursts of spike and slow-wave electroencephalographic discharges bilaterally, and his condition was diagnosed as grand mal epilepsy. The patient showed no other physical or emotional disability and did not admit to smoking cigarettes, drinking alcohol, or taking any other drugs. Plasma level of diphenylhydantoin was 7.4 mcg / ml; ohenobarbital level was 11 mcg /ml; and folic acid, 4.5mcg / ml.

The patient apparently complies with his dosage regimen, since he has a history of regular clinic visits and refilled drug prescriptions.

Comment

This case suggests that marihuana may possess an anticonvulsant

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effect in human epilepsy. Previous reports have alluded to this possibility. (1-3,5) Moreover, the antiseizure properties of delta-9-tetrahydrocannabinol have been demonstrated in a wide variety of experimental animal species. (7-9) It has been shown in laboratory-animal seizure models that the tetrahydrocannabinols show a differential activity against major seizures without altering the sequelaw of minor seizures. (7) Thus, the present case appears to bear out the prediction from the animal studies while at the same time possibly explaining marihuana's observed lack of effect in petit mal epilepsy. (4)

Theoretical calculations can be made to elucidate the probable blood level range for delta-9-tetrahydrocannabinol. A sample of the patient's marijuana was analyzed for tetrahydrocannabinol content by gas chromatography, and was found to contain 1.2% by weight total cannabinoids. One twelfth of the total cannabinoids, or 0.1% by weight, was accounted for by delta-9-tetrahydrocannabinol. Assuming 1 gm of marihuana per joint and correcting for pyrolysis (50%) and lung-absorption losses (20%), the inhalation dose of delta-9-tetrahydrocannabinol to the patient (weight, about 65 kg [143]) would be 6.15 mcg / kg. It is known that doses of 5 mcg to 7 mcg / kg of delta-9-tetrahydrocannabinol produce psychological and physiological effects in steady marihuana smokers. (10) Moreover, after an intravenous bolus of delta-9-tetrahydrocannabinol, marihuana smokers show lower blood levels and shorter half-lives (28 hours) for the drug than nonusers (half-life, 57 hours). (10) Since the half-life is 28 hours in steady smokers and this patient used two to five joints per evening, little of the drug would be eliminated and the blood levels would be expected to climb rapidly during the evening.

The subtherapeutic blood level of diphenylhydantoin in this patient, 7.4 mcg / ml (normal range, 10 to 25) was not unexpected, since phenobarbital is know to induce the formation of enzymes that metabolize diphenylhydantoin. Even when the blood levels of diphenylhydantoin are less than the normal range, the combination of the two drugs is known to be clinically effective. (11) The blood level of 11 mcg / ml of phenobarbital found in this patient is within the normal therapeutic range (10 to 20).

In summary, marihuana smoking in conjunction with routine doses of phenobarbital and diphenylhydantoin was apparently necessary for controlling seizures in one 24-year-old patient. However, the present case is in direct contrast to the single previously reported case of marihuana smoking exacerbating seizures in one patient with grand mal epilepsy. (6) The possibility that delta-9-tetrahydrocannabinol or other cannabinoids may be useful or detrimental in major seizures needs further investigation.

This investigation was supported in part by National Institute of Mental Health grant MH23414
The analysis of marihuana for tetrahydrocannabinol was performed by Pharm Chem Laboratories, Palo Alto, Calif.

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EXHIBIT F

CHRONIC ADMINISTRATION OF CANNABIDIOL TO HEALTHY VOLUNTEERS AND EPILEPTIC PATIENTS

Pharmacology 21: 175-185 (1980)

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This work was supported by grant No. ROI DA 00875 from the US National Institutes of Mental Health (principal investigator: E.A. Carlini).

Key words. Cannabidiol--Epilepsy--Healthy volunteers

Abstract. In phase 1 of the study, 3 mg / kg daily of cannabidiol (CBD) was given for 30 days to 8 healthy human volunteers. Another 8 volunteers received the same number of identical capsules containing glucose as placebo in a double-blind setting. Neurological and physical examinations, blood and urine analysis, ECG and EEG were performed at weekly intervals. In phase 2 of the study, 15 patients suffering from secondary generalized epilepsy with temporal focus were randomly divided into two groups. Each patient received, in a double-blind procedure, 200-300 mg daily of CBD or placebo. The drugs were administered for as long as 4 1/2 months. Clinical and laboratory examinations, EEG and ECG were performed at 15- or 30-day intervals. Throughout the experiment the patients continued to take the antiepileptic drugs prescribed before the experiment, although these drugs no longer controlled the signs of the disease. All patients and volunteers tolerated CBD very well and no signs of toxicity or serious side effects were detected on examination. 4 of the 8 CBD subjects remained almost free of convulsive crises throughout the experiment and 3 other patients demonstrated partial improvement in their clinical condition. CBD was ineffective in 1 patient. The clinical condition of 7 placebo patients remained unchanged whereas the condition of 1 patient clearly improved. The potential use of CBD as an antiepileptic drug and its possible potentiating effect on other antiepileptic drugs are discussed.

Anecdotal reports on the antiepileptic properties of marihuana (Cannabis sativa) are known since ancient times (Li, 1974). Rosenthal (1971) mentioned medieval Arab manuscripts in which cannabis is described as a treatment for epilepsy. During the 19th century several medical reports were published on the ameliorative effects of cannabis extracts on several forms of convulsions (O'Shaughnessy, 1842; Shaw, 1843; Reynolds, 1890).

In spite of these promising results and its low toxicity, the use of cannabis preparations for medical purposes progressively decreased. This was due to the absence of standardized preparations, the unknown chemical composition, and the psychotropic secondary effects produced by cannabis.

Cannabidiol (CBD) is the major neutral nonpsychoactive cannabinoid in most cannabis preparations. It was first isolated by Adams et al, in 1940 but its structure was elucidated only 23 years later (Mechoulam and Shvo, 1963). The main active component of cannabis is delta-1-tetrahydrocannabinol (delta-1-THC) which was isolated in pure form and its structure was determined by Gaoni and Mechoulam in 1964. It is also named delta-9-THC. Numerous other natural cannabinoids are known today (Mechoulam, 1973; Mechoulam et al, 1976).

The unraveling of the chemistry of C. sativa brought a new interest in its pharmacology, and quite expectedly many laboratories studied the anticonvulsant properties of its components especially since early reports had shown that some natural and synthetic cannabinoids protected rats from convulsions (Loewe and Goodman, 1947) and were of therapeutic value in epileptic children (Davis and Ramsey, 1949). More recently many reports have appeared attributing anticonvulsant properties to delta-1-THC and other cannabinoids, in a variety of experimental procedures (Garriott et al, 1968; Sofia et al, 1971; Consroe and Man, 1973; Karler et al, 1973, 1974; Plotnikoff, 1976). As a rule, delta-1-THC was the most studied

compound. Most of the results obtained confirmed the rather potent anticonvulsant property of this drug. Its possible use as an antiepileptic drug in humans has, however, been hindered by its known psychotropic effects.

Since Brazilian workers (Carlini et al, 1973; Izquierdo et al, 1973) first demonstrated the anticonvulsant effects of CBD, there have been several additional reports on the effectiveness of CBD and its derivatives in protecting experimental animals from convulsions induced by various procedures (Karler et al, 1973; Turkanis et al, 1974; Carlini et al, 1975; Karler and Turkanis, 1976; Consroe and Wolkin, 1977). Consroe and Wolkin (1977) demonstrated that CBD has a high protective index comparable to that of phenobarbital and a spectrum of anticonvulsant activity in rodents similar to that of phenytoin. CBD also enhances the anti-convulsant potency of both phenytoin and phenobarbital (Consroe and Wolkin, 1977; Chesher and Jackson, 1974; Chesher et al., 1975).

In addition to its favorable anticonvulsant effects and absence of toxicity in animals, CBD seems to be devoid of psychotropic activity and other undesirable side effects in humans. The lack of toxicity of CBD in animals was demonstrated by intraperitoneal injection of 50 mg / kg daily for 90 days in mice, oral ingestion of 5-20 mg / kg daily for 90 days and 50 mg / kg for 27 days by rats and intravenous injection of 1,000 mg / kg in rabbits. No toxicity was observed (Cunha and Carlini, to be published). In man, oral intake of doses from 15 to 160 mg / day (Karniol et al, 1974; Hollister, 1973; Carlini et al, 1979), inhalation of 0.15 mg / kg (Dalton et al, 1976a), and intravenous injection of 30 mg (Perez-Reyes et al, 1973; Hollister, 1973) were not followed by ill effects. Chronic oral administration of 10 mg daily for 21 days did not induce any change in neurological (including EEG), clinical (including ECG), psychiatric, blood and urine examinations (Mincis et al, 1973).

Another recent investigation in our laboratory (Consroe et al., 1979) showed that CBD neither interferes with several psychomotor and psychological functions in humans nor potentiates alcohol effects on these functions.

The above data led us to undertake the present investigation which was performed in two phases. In phase 1, 3--6 mg / kg of CBD (roughly corresponding to 200--400 mg / subject) was administered daily to healthy human volunteers for 30 days. In phase 2, patients suffering from secondary generalized epilepsy with temporal irritative activity received 200--300 mg of the drug for periods of up to 4.5 months.

Experiment 1 (Phase 1 of Study)

Material and Methods

Subjects
16 adult volunteers (11 men and 5 women) aged 22-35, with an average weight of 65 kg were chosen from the staff of Escola Paulista de Medicina. They were in good health showing neither clinical nor laboratory evidence of cardiovascular, renal, hepatic or other impairments. The institutional review committee at Escola Paulista de Medicina previously approved the protocol of the experiments.

On the first day of the experiment the patients were submitted to a complete medical check-up, including clinical and neurological examinations, EEG, ECG, blood tests (hematocrit, hemoglobin, leukocyte and erythrocyte counts, bilirubin, oxaloacetic and puruvic transaminases and creatinine) and urine tests ; (osmolarity, pH, albumin, leukocyte and erythrocyte counts, cylinders and crystals) in the Department of Medicine of the Hospital Sao Paulo of Escola Paulista de Medicina. On the 7th day, they returned to the hospital, signed the informed consent and were randomly divided in two groups of 8. Each group started the ingestion of identical gelatine capsules containing either glucose as placebo (control group) or CBD (experimental group). The experiment was performed on a double-blind basis and the subjects were instructed to ingest the assigned capsules, one in the morning and the second in the afternoon for 30 days. Each capsule contained an amount of CBD (or glucose) equivalent to 1.5 mg / kg, i.e. a daily dosage of 3.0 mg / kg. 1 volunteer took 4 capsules of CBD daily (6 mg / kg) on the last 3 days of the experiment.

On the 3rd, 7th, 15th, 31st and 37th days after the beginning of drug ingestion, the subjects returned to the hospital to undergo the

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examinations described above.

Drug

Cannabidiol, in crystalline from (m.p. 66--67) was isolated from hashish of undetermined age. It was of Lebanese origin and was supplied by the Israeli Police. The isolation procedure has been described (Gaoni and Mechoulam, 1971). Part of the CBD was a gift from Makor Chemicals, P.O.B. 6570, Jerusalem

Results

General Observations
During the entire period of the experiment, the subjects did not report any symptoms suggestive of psychotropic effect of CBD. Of the 8 volunteers receiving the placebo, 1 gave up on the 21st day of the experiment for personal reasons; a second placebo subject reported sudoresis and 'palpitations' from the 7th to the 10th day in the veins of the feet, legs and head, stating that he had to uncover his feet to feel the palpitations less in order to sleep. Clinical and laboratory examinations were normal and the symptoms subsided after the 11th day without any measures on the part of the investigators.

Of the 8 volunteers receiving CBD, 2 reported somnolence, 1 during the first week and the other throughout the entire period of the experiment. A 3rd subject, with a history of mild insomnia, reported being able to sleep better during the first week of medication.

Neurological and clinical examinations, EEG and ECG tracings, and blood and urine analyses (detailed above) were within normal limits in the 16 subjects before, during and after the experiment.

Comments

It has been suggested that delta-1-THC and other cannabinoids may possess therapeutic potential as antidepressive drugs in patients with cancer (Regelson et al., 1975) or in the treatment of glaucoma (Hepler and Frank, 1971), asthma (Tashkin et al., 1972), etc. For a recent review see Mechoulam and Carlini (1978). However, acute administration of 20--60 mg of delta-1-THC induces a marked psychic change and has peripheral effects such as an increase in heart rate (Isbell et al., 1967; Kiplinger et al., 1971; Karniol et al., 1975) which would limit its therapeutic use.

In contrast, the present experiment shows that 3 mg / kg / day of CBD administered for 30 days (1 volunteer received 6 mg / kg / day during the last 3 days of experiment) did not induce any psychic or other side effects and was well tolerated by the 8 subjects. Thus CBD does not appear to have any toxic effect in humans when administered at the above dosage over a long period. This confirms our previous data obtained in animal (Cunha and Carlini, to be published).

In our opinion these findings justified the trial of the drug in epileptic patients.
Experiment 2 (Phase 2 of Study)

Material and Methods

Subjects
15 Epileptic patients, 11 women and 4 men, aged 14-49 (average 24 years), with a documented history of frequent convulsions for at least 1 year, were selected. These patients were not reacting satisfactorily to the prescribed antiepileptic drugs they were receiving (table 1) in spite of special care to assure that the patients were taking them properly. The patients were diagnosed as cases of secondary generalized epilepsy; EEG tracings revealed irritative activity with temporal projection. They had at least one generalized convulsive crisis weekly. Clinical and laboratory examinations showed no signs of renal, cardiovascular or hepatic disease. The experiment was performed in the Neurology Out-Patient Clinics of the Hospital Sao Paulo (8 patients) and the Hospital da Santa Case (t patients). Each patient was followed by the same investigator, beginning 2 weeks before first drug administration and then throughout the whole period of drug administration. In the 2 weeks before CBD or placebo administration, the number of focal and generalized convulsive crises was

recorded and considered as the baseline to evaluate treatment. On the first day of the experiment, the patients were submitted to the examinations described in experiment 1. They were randomly divided into one group of 8 (control group) and another group of 7 (CBD group) and returned to the hospital for 2 more days. After 1 week each group received placebo or CBD capsules in a double-blind procedure in addition to the antiepileptic drugs they were already receiving (see table 1). 1 placebo patient (Z.S.M.) was transferred to the CBD group after 1 month. Half of each group of patients was treated in each hospital. The patients were instructed to take 2 or 3 capsules daily (containing 100 mg of CBD or glucose) and to return to the hospital every week for clinical and / or laboratory examinations.

Clinical evaluation of drug treatment was made weekly using a scale with score 0-3, which took into consideration absence of convulsive crises or absence of generalization and self-reported subjective improvement (see tableII). According to this criterion all patients were scored 3 during the predrug phase (baseline).

Results

General Observations
During the curse of the experiment none of the 8 patients receiving CBD showed evidence of behavioral alterations which could be suggestive of a psychotropic effect. The minimum and maximum times of drug administration were 8 and 18 weeks for most patients (control and CBD groups). 2 of the placebo patients did not return after the end of the 4th week and 1 CBD patient after the 6th week. 1 placebo patient (Z.S.M.) whose condition remained unaltered during 4 weeks, wanted to give up the experiment, but remained in it after crossing over to the CBD group.

4 patients under CBD and 1 receiving placebo complained of somnolence during the experiment. Another CBD patient (M.C.P.) complained of painful gastric sensations after drug ingestion at the 6th week. These symptoms disappeared after prescription of an antacid and did not return throughout the experiment.

Table II. Criteria used to evaluate clinical efficacy of cannabidiol in epileptic patients

Score 0.....complete improvement
Score 1.....partial improvement
Score 2.....small improvement
Score 3.....without improvement

0 = Total absence of convulsive crises and self-reported subjective improvement.
1 = Absence of generalization of crises and self-reported subjective improvement.
2 = Only self-reported subjective improvement.
3 = No reduction in crises and no self-reported improvement.

Neurological Examination and EEG
Before drug treatment 1 CBD patient (N.D.) showed paresthetic walking towards the right, with spastic hypomotility of the right arm and leg, mainly of the right hand. He also presented a decrease in psychomotor functions. 2 other patients in the CBD group (A.A.S. and Z.S.M.) showed in examinations prior to the experiment some mental underdevelopment. Neurological examinations of all other patients were within normal limits.

Table III shows the results of the EEG analysis in a condensed form. Of the patients receiving CBD, 3 showed improvement in EEG pattern with signs of decrease in frequency of crises throughout the experiment. 2 placebo patients also had improved EEG patterns (J.O.R. and J.S.V.) on one occasion, with a return to their previous condition on subsequent examination.

Clinical Evaluation of Treatment
Clinical evaluation was performed weekly, scoring 0 - 3 points to each patient compared to its own baseline (see table II and 'methods' for details). At the end of the treatment, the median of weekly score for each patient was calculated. The results are presented in table IV. During the first week of treatment there was general improvement in almost all patients (placebo and CBD groups), but from the second week, all placebo patients with one exception (M.D.M.S.) returned to their previous clinical

state. At the end of the placebo treatment, 7 patients had a median of 3 (i.e. no improvement) whereas patient M.D.M.S. showed complete improvement (median 0). 2 placebo patients (J.S. and M.G.S.) with no improvement received the capsules for the 4th week of treatment but did not return. 3 other placebo patients (J.O.R.; J.S.V.; M.L.M.) remained under treatment for the period stated in table IV, after which it was decided to withdraw them from the experiment and to change the antiepileptic drugs they were receiving (see table I) in an attempt to improve their condition. Patient R.C. remained in the placebo group for 18 weeks and received all known antiepileptic drugs without success. Patient Z.S.M. was on placebo for 4 weeks without improvement and was subsequently transferred to 200 mg of CBD daily for 6 weeks (without her knowledge) with a small improvement (median 2).

Of the 8 patients receiving CBD, 4 showed considerable improvement in their clinical condition (median 0). However, in 1 case (M.C.P.) this was achieved by increasing the dosage to 300 mg daily. Patient A.A.S., who showed much improvement from the first week, unfortunately moved to another city after completing 6 weeks of treatment with CBD. The 5th patient (F.R.F.) improved only partially (median 1) although he attained score 0 in clinical evaluation (no convulsive crisis and subjective improvement) in 7 out of the 16 weeks of treatment. 2 of the 3 remaining patients showed improvement (score 2) whereas the last patient (N.D.) did not improve at all in spite of increasing CBD to 300 mg daily for the last 2 weeks of treatment.

Table IV

JOR placebo 3
JS placebo 3
MGS Placebo 3
JSV placebo 3
MLM placebo 3
RC placebo 3
MDMSplacebo 0
ZSM placebo 3

ZSM CBD200 2
FRF CBD200 1
OEBNCBD200 0
AAS CBD200 0
ASR CBD200 2
NP CBD200
300 3
MCP CBD200
300 0

0 = complete improvement
3 = no improvement

Discussion

Treatment of epilepsy is based mainly on anticonvulsant drugs. However, even when properly administered in well-diagnosed cases, these drugs succeed in helping only about 70-75% of the epileptic patients, whereas about 30% of the patients do not benefit at all (Robb, 1975). Furthermore, all clinically effective antiepileptic drugs induce undesirable side effects at normal dosage (osteomalacia, megaloblastic anemia; gingival hyperplasia) or due to overdose (nystagmus, motor incoordination, coma and death) or to idiosyncratic reactions (Kutt and Louis, 1972).

As already stated in the introduction, many ancient reports mention the antiepileptic properties of cannabis. More recently Consroe et al. (1975) described an epileptic patient receiving phenobarbital and phenytoin without good results, who benefited by smoking marihuana. These accounts indicate that marihuana contains chemical entities which may possess anti-epileptic properties.

According to the present data, CBD may turn out to be a useful drug for the treatment of some cases of epilepsy. There is hardly any toxicity as shown in our phase 1 study; there were no changes in EEG, ECG, blood and urine analyses and neurological and clinical examinations were normal in 8 healthy volunteers receiving 3 mg / kg of CBD daily for 30 days. A similar absence of toxicity was also noted in our phase 2 study in

which 8 epileptic patients received 200 or 300 mg for up to 4 1/2 months. Furthermore, none of the 16 subjects receiving CBD showed any psychic delta-1-THC-type effects. The present data obtained after long-term administration also confirm previous reports showing the absence of toxicity in acute studies (Hollister, 1973; Carlini et al, 1979).

Somnolence reported by 3 healthy volunteers and 4 epileptic patients (43% of the subjects receiving the drug) was the only CBD side effect noted. A certain hypnotic effect is frequently observed with drugs which possess antiepileptic properties. We have in fact recently demonstrated that CBD does induce better sleep in human volunteers (Carlini et al., 1979). On the other hand, CBD induced a remarkable improvement (median 0) in 4 of 8 epileptic patients who remained almost free of convulsive crises during the entire period of the experiment. In a 5th patient (median 1), the crises were absent in 7 of the 16 weeks of treatment. All of these patients (as well as their relatives) reported subjective improvement. A similar subjective effect was also reported by 2 more patients and only in 1 patient CBD failed to induce any form of clinical benefit. This is in striking contrast to the results obtained with the 8 patients receiving placebo of whom 7 showed no improvement in their clinical condition.

However, EEG results were not as consistent as the clinical evaluation. As seen in table III, clinical improvement was not always followed by positive changes in the tracings. As the International League against Epilepsy (Commission on Antiepileptic Drugs) does not consider EEG mandatory in this type of research (Penry, 1973), EEG data were not included in the overall clinical evaluation of CBD effects. It should also be emphasized that the abnormal EEGs were present from the beginning of the experiment even though all patients were receiving known antiepileptic drugs. Furthermore, phenytoin and barbiturates fail to control the EEG abnormalities of epileptics in spite of being able to abolish their behavioral convulsions; phenytoin may even increase the prominence of focal spikes (Morrel et al., 1959; Millichap, 1969).

Wall et al. (1976) have reported pharmacokinetic studies in man with 3H-CBD injected intravenously into 5 healthy volunteers. They observed that 8% of the total initial dose (20 mg of CBD) was present in plasma 30 min after injection, to fall to 3% after 60 minutes. 3 days later, 33% was excreted in the feces and 16% in the urine, with 50% remaining in tissues and organs. Therefore, CBD seems to have a relatively long half-life, which favors its use as a drug in epileptics.

However, in spite of the large number of reports showing beneficial effects of cannabis and its preparations in many forms of experimental convulsions and in human epilepsy, a few reports claim the contrary. Feeney et al. (1976) showed that delta-1-THC in cats induced EEG changes resembling those observed in convulsions, and Perez-Reyes and Wingfield (1974) described a similar effect of CBD in man. In neither case, however, were behavioral convulsions observed. It is interesting in this context that phenytoin may increase activity of focal spikes (Millichap, 1969). To the best of our knowledge there is only one report attributing a worsening of an epileptic convulsive crisis (grand mal) following use of marihuana smoking (Keeler and Reifler, 1967), and we do not know of any cases described for CBD. Furthermore, in none of our 8 epileptic patients did we observe deterioration of clinical symptomatology or of EEG, but rather the opposite effect was true.

The mechanism by which CBD benefited our epileptic patients is not known. All 8 patients were also receiving known antiepileptic drugs which were by themselves, however, ineffective. One possibility is that CBD potentiated their action since enhancement by CBD of anticonvulsant activity of phenobarbital and phenytoin in animals has been demonstrated (Consroe and Wolkin, 1977; Chesher and Jackson, 1974; Chesher et al., 1975). In man, however, 50--500 mcg / kg CBD given in cigarette form is not able to alter plasma concentrations of secobarbital (Dalton et al., 1976b). The possibility that CBD acts per se should also be taken into consideration, as shown by several reports describing its direct anticonvulsant effects in animals.

In conclusion, we have found that CBD had a beneficial effect in patients suffering from secondary generalized epilepsy with temporal foci, who did not benefit from know anti-epileptic drugs. Further research with more patients and other forms of epilepsy is needed to establish the scope of the antiepileptic effects of CBD in humans.

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EXHIBIT G

Petro/MS/1981

TREATMENT OF HUMAN SPASTICITY WITH DELTA-9-TETRAHYDROCANNABINOL

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J Clin Pharmacol. 1981; 21: 413S--416S

Abstract: Spasticity is a common neurologic condition in patients with multiple sclerosis, stroke, cerebral palsy or an injured spinal cord. Animal studies suggest that THC has an inhibitory effect on polysynaptic reflexes. Some spastic patients claim improvement after inhaling cannabis. We tested muscle tone, reflexes, strength and performed EMGs before and after double-blinded oral administration of either 10 or 5 mg THC or placebo. The blinded examiner correctly identified the trials in which the patients received THC in seven of none cases. For the group, 10 mg THC significantly reduced spasticity by clinical measurement ($P<0.01$). Quadriceps EMG interference pattern was reduced in those four patients with primarily extensor spasticity. THC was administered to eight other patients with spasticity and other CNS lesions. Responses varied, but benefit was seen in three of three patients with "tonic spasms." No benefit was noted in patients with cerebellar disease.

Several patients with multiple sclerosis reported to us that their spasticity improved after smoking marihuana. Preliminary uncontrolled observations of these patients before and after inhalation of the drug suggested to us that the improvement in spasticity was a specific effect of the marihuana and not merely a result of the well-recognized euphoria or altered perception experienced by social users of the drug.

Methods

We entered nine patients with spasticity, presumably of spinal origin and related to multiple sclerosis, into a double-blinded pilot study. The blinded observer examined each patient on three separate days, before and at 1 1/2-hour intervals after oral administration of a capsule containing either 10 mg, 5 mg, or no synthetic delta-9-tetrahydrocannabinol (THC). Absorption of oral THC is variable, about 90 per cent, but generally slower than that of inhaled THC. Blood levels and psychologic effects peak at 3 hours after ingestion. Because blood level determination is costly and may be unreliable, we did not determine levels.
The examiner rated deep tendon reflexes, muscular resistance to stretch in the legs, and abnormal reflexes each on a scale of 0 (absent) to 4 (abnormally increased) and tabulated the total divided by the number of observations as the "spasticity score" at 1 1/2 -hour intervals. For example, if both knee jerks were 3+, both ankle jerks were 3+, and both adductor jerks were 3+, the total was 18 and the spasticity score was 18/6= 3.0. Babinski signs were rated as 4+, their absence as 3+.
The examiner viewed the EMG interference pattern of the quadriceps muscle as the knee joint was flexed from 0 to 90 degrees at varying velocities. The examiner also assessed walking ability, inquired about the patient's subjective response and side effects of the drug, and measured vital signs.

Results

Three patients reported feeling "loose" and better able to walk after receiving either 5 or 10 mg THC. The changes in spasticity scores for the treated and placebo groups are illustrated in Fig. 1. Differences between the groups at 180 minutes are significant ($P<0.01$); summed scores for the two treated groups differed significantly from summed scores of the placebo group ($P<0.005$). The spasticity scores of four patients improved more than two standard deviations from the mean after either 5 or 10 mg THC; one patient improved after placebo. Only two of the three patients who felt improved actually did so by objective criteria. On the basis of the spasticity scores, the blinded examiner identified correctly the placebo trials in seven of the nine patients.
The EMG index of spasticity proved to be impractical in five patients—in three because resistance to stretch was too severe and in two because electrical activity was too little to record. Among the remaining four patients, the interference pattern, by visual inspection, was reduced after treatment from the pretreatment pattern at comparable velocity of stretch.
Side effects of the 5- or 10-mg oral dosage were minimal. One

patient reported feeling "high" after 10 mg, and another reported a "high" after placebo. No other patients reported side effects at the relatively low doses we used.

Discussion

Our preliminary results suggest that THC or one of its synthetic derivatives warrants further study as a potential treatment for spasticity. Although many previous investigators have studied the effects of marihuana on complex motor tasks, we were not able to find previous studies of the effects of marihuana on spasticity in the medical literature. Experimental studies in animals suggest that THC has an inhibitory effect on polysynaptic reflexes mediated through the spinal cord. The results of differential sectioning of the neuraxis in cats by Dagirmangian and Boyd (1) suggest that the ability of several tetrahydrocannabinols to decrease polysynaptic flexion reflexes relates to its action in the region between the mesencephalon and first cervical segment. Kayaalp et al. (2) postulate that THC has an effect on both nerve conduction and skeletal muscle contraction. Sullivan (3) and colleagues found a dose-dependent loss of reflexes and muscular weakness in dogs.
Although THC has proved to be clinically useful in the treatment of nausea induced by cancer chemotherapy and in reducing intraocular pressure in glaucoma, the results of these trials have demonstrated several disadvantages of the drug. The first is its potential for psychologic effects that limits usage in higher doses than those we employed. The second drawback to regular clinical use of the drug and of its many derivatives is the observation that many of its therapeutic effects may diminish after a relatively short period of regular usage.

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Discussion of the Paper

Dr. Nahas: Were the subjects that you studied naive toward marijuana, and did you observe tolerance?

Dr. Petro: All of our patients were naive to marijuana. Anecdotally, other patients claim that they have been using marijuana for periods up to 15 years for control of spasticity, but research needs to cover a larger and better controlled sample before any definitive statement would be possible. No chronic studies have been done to evaluate drug tolerance in spasticity.

Dr. Ungerleider: Did you, as blinded examiner, interview the patients and perform the tests?

Dr. Petro: I did all of the evaluations of neurologic function.

Dr. Ungerleider: Did you know that they felt better before you evaluated them objectively?

Dr. Petro: No; I used only objective measures, the EMG criteria and the spasticity scores.

Dr. Lindblom: Have you considered the use of patients other than those with multiple sclerosis (MS)? We studied the effect of baclofen on spasticity, and found much spontaneous variability in MS patients. In addition, some are euphoric from the disease and cannabis might add to the euphoria and confuse the results with unspecific effects. Furthermore, there are several types of spasticity, and in the case of baclofen, we found that gamma-spasticity was reduced but alpha-spasticity was unaffected.

Dr. Petro: We had a population of MS patients that was rather large and

readily accessible. Certainly, in subjects with significant cerebellar disease, marijuana (or its derivatives) would appear to be contra-indicated because of relaxant effects. We examined the patient population readily available for study, which was MS patients, but as you suggest this is not the ideal group to study.
Dr. Gilbert: Poly-synaptic reflexes in the dog are very sensitive to THC. In the morphine-dependent animal during abstinence there is an increased activity in the hind limbs. That activity can be blocked with very low doses of THC, nantradol and nabilone, before we see any other effects of the drugs (see Gilbert et al., this monograph).

Dr. Dow: Could you elaborate on your conclusion that THC is not the ideal drug for spasticity?

Dr. Petro: Patients that report effects from marijuana don't like taking THC; after smoking a marijuana cigarette, they clearly have an improvement that is different from that seen from THC. As other related substances with more specific CNS effects become available, these should be studied in the treatment of spasticity.

EXHIBIT H

3RD ARTICLE of Level 1 printed in FULL format.

The New England Journal of Medicine (R)

N Engl J Med 1994; 331: 1675-1679

December 22, 1994

SECTION: ORIGINAL ARTICLES

LENGTH: 3337 words

TITLE: **Risk Of Kidney Failure Associated With The Use Of** Acetaminophen, Aspirin, And Nonsteroidal Antiinflammatory Drugs.

SOURCE: From the Welch Center for Prevention, Epidemiology, and Clinical Research (T.V.P., P.K.W., M.J.K.) and the Departments of Epidemiology (T.V.P., P.K.W., M.J.K.), Health Policy and Management (M.J.K.), and Medicine (P.K.W., M.J.K.), Johns Hopkins University School of Hygiene and Public Health and School of Medicine, Baltimore; and the Institute of Social and Preventive Medicine, University of Geneva, Geneva, Switzerland (T.V.P.). Address reprint requests to Dr. Perneger at the Institute of Social and Preventive Medicine, University of Geneva, Centre Medical Universitaire Case Postale, 1211 Geneva 4, Switzerland.

Supported by grants from the Swiss National Science Foundation (823B-025121 and 32-32609), the Schmidheiny Foundation, the American Heart Association, the National Kidney Foundation, and the Agency for Health Care Policy and Research (R03 HS 06978-01); by General Clinical Research Center grants (5MOIRR00722 and RR00035) from the National Center for Research Resources; and by a Health of the Public Award from the Pew Charitable Trusts and the Robert Wood Johnson Foundation. Dr. Klag is an Established Investigator of the American Heart Association.

AUTHOR: Perneger, Thomas V.; Whelton, Paul K.; Klag, Michael J.

ABSTRACT: Background. People who take analgesic drugs frequently may be at increased risk of end-stage renal disease (ESRD), but the extent of this risk remains unclear.

Methods. We studied 716 patients treated for ESRD and 361 control subjects of similar age from Maryland, Virginia, West Virginia, and Washington, D.C. The study participants were interviewed by telephone about their past use of medications containing acetaminophen, aspirin, and other nonsteroidal antiinflammatory drugs (NSAIDs). For each analgesic drug, the average use (in pills per year) and the cumulative intake (in pills) were examined for any association with ESRD.

Results. Heavier acetaminophen use was associated with an increased risk of ESRD in a dose-dependent fashion. When persons who took an average of 0 to 104 pills per year were used for reference, the odds ratio of ESRD was 1.4 (95 percent confidence interval, 0.8 to 2.4) for those who took 105 to 365 pills per year and 2.1 (95 percent confidence interval, 1.1 to 3.7) for those who took 366 or more pills per year, after adjustment for race, sex, age, and intake of other

analgesic drugs. When persons who had taken fewer than 1000 pills containing acetaminophen in their lifetime were used for reference, the odds ratio was 2.0 (95 percent confidence interval, 1.3 to 3.2) for those who had taken 1000 to 4999 pills and 2.4 (95 percent confidence interval, 1.2 to 4.8) for those who had taken 5000 or more pills. Approximately 8 to 10 percent of the overall incidence of ESRD was attributable to acetaminophen use. A cumulative dose of 5000 or more pills containing NSAIDs was also associated with an increased odds of ESRD (odds ratio, 8.8), but the use of aspirin was not.

Conclusions. People who often take acetaminophen or NSAIDs have an increased risk of ESRD, but not those who often take aspirin. (N Engl J Med 1994;331:1675-9.)

TEXT:

Analgesic nephropathy was first described in the 1950s n1. Phenacetin was subsequently identified as the chief culprit and was withdrawn from the market. Evidence of the nephrotoxicity of other analgesic drugs -- acetaminophen, aspirin, and other nonsteroidal antiinflammatory drugs (NSAIDs) -- is scanty and inconsistent n2. In a prospective study of Swiss factory workers, subjects who took salicylates had no excess of kidney disease n3. Of four case-control studies, one n4 reported no association between the ingestion of analgesic drugs and end-stage renal disease (ESRD), but the others found associations between ESRD and salicylates, n5 pyrazolones, n5 aspirin, n6 acetaminophen, n6 n7 and NSAIDs n8.

None of these case-control studies were entirely population-based. In three, patients with ESRD were drawn from the general population but were compared with hospitalized control subjects, n4 n5 n6 and in the fourth study subjects from the general population were compared with hospitalized patients with chronic kidney failure n7 n8. Because hospitalized patients may differ from members of the general population in their analgesic-drug use regardless of the presence of kidney disease, the associations found in these studies between renal failure and the use of analgesic drugs may be spurious. We report here a case-control study of over-the-counter analgesic drugs as risk factors for ESRD in which both the case patients and the control subjects were drawn from the general population.

Methods

The study protocol was approved by the institutional review boards at Johns Hopkins University and the Health Care Financing Administration.

Study Participants

We studied residents of Maryland, Virginia, West Virginia, and Washington, D.C., who were 20 to 64 years old and had telephones in their homes. People who lived in institutions, were absent from their homes for more than two weeks, or were unable to complete the interview (because of deafness or a language

barrier) were excluded from the study.

The case patients had to have ESRD and had to have started long-term dialysis between January and July 1991. They were drawn from the Mid-Atlantic Renal Coalition, a population-based registry of patients with ESRD. Of 978 persons in the registry, 752 were eligible to participate. The others were excluded for the following reasons: 93 did not have a private telephone, 65 had died, 19 were institutionalized, 14 had moved out of the study area, 8 had recovered their renal function, 8 were too sick to be interviewed, 7 had hearing problems, 5 did not speak English, 5 were hospitalized for more than two weeks, and 2 were more than 64 years old. Of the 752 eligible persons, 716 (95 percent) were interviewed (of the others, 16 declined to be interviewed, 5 did not complete the interview, and 15 could not be reached). A median of five months elapsed between the start of therapy for ESRD and the time of the interview.

The control subjects lived in the same area as the patients n9 and were selected by random-digit dialing so that their age distribution matched that of the case patients. We sought to enroll half as many control subjects as case patients. Of 1311 residences reached by telephone, 1259 (96 percent) were screened for eligible residents, and 402 were found to contain one or more eligible residents. Of the remaining 857 households, 846 contained no members in the required age group, 7 contained no English-speaking respondents, 3 contained respondents who had difficulty hearing, and 1 contained a respondent who had ESRD. When several eligible control subjects lived in the same household, one was selected at random. Of the eligible control subjects, 361 (90 percent) completed the interview.

Data Collection

Trained interviewers contacted potential participants by telephone, explained the purpose of the study, provided a telephone number to call for additional information, obtained informed consent, and asked a set of standard questions. The interview lasted 24 minutes on average. People who initially declined to participate were contacted again after two weeks; about 40 percent agreed to participate when approached a second time.

Exposure Variables

The participants were asked separately about their lifetime exposure to the following five types of analgesic drugs, referred to by their common brand names: single drugs or mixtures containing acetaminophen, but not aspirin or phenacetin; single drugs or mixtures containing aspirin, but not acetaminophen or phenacetin; mixtures containing acetaminophen and aspirin, but not phenacetin; single drugs or mixtures that contained phenacetin before its withdrawal from the market; and common NSAIDs containing ibuprofen, naproxen, or indomethacin.

The list of NSAIDs was based on a review of over-the-counter medications sold in Baltimore pharmacies in 1990; indomethacin was included because it was one of the first NSAIDs on the market. The other lists of medications were based on an update of the information used by Sandler et al in their studies n7 n8. Phenacetin-based medications were identified in order to adjust the analysis for exposure to this substance known to be nephrotoxic.

For each type of analgesic drug, the study participants were asked whether they had taken one or more brands more than 10 times in their lives (before starting dialysis, in the case of the case patients). Those who said they had done so were asked about the average frequency of their analgesic-drug use (days per week, month, or year), the age at which they began to take the drugs regularly, and the average number of pills consumed per day when they took the drugs. Average intake (in pills per year) and cumulative intake (in pills, calculated as the average intake multiplied by the number of years since the first regular use) were computed. In the case of mixtures containing both acetaminophen and aspirin, the total consumption was considered to include equal amounts of each primary drug. Average intake was categorized as light (0 to 104 pills per year, or 0 to 2 pills per week), moderate (105 to 365 pills per year, or up to 1 pill per day), or heavy (366 or more pills per year, or more than 1 pill per day), and cumulative intake was categorized as low (0 to 999 pills), medium (1000 to 4999 pills), or high (5000 or more pills).

Statistical Analysis

The case patients and control subjects were compared by cross-tabulation and logistic-regression modeling n10. Odds ratios were used to estimate relative risks. Tests of linear trend were performed when appropriate. Population-attributable risks were computed to estimate the potential effect of withdrawing a given analgesic drug on the incidence of ESRD n11. To examine the association of analgesic-drug use with different types of kidney disease, we used a five-level categorical outcome variable, with one level assigned to the control subjects and four levels assigned to the case patients according to the ascribed cause of ESRD: diabetes mellitus, hypertension, other specified causes, or no definite origin. The presumed cause of renal failure was based on each patient's recall of the diagnosis by his or her nephrologist. Polychotomous logistic-regression analysis n10 was used to analyze multilevel outcomes. All statistical tests were two-tailed, and a P value of less than 0.05 was considered to indicate statistical significance. The analyses were conducted with Systat software n12.

Results

The case patients and the control subjects differed significantly with respect to sex and race. Of the 716 case patients, 304 (42 percent) were women; 310 (43 percent) were white, 384 (54 percent) were black, and 22 (3 percent) were of other races. Of the 361 control subjects, 235 (65 percent) were women; 303 (84 percent) were white, 51 (14 percent) were black, and 7 (2 percent) were

of other races. The age distributions were similar in the two groups (mean +/- SD , 47 +/- 12 years in both), indicating successful matching.

A majority of the study participants had taken analgesic drugs either sporadically or regularly. Of the case patients, 77 percent had taken acetaminophen, 77 percent had taken aspirin, and 31 percent had taken NSAIDs more than 10 times in their lives. Among the control subjects, the rates were 75 percent for acetaminophen, 86 percent for aspirin, and 46 percent for NSAIDs. Similar proportions of case patients (15 percent) and control subjects (17 percent) had taken analgesics that may have contained phenacetin.

Frequency of Use

In the univariate analysis, heavy users of acetaminophen (more than 365 pills per year) had an increased risk of ESRD, whereas moderate users (105 to 365 pills per year) did not (Table 1). No statistically significant associations were noted for aspirin and NSAIDs. Adjustment for age, sex, race, and the use of other analgesic drugs strengthened the odds ratios for acetaminophen use and revealed a significant dose-response relation (P for linear trend, 0.009). In contrast, this adjustment weakened the associations of ESRD with the use of aspirin and NSAIDs.

*Table 1. Average Annual Intakes of Acetaminophen, Aspirin, and NSAIDs as Risk Factors for ESRD in Maryland, Virginia, West Virginia, and Washington, D.C., in 1991 *.

TABLE OMITTED

Cumulative Intake

The odds of ESRD increased with increasing cumulative intake of acetaminophen (Table 2), whereas persons who had taken 1000 to 4999 pills containing aspirin had a lower risk of ESRD than those with a lower cumulative intake. In contrast to heavy average intake, a high lifetime intake of NSAIDs was associated with a fourfold increase in the odds of ESRD. Although the confidence intervals were wide, the odds of ESRD were lowest with moderate intake of aspirin or NSAIDs. Adjustment for age, sex, race, and the intake of other analgesic drugs strengthened the associations between the cumulative intake of acetaminophen and ESRD (P for linear trend, <0.001) and between high doses of NSAIDs and ESRD.

*Table 2. Cumulative Lifetime Intakes of Acetaminophen, Aspirin, and NSAIDs as Risk Factors for ESRD in Maryland, Virginia, West Virginia, and Washington, D.C., in 1991 *.

TABLE OMITTED

Effect of Race

Black subjects reported less use of analgesic drugs than white subjects, but the associations between the use of analgesic drugs and the risk of ESRD did not differ according to race (data not shown). In analyses of both average and cumulative intake, adjustment for race accounted for most of the difference between the unadjusted and the adjusted results; this was due to the large disparity between blacks and whites in the base-line risk of ESRD.

Risk Factors According to Cause of ESRD

The pattern of risk associated with a person's average intake of analgesic drugs differed little according to the causes of ESRD that we studied: diabetes mellitus, hypertension, any other specified cause, or no known cause (Table 3). Since there were only 20 patients with ESRD who had underlying diagnoses of interstitial nephritis, no separate analysis of that subgroup was performed. The patterns of risk associated with cumulative intake of analgesic drugs were also similar in the various subgroups (Table 4): a high intake of acetaminophen or NSAIDs was apparently harmful, whereas a medium intake of aspirin appeared to be protective.

*Table 3. Adjusted Odds Ratios and 95 Percent Confidence Intervals for the Average Annual Intakes of Acetaminophen, Aspirin, and NSAIDs as Risk Factors for ESRD According to the Ascribed Cause of ESRD *.

TABLE OMITTED

*Table 4. Adjusted Odds Ratios and 95 Percent Confidence Intervals for the Cumulative Lifetime Intakes of Acetaminophen, Aspirin, and NSAIDs as Risk Factors for ESRD According to the Ascribed Cause of ESRD *.

TABLE OMITTED

Population-Attributable Risks

Estimation of the population-attributable risk of ESRD suggested that if each participant consumed fewer than 105 pills containing acetaminophen per year (fewer than 2 pills per week), the incidence of ESRD would decrease by 7.7 percent (Table 5). Changes in the average intake of aspirin and NSAIDs would have negligible effects on the incidence of ESRD. A reduction in lifetime acetaminophen use to fewer than 1000 pills could potentially lower the incidence of ESRD by 10.5 percent. Reducing the intake of aspirin would have the opposite effect, resulting in an increase in ESRD. These inferences assume that the observed associations (harmful in the case of acetaminophen and protective in the case of aspirin) are causal and correctly estimated.

*Table 5. Population-Attributable Risk of ESRD According to Average Intake and Cumulative Life-time Intake of Acetaminophen, Aspirin, and NSAIDs *.

TABLE OMITTED

Discussion

This study revealed several meaningful relations between analgesic-drug use and ESRD. The strength of these relations may have been underestimated, because drug use was measured rather imprecisely. These findings pertain only to adults 20 to 64 years of age who survived for about six months after the initiation of ESRD therapy.

Both heavy average intake (more than 1 pill per day) and medium-to-high cumulative intake (1000 or more pills in a lifetime) of acetaminophen appeared to double the odds of ESRD. These findings support those in two previous reports n6 n7. In our study, the estimated odds ratio of ESRD associated with daily use of acetaminophen was lower than that reported by Sandler et al n7; unlike them, we report a significant dose-response gradient. These discrepancies may be explained by differences in study methods: Sandler et al n7 measured analgesic use more precisely than we did, and they enrolled hospitalized case patients and control subjects drawn from the community, interviewed proxy respondents, and included patients at various stages of renal insufficiency.

Acetaminophen use apparently increased the odds of ESRD in patients with a variety of underlying renal diseases, including diabetic nephropathy. This may reflect the fact that tubulointerstitial changes (the typical analgesic-mediated injury) influence the progression of damage in a variety of renal diseases n13. Alternatively, acetaminophen can harm the kidney through several different pathogenic pathways n2. Because the diagnoses of underlying kidney disease were not validated in our study, misclassification may have obscured the differences between the effects of different diseases.

The potential effect of acetaminophen use on the overall incidence of ESRD is considerable. If our estimated odds ratios are valid and the association between acetaminophen use and ESRD is causal, reduced consumption of acetaminophen could decrease the overall incidence of ESRD by approximately 8 to 10 percent. This is 10 times more than would be inferred from the prevalence of analgesic nephropathy in patients with ESRD, as diagnosed by attending physicians (1 percent among patients 20 to 64 years of age in the United States from 1987 through 1990 n14). If our estimates could be extrapolated to the entire United States (which may not be possible, given the geographic variability in analgesic use n2) and to all age groups, such a reduction would represent a savings of $ 500 million to $ 700 million in costs for ESRD care each year. Because estimates of analgesic use based on recall by participants may be subject to misclassification, n15 the population-attributable risks provided by this study may underestimate the true potential benefits of reducing or stopping the consumption of acetaminophen.

Establishing the causality of the association between acetaminophen use and ESRD is critical. The association was dose-dependent, specific (i.e., unlike the

associations between other analgesics and ESRD), consistent with several previous reports, and biologically plausible, since acetaminophen is a metabolite of phenacetin. Thus, several criteria for causality were fulfilled. Nevertheless, the temporal precedence of the presumed cause still needs to be demonstrated, and experimental evidence for causality produced.

Unlike acetaminophen, aspirin did not increase the risk of ESRD. This confirms the results from some studies, n3 n7 but not others n5 n6. In our analysis, the risk of ESRD was slightly lower in persons taking an annual average of 105 to 365 pills and significantly lower in those who took 1000 to 4999 pills in their lifetime, as compared with persons who took aspirin less often. It is unlikely that aspirin has a true protective effect against renal failure. The J-shaped association, also observed for NSAIDs, may occur because persons with renal insufficiency (who are at high risk of ESRD) abstain from using aspirin. Heavy aspirin users may take analgesic drugs for serious indications, such as intense, protracted pain, and may be less concerned than moderate users about potential renal side effects. We cannot verify this hypothesis, because we did not investigate the reasons for analgesic use.

We detected no increase in the risk of renal failure among daily users of NSAIDs. An association of this type has been reported for men more than 65 years old, n8 but the age limits we used precluded verification of that finding. On the other hand, we found a steep increase in the odds of ESRD in persons who consumed 5000 or more pills containing NSAIDs during their lifetime. Although this finding is based on few observations (only 18 case patients and 2 control subjects reported taking NSAIDs in these quantities), it arouses concern about the safety of persons taking large quantities of NSAIDs. Our results may underestimate the toxicity of NSAIDs, because we did not thoroughly explore the use of preparations obtained by prescription and because patients with progressive kidney insufficiency may have been discouraged from using this class of drugs.

Previous research suggests that NSAIDs cause renal damage in persons with renal insufficiency by lowering the glomerular filtration rate through an anti-prostaglandin effect n16 n17. However, all NSAIDs may not have the same renal effects: ibuprofen may be more nephrotoxic than sulindac or other drugs n16 n17.

This study questions the safety of long-term acetaminophen use (more than 2 pills per day, or more than 1000 pills overall) and of consumption of large quantities of NSAIDs, but it suggests that aspirin use confers little or no excess risk of renal failure. Public health authorities should consider more careful oversight of the long-term use of acetaminophen in the general population. Possible options include using warning labels on packaging or requiring a prescription to purchase large amounts of acetaminophen. Any such decision must consider the substantial beneficial effects of this analgesic drug and the possible adverse effects of restricting access to it, such as a switch

by habitual acetaminophen users to other medicines, including NSAIDs, whose safety may also be questionable. Meanwhile, people requiring large quantities of analgesic medicines and those at high risk of renal failure may be best advised to use aspirin for pain control.

We are indebted to Ms. Tamra Myers for data-collection management; to Mrs. Shirley Kritt and Mrs. Jennifer Sykes for interviewing; to our collaborators at the Health Care Financing Administration (Dr. Zermain Breidenbaugh, Dr. Paul Eggers, Mrs. Pamela Frederick, Ms. Michael McMullan, Mr. Paul Mendelsohn, and Mr. Izzy Oppenheimer) and at the Mid-Atlantic Renal Coalition (Mrs. Nancy Armistead and Ms. Arlene Skinner); and to Dr. Dale P. Sandler, of the Epidemiology Branch, National Institute of Environmental Health Sciences, for kindly sharing information about analgesic medicines on the market in the past several decades.

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EXHIBIT I

Analgesic Effect of Delta-9-Tetrahydrocannabinol

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CRUDE preparations of cannabis sativa were recommended for a variety of painful conditions toward the end of the 19th century.[1-3] As analgesics they were regarded as especially effective in conditions having a large functional or psychic contribution to the pain such as migraine, dysmenorrhea, and the pain of terminal illness. Yet they proved no match for the potent and rapid acting narcotics and eventually lost favor because their effects were milder and less predictable. In contrast to the narcotics, however, their toxicity was observed to be low, their disturbance of vegetative functions minimal, and their potential for addiction practically nonexistent. Recent identification and synthesis of delta-9-tetrahydrocannabinol (THC), the psychoactive ingredient of cannabis, has made systematic administration of the compound possible and has rewakened interest in its therapeutic potential.[4,5]

This preliminary investigation was designed to demonstrate an analgesic effect of orally administered THC in patients suffering from cancer pain. Its specific purpose was the identification of a dosage range within which the drug might relieve pain without at the same time producing disturbing toxic effects. Placebo and randomly allocated, graded doses of THC were administered to hospitalized cancer patients who volunteered for a trial of this medication.

Materials and Methods

Ten cooperative subjects, eight women and two men, were selected for participation in this study from among advanced cancer patients being followed at the University of Iowa Hospital. These patients, having a mean age of 51 years and a mean weight of 62 kg, reported continuous pain of moderate severity that was attributable to their disease. Five patients suffered from carcinoma of the breast, two from malignant lymphoma, one from carcinoma of the cervix, one from carcinoma of the colon, and one from lymphoepithelioma. Patients receiving large doses of narcotics were excluded from the study although seven had received methadone as part of their regular analgesic regimen. All were admitted to the University of Iowa Clinical Research Center where they were maintained on their usual analgesic program. Each was informed that, while on the study, he would receive varied doses of the active ingredient in marijuana. Each was further advised that doses would not be of equal strength and that the objective of the study was to determine which were the most effective in relieving pain. Informed consent was obtained in writing from all patients.

Regular analgesics were withheld after 4:00 A.M., and test medications were administered once daily at approximately

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8:30 A.M., 1 hour after eating. On successive days, placebo and 5, 10, 15, and 20 mg THC, all identical in appearance, were administered double blind in a random sequence.* A full-time registered nurse assigned to the study administered test medications and interviewed subjects hourly regarding the severity of pain and the extent of relief experienced. The categories of slight, moderate, and severe pain all represented subjective judgments on the part of the patients at the time of being interviewed. The nurse's observations, including evident or reported side effects, were recorded on a pain chart designed for that purpose.[6,7] This observer also administered an 11-item subjective effects questionnaire hourly and a side effects inventory at the end of each 6-hour observation period. The subjective effects questionnaire consisted of the following seven-point scales: sleepy–awake, energetic–fatigued, sad–happy, quiet–restless, sociable–unsociable, dreamy–clear-headed, calm–uneasy, alert–dull, worried–peaceful, time slowed–time speeded up, and trouble thinking–thinking clearly. Hourly recordings of blood pressure and heart and respiration rates were also made.

Hourly ratings of the severity of pain (0=absent, 1=mild, 2=moderate, and 3=severe) were used to arrive at hourly pain *reduction* scores. These scores were obtained by subtracting the hourly ratings from that recorded prior to the drug's administration. If, for example, severe pain was reported before the drug was given, then mild pain 3 hours afterward would be assigned a reduction score of two. Pain *relief* scores were recorded as follows: 0=none, 1=slight, 2=moderate, 3=a lot, 4=complete. The sum of hourly pain reduction or relief scores for a given 6-hour observation period (total reduction or relief scores) were used as a basis for statistical analysis. Hourly scores on the subjective effects questionnaire were assigned to the number of points a subject moved away from a pre-drug reference on a particular scale.

Results

Table I shows mean total pain reduction and relief scores for placebo and THC. Application of Edward's method of trend analysis of variance revealed a significant trend toward progressive relief of pain with increasing doses of the drug ($P<0.001$).[8] Since a comparison of pain relief scores between adjacent dose levels yielded no significant differences, scores for combined low dose levels (5 and 10 mg) were compared with scores for combined high dose levels (15 and 20 mg).

Here, a significant difference in the expected direction of greater pain relief with high doses of THC was demonstrated ($P<0.025$, paired observation method). Due to the small number of patients and the variability between them, further statistical analysis of these data did not seem appropriate. Mean hourly relief scores for placebo and 10, 15, and 20 mg THC are plotted in Fig. 1. They show that the analgesic effect of THC developed gradually and was prolonged. While the

TABLE I

Total Pain Reduction and Relief Scores Following Oral THC

Dose	Scores (mean ± S.E.)	
	Pain reduction	Pain relief
Placebo	0.9 ± 0.30	2.8 ± 0.61
THC, 5 mg	2.6 ± 0.53	4.7 ± 0.95
THC, 10 mg	1.4 ± 0.42	4.4 ± 0.95
THC, 15 mg	3.6 ± 0.65	5.6 ± 0.84
THC, 20 mg	4.6 ± 0.66	10.8 ± 1.19

* Delta-9-tetrahydrocannabinol in capsules containing a sesame oil vehicle was obtained from the National Institute of Mental Health.

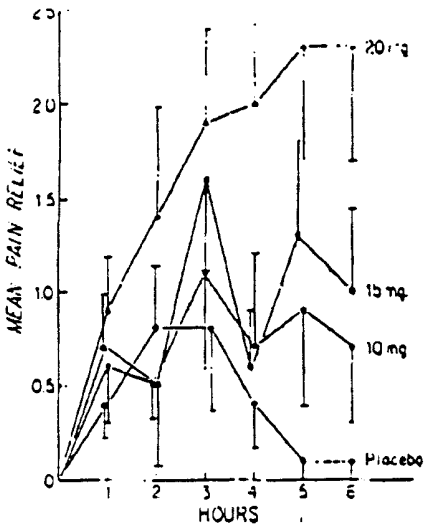

Fig. 1. Mean (± standard error) hourly pain relief in ten patients following the administration of THC.

peak effect occurred at 3 hours following 10 and 15 mg, it did not develop until 5 hours following a dose of 20 mg. A second peak observable at 5 hours after drug administration may have been the result of THC's mobilization from the gall bladder and reabsorption following food ingestion.[9] One patient with a lymphoepithelioma experienced no pain relief from THC at any dose. She differed from the others in having pain that was sharply localized, questionably related to her disease, and unresponsive to other analgesic medications. Five patients received substantial relief (total relief scores of greater than 6) from 15 mg and seven, from a dose of 20 mg.

Table II shows the frequency with which commonly experienced side effects were reported by the ten patients in this study. Patients receiving 20 mg THC were heavily sedated and even at 15 mg reported considerable drowsiness. This sedative effect was also apparent from responses on the subjective effects questionnaire. Table III shows total 6-hour change scores for three scales revealing a progressive reduction in arousal produced by the drug. Also shown in Table III is evidence of progressive mental clouding that made its appearance at 5 mg and became marked at 20 mg.

Other questionnaire scales showed no change. Euphoria was infrequently reported and was grossly evident in only two patients following the 15- and 20-mg doses. One of these was the only patient in the series giving a history of marijuana use. Several others reported minor elevations of mood when specific inquiry regarding such charges was made.

Both heart rate and blood pressure decreased following 15- and 20-mg doses of THC. The mean (± standard error) hourly decline in heart rate was 2.3± 1.93 beats per minute following 15 mg and 3.9±1.43 beats per minute following 20 mg. The mean hourly fall in blood pressure over the 6-hour observation was 11/7±1.48/1.31 mm Hg after 15 mg and 5/1±1.72/1.39 mm Hg following 20 mg. No change in respiration rate was observed.

Discussion

This preliminary trial of THC on a limited number of patients has demonstrated an analgesic effect of the drug. Attempts to establish its potency relative to standard analgesics of mild to moderate strength such as aspirin and codeine appear warranted and are currently in progress. In a dose of 20 mg, the drug is highly sedating and, consequently, of limited value for most patients. Doses of 5 and 10 mg, which showed a trend toward pain relief greater than placebo, might or might not maintain their superiority in trials involving large numbers of patients.

In the setting of this experiment, THC demonstrated sedating effects in contrast

TABLE II

Side Effects After Oral THC

Side effect	Number of patients experiencing side effects (N = 10)				
	20 mg THC	15 mg THC	10 mg THC	5 mg THC	Placebo
1. Drowsiness	10	7	5	7	3
2. Slurred speech	8	8	4	4	2
3. Blurred vision	7	7	4	2	0
4. Mental clouding	6	7	4	5	2
5. Dizziness	6	4	4	2	1
6. Headache	4	3	5	5	2
7. Increased appetite	4	5	5	2	0
8. Ataxia	5	7	3	3	3
9. Dreaminess	3	6	3	4	3
10. Disconnected thought	5	1	2	2	0
11. Numbness	4	3	2	1	0
12. Euphoria	5	4	1	0	0
13. Visual hallucinations	3	0	1	0	0
14. Tinnitus	0	2	4	0	0

TABLE III

Subjective Effects After Oral THC

Effect	Mean total deviations from predrug reference points on scales				
	Placebo	5 mg THC	10 mg THC	15 mg THC	20 mg THC
Sedation					
1. sleepy–awake	+6.5	−4.4	−4.9	−6.8	−9.8
2. fatigued–energetic	+1.0	−2.1	−2.2	−6.9	−7.0
3. dull–alert	+4.9	−1.5	−3.2	−2.7	−8.7
Mental clouding					
4. dreamy–clearheaded	+0.9	−2.6	−3.6	−9.1	−11.8
5. trouble thinking–thinking clearly	+2.2	−3.3	−3.8	−6.7	−6.7

to the stimulating ones commonly associated with its social use.[10] In place of heightened perception, numbness and pain reduction occurred; in place of euphoria and enhanced sociability, a dreamy social withdrawal developed. Associated with the latter, a fall in heart rate and blood pressure occurred in contrast to the increase in pulse which is typically reported.[11] Patients in this study were exposed to little stimulation, were relatively ill, and were, for the most part, socially isolated. These circumstances may well have been determinants of the drug's depressant effects.

Finally, the preliminary data reported here suggest that an association exists between the pain reduction caused by THC

and the reduction in arousal and attention produced by this drug. On the other hand, the reduction in pain appears to be independent of the compound's euphoric and antianxiety effects. Attempts to correlate physiologic measures of arousal and psychological assessments of attention with pain relief may provide clues to an understanding of the drug's mechanism of analgesic action.[12]

Summary

A preliminary trial of oral delta-9-tetrahydrocannabinol (THC) demonstrated an analgesic effect of the drug in patients experiencing cancer pain. Placebo and 5, 10, 15, and 20 mg THC were administered double blind to ten patients. Pain relief significantly superior to placebo was demonstrated at high dose levels (15 and 20 mg). At these levels, substantial sedation and mental clouding were reported.

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EXHIBIT J

Psychopharmacology 49, 79 – 84 (1976)

Psycho pharmacology

Effects of Marihuana Use on Body Weight and Caloric Intake in Humans

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Abstract. Body weight and caloric intake were measured in a group of heavy and casual marihuana users prior to, during and following 21 days of marihuana smoking under research ward conditions. A group of control subjects were studied under identical conditions, but they did not smoke marihuana. Both heavy and casual marihuana users had a significant increase in caloric intake and gained weight during the marihuana smoking period. Heavy and casual users gained an average of 3.7 and 2.8 lbs respectively during the first 5 days of marihuana smoking. In contrast, control subjects gained only a small amount of weight (0.2 lbs) during the same time interval. Water retention did not appear to be a major factor in weight gain by the marihuana users. These findings are in agreement with both anecdotal reports and previous experimental data that marihuana use is associated with increased caloric intake and weight gain.

Key words: Marihuana smoking – Weight gain – Experimental setting – Caloric intake.

Marihuana is commonly believed to enhance food intake in man. Anecdotal accounts of increased food ingestion associated with marihuana smoking (Siler et al., 1933; Haines and Green, 1970; Snyder, 1971) have only recently been assessed in clinical studies (Hollister, 1971; Williams et al., 1946). Hollister (1971) found that subjects ingested more of a chocolate milkshake preparation after 0.5 mg/kg oral delta-9 THC than after placebo. When offered the milkshake 3 h post-drug, marihuana subjects consumed 731 ml vs. 503 ml ingested by the placebo group. Chronic exposure to marihuana (39 days) or pyrahexyl, a THC analogue, (28 days) was also associated with weight gain (Williams et al., 1946).

In a recent study, Regelson et al. (1974) administered delta-9 THC to patients with cancer to determine if the drug would retard chronic weight loss. In a preliminary communication, these investigators report the delta-9 THC appeared to stimulate appetite and the patients gained weight. However, no data concerning amount of weight gained or calories ingested was reported.

The present study was part of a larger group of experiments designed to assess the effects of chronic marihuana use on various biological and behavioral functions (Mendelson et al., 1974). This report focuses upon the influence of marihuana smoking on food intake and body weight.

METHODS

Subjects. Male volunteers were recruited through advertisements placed in local newspapers. Psychiatric and medical examinations were carried out, and only those subjects in good physical and mental health were selected for participation in the study. Twelve 'casual' and fifteen 'heavy' marihuana users were studied compared with ten subjects who served as controls.

Casual users reported a mean duration of 5.3 years marihuana use with a monthly smoking frequency of 11.5 times. Heavy users reported a mean duration of marihuana use of 5.6 years and a monthly smoking frequency of 42 times. Both groups were matched as closely as possible with regard to socioeconomic background, intelligence and level of education. Further background information about the subjects is presented in Table 1.

Ten control subjects were exposed to identical ward conditions. These subjects had a past history of casual alcohol use and could work for money or alcohol on the research ward. Control subjects did not have access to marihuana or other drugs. As Table 1 indicates, the backgrounds of the control subjects were comparable to the casual marihuana users in all relevant respects. During the study they drank virtually no alcohol (average 1.5 oz. per day) and therefore qualify as drug-free controls.

Marihuana. All marihuana smoking had to be done at time of cigarette purchase, under the observation of a staff member.

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Table 1. Background characteristics and previous drug-taking experience: casual and heavy marihuana smokers

	Casual users ($N = 12$)		Heavy users ($N = 15$)		Controls ($N = 10$)	
	Mean	(SD)	Mean	(SD)	Mean	(SD)
Age	23.3	(1.1)	23	(1.6)	23	(1.5)
Years formal education	14.5	(1.4)	13.6	(1.5)	15.1	(1.6)
Years used marihuana	5.3	(1.1)	5.6	(1.9)	6.4	(2.3)
Marihuana use (times/mo)	13.0	(6.2)	41.0	(26.4)	3.4	(1.3)
Alcohol use (times/mo)	9.3	(8.0)	19.9	(10.0)	6.9	(4.1)

A detailed report of the experimental analysis of marihuana acquisition and use has been presented elsewhere (Mendelson et al., 1972). Unused portions of smoked marihuana cigarettes were returned to the staff to insure that 'roaches' were not accumulated and smoked without staff knowledge. Since studies were carried out on an inpatient hospital research ward, staff were able to insure that subjects did not use drugs other than marihuana.

Cigarettes containing approximately 1 g of marihuana were obtained from the National Institute of Mental Health (NIMH) in lot standard dosage form. Each cigarette contained approximately 1.8–2.3% THC as assayed by the NIMH. Actual content analysis of the marihuana using ethanol-Soxhlet and Modified Lerner extraction procedures was as follows: cannabidiol, 0.18% ± 0.04%; Δ^8THC, 0.002; Δ^9THC, 2.06% ± 0.08%; cannabinol, 0.08% ± 0.012%.

General Design. The investigation was carried out on a four-bed clinical research ward of the Alcohol and Drug Abuse Research Center at the McLean Hospital. Each study consisted of three consecutive phases: (1) a pre-drug 5-day baseline, (2) a 21-day period during which marihuana (or alcohol for control subjects) was available, and (3) a post-drug period of 5 days duration. All other conditions were identical for the marihuana and for the alcohol control subjects.

Food was prepared in the cafeteria of McLean Hospital and was brought to the research ward and served by nurses or mental health workers. The type and amount of food eaten was recorded and caloric intake calculated. Subjects were also permitted to choose their favorite snack foods and both the cafeteria and snack foods were supplied free to the subjects. Body weight was recorded each morning at 8.00 a.m. Urine samples were collected on a 24-h basis for all the casual and 11 of the 15 heavy marihuana users.

RESULTS

Daily body weight and caloric intake are reported for the heavy and casual users and the control group. Changes in body weight and caloric intake during successive 5-day periods of the study were analyzed with paired *t*-tests. Comparisons were made between the pre-drug control period and the first 5 drug days (study days 6–10) and also between the last five drug days (study days 22–26) and the post-drug phase. Body weights were obtained at 8:00 a.m. and represent food consumption during the previous day. Thus, post-drug body weights are plotted for a 4-day (days 28–31) rather than a 5-day (days 27–31) period in Figure 1.

Heavy marihuana users showed a significant ($P < 0.01$) increase in caloric intake and body weight following initiation of drug use (Fig. 1). Although body weight continued to increase during the drug phase, caloric intake decreased, but remained above baseline pre-drug levels. Upon termination of the smoking phase of day 26, both body weight and caloric intake decreased significantly ($P < 0.01$). The number of marihuana cigarettes smoked per day, displayed across the top of Figure 1, progressively increased during the 21-day drug phase; there was no clear relationship, however, between the number of marihuana cigarettes smoked by any single subject and the amount of food consumed. In fact, as Figure 1 indicates, the highest weight gains during the first five drug days corresponded to the least amount of marihuana use (4.29 cigarettes per day).

The casual user group (Fig. 2) also demonstrated increases in both body weight and caloric intake. Both measures increased significantly during drug availability and use ($P < 0.05$) and caloric intake decreased significantly following cessation of marihuana use ($P < 0.01$). However, body weight loss following cessation of marihuana use did not reach a statistically significant level. As with the heavy user group, no clear dose-weight relationship emerged for any subject. Once more, the high initial increases in body weight corresponded with relatively low levels of drug use (2.02 cigarettes per day).

Control subjects (Fig. 3) sustained monotonic increases in both body weight and caloric intake during the 30-day study. This pattern is in sharp contrast to the curvilinear changes seen in both marihuana groups. Further, the magnitude of weight and caloric intake changes in the control subjects was well below that seen in the marihuana groups. Weight gain comparisons between either marihuana group and the control group were statistically significant. (Casual users vs. control: $t = 4.13$, $P < 0.005$; heavy users vs. control: $t = 4.09$, $P < 0.005$.) The control sub-

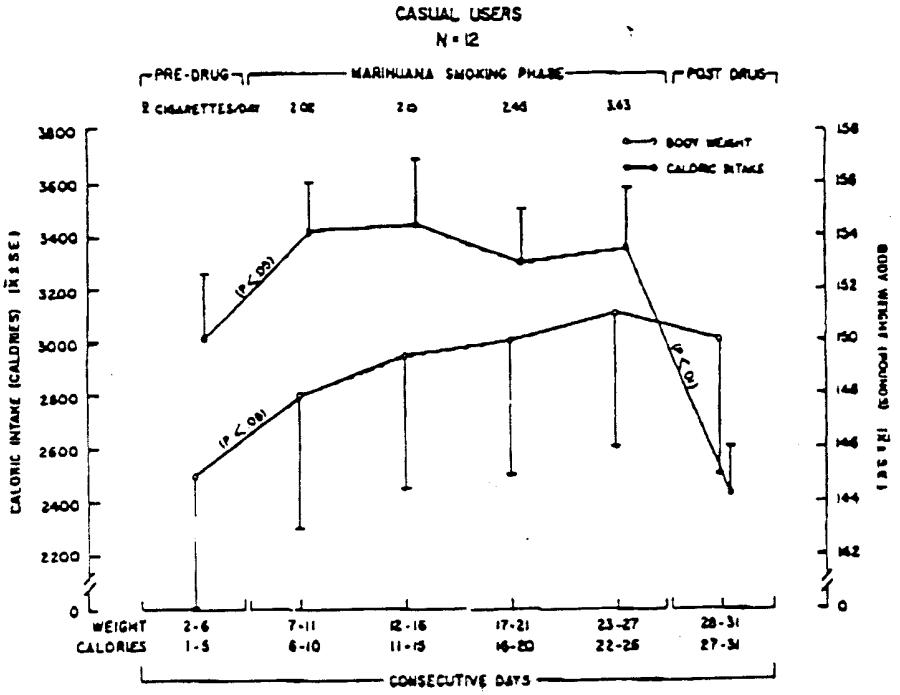

Fig. 1. Casual users ($N = 12$) patterns of body weight (O·——O) and caloric intake (● ●) are shown for consecutive 5-day blocks (see text). All points are group means ± standard error of the mean. At top of figure, the mean daily number of marihuana cigarettes smoked is listed for each 5-day period

jects continued to ingest food in increasingly greater amounts during the last five days of the study, while both marihuana groups had significantly depressed food ingestion levels during this period of time.

To determine if fluctuations in body-weight might be due to water retention, urine volume output was plotted as a function of time and drug phase (Fig. 4). If water retention were a function of drug use, urine volume output should have decreased upon initiation of marihuana use and should have increased with cessation of marihuana use. However, the opposite phenomena was found in the twelve casual and eleven heavy users, indicating that increased fluid intake paralleled increased food intake.

DISCUSSION

Results obtained in this study are in agreement with the findings of others on acute (Hollister, 1971) and chronic (Williams et al., 1946) effects of marihuana use on food ingestion. Hollister (1971) found that increased caloric consumption associated with acute delta-9 THC administration could be measured 3 h following drug administration. Williams et al. (1946) found that an increase in body weight occurred during a 39 day period of marihuana use. Caloric intake, however, only increased in a transient manner and then fell steadily to below pre-drug baseline levels. Evaluation of these data is difficult since the type, content and potency of the marihuana preparation smoked is not specified. Moreover, control groups were not studied to determine if non-drug related variables such as experimental setting, prison routine, type of food available, eating schedules, etc., had any influence on patterns of food ingestion. In the present study, high caloric intake was recorded throughout the smoking period for casual users, but showed a trend toward a sustained decrease below initial values for the heavy users. Since marihuana was available in our study for 21 days (vs. 39 days as described by Williams et al., 1946), it is possible that a longer period of marihuana availability would produce an initial increase followed by a depression of caloric intake.

A possible reason for a relative decrease in caloric intake after a significant initial increase at the onset of marihuana smoking may be related to gradual

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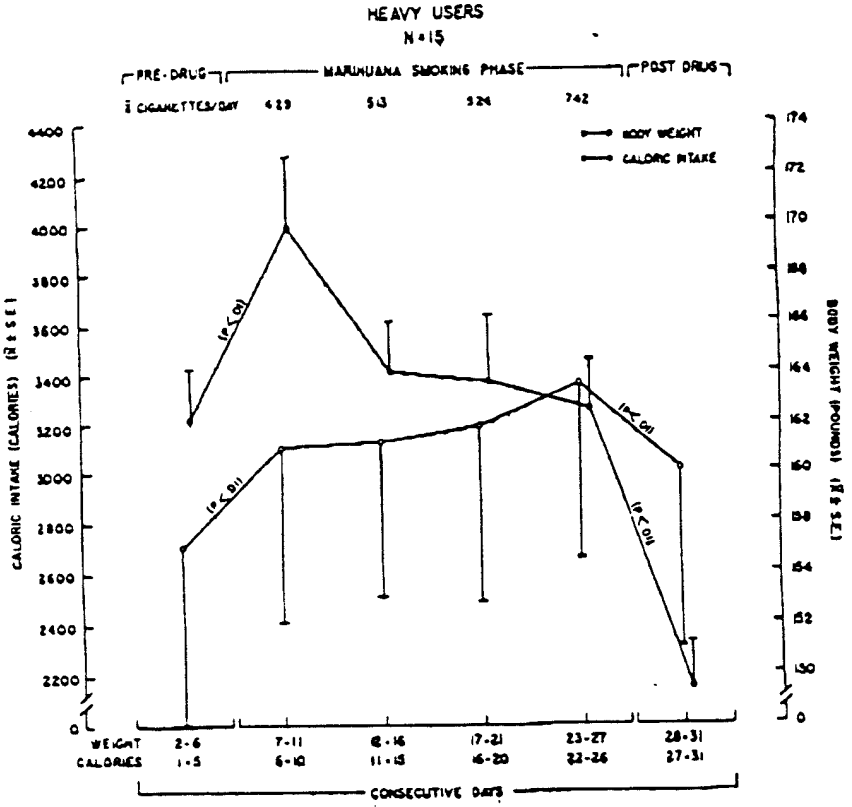

Fig. 2. Heavy users ($N = 15$) patterns of body weight (O —O) and caloric intake (● —●) are shown for consecutive 5-day blocks (see text). All points are group means ± standard error of the mean. At top of the figure, the mean daily number of marihuana cigarettes smoked is listed for each 5-day period

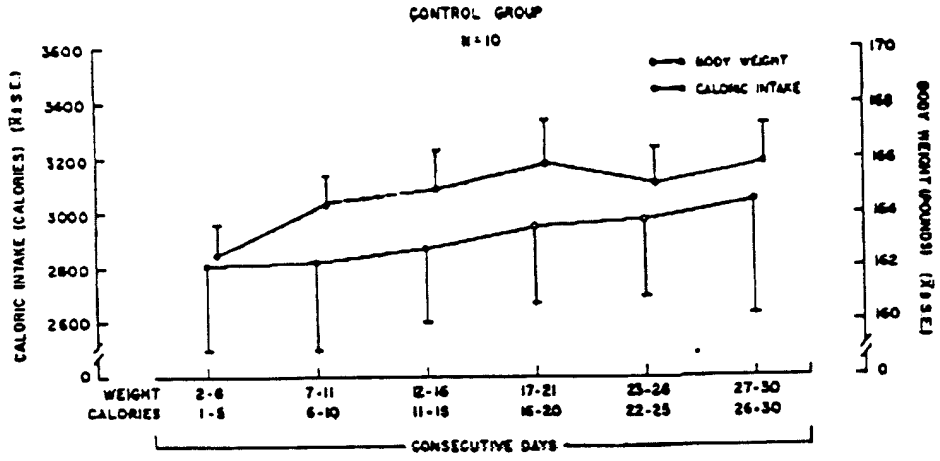

Fig. 3. Non-smoking controls ($N = 10$) patterns of body weight (O —O) and caloric intake (● —●) are shown for consecutive 5-day blocks (see text). All points are group means ± standard error of the mean

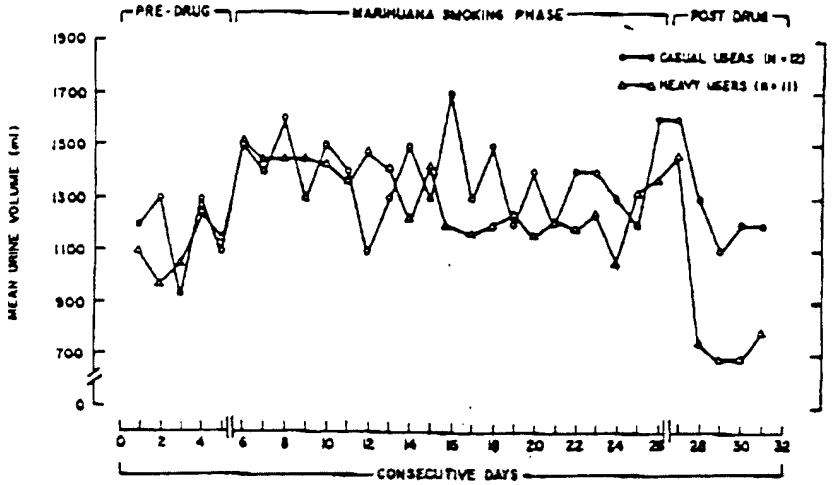

Fig. 4 Heavy (Δ—Δ) (N = 10) and casual (O—O) (N = 12) user urine volume output as a function of experimental phase

development of marihuana tolerance. It is also possible that the initial increase in food intake at the beginning of the marihuana smoking phase may have generated aversive consequences (e.g., fear of being overweight) and induced subjects to reduce food intake during subsequent marihuana smoking. In fact, subjects often verbalized their concern about gaining too much weight, but when overt dieting was reported, it began during the 5-day post-smoking period.

Control subjects gained very little weight as the study progressed. Increases averaged just over two pounds during 30 days and showed a linear trend. This phenomena might be expected considering restricted ward environment and the availability of free food.

Although there was no clear evidence that marihuana use resulted in marked fluid retention, this possiblity cannot be entirely ruled out. Benowitz and Jones (1975) have recently reported that weight gain in subjects administered daily Δ^9 THC may have been due to fluid retention and plasma volume expansion. Caloric intake was not presented in their report. The subjects in the present study showed clear changes in caloric consumption accounting for at least part of the significant weight changes. More detailed studies of total body water content are now being conducted to determine how caloric intake and changes in body water influence the weight of marihuana users.

Following administration of either pyrahexyl or delta-9 THC, rats show a decrease in food intake and in body weight (Abel and Schiff, 1969; Manning et al., 1971; Sjoden et al., 1973; Sofia and Barry, 1974). Why marihuana administration depresses food intake in laboratory animals but elevates caloric intake in humans remains unknown. Dosage factors may be as important as species differences. Human subjects control the amount of marihuana they smoke, while animals are usually given dosages proportionately many times greater than those used by humans (Elsmore and Fletcher, 1972). In the single report of THC- or marihuana-related weight gain in animals, rats were first adapted to a deprivation schedule for 150 days and then given delta-9 THC (Gluck and Ferraro, 1974). Under these conditions, rats consumed food during their daily 1 h access period in contrast to non-drug conditions. Thus, long-term adaptation to limited food access may be a necessary prerequisite for marihuana-related enhanced food intake in animals. Humans are under no such deprivation schedule, and the seemingly contradictory results between humans and laboratory animals may due be to species differences or to variables which, to date, have not been identified.

Acknowledgements. This study was supported, in part, by Contract No. DADA17-73-C-3082 from the Department of the Army and Grant No. DA4RG010 from the National Institute on Drug Abuse, ADAMHA.

We wish to thank Miss Lorraine DeRubeis for her assistance in data analysis.

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Received February 2, 1976, Final Version April 15, 1976

EXHIBIT K

EXHIBIT K, *IN DRUGS BETWEEN RESEARCH AND REGULATIONS*, IS A BOOK. DEFENDANTS WILL PROVIDE A COPY OF THIS BOOK TO THE COURT UPON REQUEST

EXHIBIT L

Specialty Conference

N-of-1 Clinical Trials

A Technique for Improving Medical Therapeutics

Discussant
ERIC B. LARSON, MD, MPH, *Seattle*

This discussion was selected from the weekly Grand Rounds in the Department of Medicine, University of Washington School of Medicine, Seattle. Taken from a transcription, it has been edited by Paul G. Ramsey, MD, Associate Professor of Medicine, and Philip J. Fialkow, MD, Professor and Chair of the Department of Medicine.

ERIC B. LARSON, MD*: Most clinicians have a keen interest in therapeutics and especially therapeutic efficacy. In fact, medical therapeutics can be viewed as a series of therapeutic experiments as follows:

A				*B*
Initial State	→	Therapy	→	Subsequent State

The patient comes to the physician in an initial state, *A*, and is offered treatment. The patient then assumes a subsequent state, *B*.[1] If *B* is more desirable, we typically judge that therapy was effective. If *B* is no different or is less desirable, we judge that therapy made no difference or was ineffective. Although this account seems straightforward, such simple assertions may not be true because of confounding factors.[2]

Effectiveness may be overestimated because of several factors. First, a patient can recover spontaneously coincident with treatment, an especially well-known occurrence for self-limited conditions. Second, patients commonly present when their symptoms are worse, especially patients with a chronic disease. Coincidental treatment appears to cause the problem to subside when the patient has simply returned spontaneously to the average, so-called baseline state of a chronic disease. This has been referred to as "regression toward the mean."[3] A third factor that may lead to an overestimation of effectiveness is a placebo effect. For some therapies, as much as 30% or more of the benefits may be due to the well-known placebo effect.[4] Finally, the expectation of a beneficial response and a willingness-to-please effect[4] are related to the placebo effect. In many patients, the simple "expectation" that a treatment will be beneficial may often be sufficient to promote a beneficial effect. The willingness-to-please effect results from the so-called obsequiousness bias[4] in which a patient gets better to please an expectant physician.

Similar confounding forces can obscure therapeutic effectiveness. Coexistent illness can coincidentally exacerbate the underlying problem. Chronic diseases have spontaneous exacerbations, and when these occur coincident with treatment, it appears that therapy is ineffective. Malingering or a secondary gain in which the patient experiences benefit from not getting better can make a patient resistant to the true effect of treatment. An age-related (physiologic) decline superimposed on a beneficial treatment effect may combine to cancel each other. Finally, if an incorrect diagnosis has been made, treatment will appear to be ineffective. For example, if a patient's symptoms or signs represent the upper or lower limits of a normal variation, then the treatment received, although usually effective, is ineffective in the misdiagnosed case.

Randomized Clinical Trials

Fortunately, randomized clinical trials (RCTs) have been used to evaluate medical therapeutics since the late 1940s.[4] Because such trials help eliminate the confounding factors outlined above, they have become the gold standard by which clinicians judge therapeutic efficacy. An RCT allocates consecutive patients to different treatments or randomly allocates the order of treatment in crossover experiments. When done carefully with enough patients, the randomization eliminates bias that might confuse the interpretation of the therapeutic experiment.

Unfortunately, many of a clinician's day-to-day treatment decisions cannot be based on the results of randomized trials. Table 1 shows examples of situations or problems in which RCTs may not be appropriate for making therapeutic choices. Unavailability of randomized clinical trials may be encountered in the case of a rare or unusual disease. Randomized trials may also not be available for some older treatments and for newer or novel treatments. Because RCTs have been widespread only since 1970, older treatments were often not evaluated by them. Newer or novel treatments, especially those devised by clinicians for single patients, are typically not subjected to randomized trials.

Even when there are good randomized trials showing efficacy, several factors limit their generalizability to a specific patient. For example, the patient might be outside the eligibility requirements for entry into an RCT. Eligibility criteria for most trials are so restrictive that less than 10% of patients with the disease in question may be accepted. Not surprisingly, the patients who are excluded are the ones in whom therapeutic dilemmas and an evaluation of therapeutics are often the most troublesome. Thus, their omission

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(Larson EB: N-of-1 clinical trials—A technique for improving medical therapeutics [Specialty Conference]. West J Med 1990 Jan; 152:52-56)

This work is supported by grant 1 RO3 HS 6006 from the National Center for Health Services Research and Health Care Technology Assessment.
Reprint requests to Department of Medicine, RG-20, University of Washington School of Medicine, Seattle, WA 98195.

TABLE 1.—*Limits of Randomized Clinical Trials (RCTs) for Care of Individual Patients*

RCT unavailable or impossible
Good RCTs show benefit but may not be generalizable
Eligibility criteria too restrictive
Some patients are nonresponders
Side effects
Good RCTs show *no* benefit but may not be generalizable
Atypical patients
Treatment response is idiosyncratic

from RCTs allows investigators to assess efficacy with fewer complicating factors. Another problem arises from the fact that even though a randomized trial has shown efficacy, not all patients will benefit from treatment. In addition, some patients may experience enough side effects that the net effect of treatment is harmful. The single patient who does not have a beneficial response experiences that event with 100% certainty even when generalizations based on populations studied by RCTs indicate the net effects are likely to be beneficial.

There are also limits to the generalizability of RCTs that show no apparent benefit. Good randomized clinical trials may not show any net benefit, but an individual patient may still benefit from treatment, especially if the treatment has biologic plausibility. Some RCTs have inadequate sample sizes and, hence, inadequate statistical power to show efficacy.[7] An individual patient could also be an atypical responder, or responsiveness to treatment may be idiosyncratic and difficult to demonstrate by an RCT.

In summary, even though randomized clinical trials are widely used for assessing therapeutic efficacy, their results may not apply to single patients or they may be unavailable for certain treatments, thus leaving clinicians in a quandary about therapeutic efficacy. Because of this quandary, there is increasing interest in single-patient experiments. A number of terms have been used to describe single-patient experiments, including N-of-1 trials, single-patient clinical trials, single-case analysis, crossover and self-controlled research designs, and single-patient RCTs. The field has an interesting history and holds great promise for improving the science of medical therapeutics.

Case Reports

Because case reports can be useful ways to illustrate valuable clinical lessons, I will present three single-case analyses in the order of my exposure to them. The first, a "case report" presented at the American Federation of Clinical Research meetings in 1985, was the case that piqued my interest in single-patient trials.[2] The second, a classic case that occurred at the interface of the developing science of statistics and popular culture, is intriguing for both its contents and the statistical power of its design.[8] The final case illustrates a single-case clinical trial that, although not random and only "single blinded," was convincing and influential.[9]

The first case was reported by Guyatt and co-workers from McMaster University, Hamilton, Ontario.[2] The patient, a 65-year-old man with uncontrolled asthmatic bronchitis, was becoming progressively more disabled by dyspnea with even simple daily activities. His therapeutic regimen eventually consisted of albuterol inhaler, ipratropium bromide, theophylline, and daily doses of prednisone. The clinician and the patient were uncertain whether the theophylline or ipratropium therapy was beneficial. Both suspected that theophylline was helpful and ipratropium was not. To optimize the therapeutic regimen, a single-patient trial was designed. Either theophylline or placebo, in a random order, was given for ten-day crossover periods. Three 10-day crossover pairs were planned. The end points included dyspnea, the need for albuterol inhaler, and the amount of sleep disturbance. During the first period, the patient did better than during the second ten days of the crossover trial. The same pattern then appeared during the second crossover period. The trial, which was originally scheduled to go for three crossover periods (about 60 days), now seemed too long to both the clinician and the patient. Both agreed that the trial should be terminated, presumably to allow the patient to resume taking theophylline. They were surprised when the placebo was associated with scores indicating increased well-being. Based on a review of the literature and the patient's course, it was determined that the seemingly anomalous results were most likely explained by gastroesophageal reflux (a xanthine side effect) and aspiration.[10] The theophylline therapy was stopped, and subsequently an N-of-1 trial of ipratropium revealed the beneficial therapeutic effects of its use. Eventually the patient was treated with a regimen of albuterol and ipratropium. He then tolerated a prednisone taper so that he could comfortably complete most of his activities of daily living on a regimen of 10 mg of prednisone every other day.

The second "case report" is not a medical case but represents a particularly famous single-case experiment. The case was an important one in the development of principles of experimentation and illustrates some useful points about randomization and statistical power. In 1935, R. A. Fisher, a British statistician whose name is most often linked with multiple-subject experiments, reported an example of how to conduct an experiment with a single subject and used that example to explain basic notions that underlie all experiments. This was the "lady tasting tea experiment."[8]

The case involved a tea-drinking English woman who claimed that she could tell whether the tea was added to the milk or the milk was added to the tea. Four cups of tea were prepared one way and four cups the other way, and the eight cups were then presented to her in a random sequence. She was told in advance that she was to identify the four cups that were prepared each way. The lady correctly identified all eight cups, and the *P* value was determined by the randomization test procedure. The null hypothesis was that her response at any treatment time was the same as it would have been at that time if any of the other cups had been presented. There are $8!/4!4! = 70$ ways in which eight cups can be presented with respect to milk first or tea first, given that four cups were milk first and four tea first. Thus, Fisher computed the *P* value as 1/70 because only 1 of the possible sequences of 4 *M*s and 4 *T*s correctly matched the woman's responses ($P = .014$).

An important feature of this experiment, in contrast to the first case report, is that the randomization occurred in blocks of eight treatments, not blocks of two as in the typical crossover experiment. Thus, the statistical power was considerably greater.

The third case report is a more primitive example of a single-patient trial.[9] Nonetheless, it also shows the value of single-patient experimentation. The report entitled "Inter-

nal-Mammary-Artery Ligation for Coronary Insufficiency—An Evaluation" was based on a presentation made in 1957 to the New England Surgical Society. This topic would later be investigated in a widely quoted article from the University of Washington describing a randomized, single-blind trial that compared a sham operation with internal mammary ligation.[11] Ralph Adams, MD, in the 1958 paper,[9] reported four cases, one of which was of a 60-year-old man admitted "three days after occurrence of his known episode of coronary thrombosis."

> His case was well known to the hospital because of previous attacks of deep thrombophlebitis, pulmonary embolism and hypercholesterolemia, and prior episodes of coronary occlusion. Precordial pain was intense and he was apprehensive that he would die. He was a highly educated man, well informed for a layman, on medical matters and in a position of considerable community responsibility. Admission was for the specific purpose of altering internal mammary circulation in the hope of giving him some cardiac protection. He was told . . . that this procedure was currently being widely discussed and, in some quarters, enthusiastically recommended. He was also informed that the hospital was in the process of evaluating the procedure as definitely as possible. These background facts led him to request that the operation be tried in the hope that he might be helped. . . .
>
> At operation, on the day of admission, a short incision was made in the second intercostal space lateral to each sternal border and each internal mammary artery was exposed. A silk ligature was placed about each artery but neither was tied. Thus, only a first-stage operation had been done, consisting of a skin incision and encirclement but not ligation of the internal mammary arteries.
>
> On awakening from the brief and light anesthetic, the patient reported that he was free of pain. He has had no pain since that date. An electrocardiogram on the day after operation showed no detectable change from preoperative tracing. Two days after the operation the ligatures from the internal mammary arteries were tied. Subsequent electrocardiographic tracings gave no evidence of improvement.

The author goes on to describe follow-up, which included no recurrence of symptoms, and states that

> in this case, there was not a fair chance to assay the relief of symptoms to be obtained by internal mammary artery ligation because the patient lost all symptoms after the first portion of a staged procedure that he believed to be the completed operation.

Adams reported what we would call a nonrandomized single-patient crossover experiment. A sham operation was followed by a real operation—dramatically showing what many might now call a placebo effect of internal mammary exposure.

Formation of an N-of-1 Clinical Trial Service

Before establishing a single-patient trial service, we contacted Dr Gordon Guyatt, who has actively investigated single-patient trials. He provided us with great encouragement and a summary of the experience of an N-of-1-trials service at McMaster University.[3] Most of his trials had been in the subspecialties of pulmonary medicine and rheumatology. Of the first 42 trials done at the center, 29 gave definitive results. In 11, active treatment was found to be effective, in 17 it was ineffective, and in 1 it was harmful (the theophylline case). Eight other trials gave less definitive results. Five were judged unsuccessful, three because, despite definitive outcomes, the results did not lead to action (G. Guyatt, written communication, June 1987).

Based on this encouraging report, we submitted a small grant proposal to the National Center for Health Services Research. Our research group, which includes Allan Ellsworth, PharmD; Jim Nuovo, MD (family medicine); Ina Oppliger, MD (rheumatology); Gerald van Belle, PhD; and Alice Arnold, MS (biostatistics), is now funded to establish and evaluate a single-patient trial service. We have announced our intentions to workers in other specialties and are currently receiving patients.

Because the objective of the "N of 1" experiment is to find the best treatment for a particular patient, we and others believe that some of the ethical questions asked of the standard randomized trial no longer apply.[3] For example, does the potential benefit to other patients outweigh the possible risk to this patient? Nonetheless, three ethical requirements do apply. First, a patient's free and informed consent should be requested after the clinician has described every feature of the trial that would materially affect the patient's decision to take part, including the reported effectiveness and safety of alternative treatments, the treatment targets to be used, and the duration and number of treatment periods to be executed. The second ethical requirement is that a patient must be free to withdraw at any time without loss of care. The third is that the same degree of confidentiality applied in other clinical situations must apply to the study results. One of our first tasks as an N-of-1 clinical trial service was to approach the Human Subjects Committee (Institutional Review Board) and seek approval for pending single-patient trials. They have developed an expedited approval process that facilitates the prompt institution of clinical trials.

When to Do a Clinical Trial

Perhaps the most germane issue in single-patient trials is when to do them. That is, when is a patient most likely to benefit from the results of a single-patient trial? The most important issue here is whether there is doubt about efficacy. Doubt may occur because neither the patient nor the physician is certain an existing treatment is working. In this setting, a patient with a chronic disease may be doing poorly or not improving on a medication regimen that could also be causing side effects, as exemplified by the theophylline case.

Another instance when efficacy may be in doubt is during the institution of a new treatment. Here the patient is being offered a new drug and the question is, "Will it work?" The clinician may be uncertain when the literature is equivocal about the drug, the risk-to-benefit ratio is less favorable, or the patient is reluctant to comply with presumably efficacious treatment.

For patients with rare or unusual conditions, the use of the single-patient trial may not only benefit the patient but also add to knowledge about the management of unusual conditions. The literature contains numerous examples of single-patient experiments where treatments of conditions like familial Mediterranean fever and narcolepsy were evaluated with N-of-1 trials.

Doubt about efficacy may be a motivating factor for a single-patient trial also when a patient insists on a treatment as necessary or effective in contradiction to medical advice or practice. The single-patient trial can be used when the physician is unable to convince the patient otherwise. In this case, a negative clinical trial should not surprise the physician but may be convincing to the patient.

After determining whether therapeutic efficacy is in doubt and deciding whether one wishes to demonstrate efficacy or a lack thereof, the clinician will need to consider other questions that affect the feasibility and worth of a single-patient trial. First is whether a treatment will likely be long term. Given the time required to conduct such a trial, single-patient trials of short-term therapies tend not to be

worth the effort required of the patient, and they are less likely to have value for the individual patient unless the patient will require the short-term treatment repeatedly.

Several questions related to the pharmacokinetics of a possible therapeutic agent affect the logistics and ease of doing single-patient trials.[12] The ideal treatment for single-patient trials is one that can be rapidly started and stopped. Thus, outcomes can be assessed starting relatively early in the trial, and there is little or no carryover between treatment periods. When these criteria are not met, carryover or period effects may complicate the interpretation.[13] These effects may require trials that are much more time consuming (for example, involving washout periods) or involve special design modifications. In general, single-patient trials are less likely to be useful for curative treatments (so-called period effects) or for long-acting treatments (due to carryover effects).

How to Do a Clinical Trial

There are three critical components of the single-patient trial: randomization, blinding of patient and physician to treatment assignment, and defining and quantitating the outcomes. The last, establishing explicit criteria for evaluating the efficacy of treatment, is a feature of the single-patient trial that is also important for medical therapeutics in general.

Randomization is necessary to minimize systematic biases that will occur related to the order of treatment and to permit double blinding to occur. Randomization is usually accomplished in a crossover style, that is, in blocks of two. If, however, it is predetermined that four, six, or eight trials will be done, the statistical power of the trial is improved considerably by randomization in larger blocks.[13] For example, when six trials are planned, the possible P values range from .125 for the paired experiment in which three crossover pairs occur ($[1/2]^3$) to .03 when all six trials are randomized independently ($[1/2]^6$). Intermediate values are possible when constraints are added.

Blinding is a key element to minimize observer-induced bias. In most single-patient trials, the patient records symptoms and, in some cases, signs. Ideally both patient and physician are blind to the treatment assignment. Records of assignment are kept with one of the trial service staff and, if a drug is involved, the pharmacist who has prepared the treatment packages.

Single-patient trials require that the goals of treatment be explicitly identified at the time the patient enters the trial. Ideally, three to five key variables are determined. The variables may reflect disease activity or symptom severity. Usually the most important variables measure patient functioning, reflecting the value of treatment for the patient. In the ideal case, outcomes would include the measurement of a physical sign, a subjective or objective rating of performance in conjunction with, for example, a laboratory measurement reflecting disease activity. The patient's goals must be assayed to be certain that the measures of performance are compatible with the patient's wishes, especially regarding quality of life.

Systematic measurement of a limited number of variables is important for a successful single-patient trial. We typically use self-administered questionnaires that rely on 7-point Likert scales or tabulate the frequency of events. We also teach patients to measure biologic variables like the forced expiratory volume in one second, peak flow, and walk time. We have found it easier to use 7-point Likert scales than visual analog scales. In the standard crossover design, the patient can be asked to state a preference for one treatment period compared with the other.

There are other issues that must be solved when designing a clinical trial. A critical question is the duration of treatment. In general, we believe the old adage, "shortest is easiest." Treatment often takes longer than expected, however, because time is required for peak effects to develop or for treatment effects to dissipate. For drug regimens that are rapidly started and stopped, treatments can be shorter and a random block design of six or eight trials of active drug and placebo can be evaluated in less than two weeks.

A special case occurs when a drug is being used to minimize or prevent attacks or exacerbations of a recurrent disease. To determine duration, the frequency of exacerbation needs to be estimated. Given a reasonable estimate of the frequency, the duration can be based on the "rule of 3s." This rule states that if an event occurs once every x days, the duration of observation must be three times x days to be 95% certain to observe one event. In the case of familial Mediterranean fever where an attack may occur once every two weeks, the treatment period would need to last six weeks to be reasonably certain to observe an effect.

Another question that affects the duration of the trial is how many pairs or trials are needed. The answer to this is the tautology, "as many as are needed." In some trials, we have recommended that a single pair may provide an adequate demonstration of efficacy. Such a demonstration lacks statistical power, but the demonstration of effect may be so compelling as to convince both patient and physician that efficacy is no longer in doubt. On the other hand, when the probability of a treatment being effective is about 50% before the

TABLE 2.—*Posterior Probabilities as Function of Prior Probabilities and Likelihood Ratio*

Prior Belief Treatment Is Effective, P	Likelihood That Treatment Is Better Than Spontaneous	Patient Improves	Posterior Probability, P
.01	3	Yes	.030
	5	Yes	.051
	1/3	No	.003
	1/5	No	.002
.10	3	Yes	.25
	5	Yes	.55
	1/3	No	.032
	1/5	No	.022
.50	3	Yes	.75
	5	Yes	.83
	1/3	No	.25
	1/5	No	.17
.80	3	Yes	.92
	5	Yes	.95
	1/3	No	.57
	1/5	No	.44
.90	3	Yes	.96
	5	Yes	.98
	1/3	No	.75
	1/5	No	.64
.95	3	Yes	.98
	5	Yes	.99
	1/3	No	.86
	1/5	No	.79

trial, and there are major risks of side effects, anything short of a statistical certainty may not be satisfactory. In the case of a paired crossover trial, the binomial distribution suggests that after four trials, the probability of treatment being repeatedly favored over placebo is .5 after the first trial, .25 after the second trial, .125 after the third trial, and .0625 after the fourth trial, which is $(1/2)^4$.

In general, the issue of "statistical" certainty—the mythical $P < .05$—is less critical in single-patient trials. An interesting perspective is added by assaying the clinician's estimate of the likelihood of success in that patient (the prior probability) and determining the estimated likelihood that the treatment is efficacious based on the literature. Using a Bayesian analysis, a posterior probability based on the patient outcome in a single-patient trial can be calculated as shown in Table 2 (G. van Belle, written communication, June 1987). These posterior probabilities show the effect that a single-patient trial can have on a clinician's level of certainty that treatment will be helpful for a patient.

Conclusion

We formed the trial service to simultaneously establish, demonstrate, and determine the value of single-patient trials in clinical practice and to help do the clinical trials. Our involvement ranges from being limited consultants providing study drugs and simply reviewing the protocol, to providing detailed, in-depth consultation regarding the value of a clinical trial in a particular patient, developing a study design, interviewing the patient, developing target outcomes, printing forms, preparing placebo drug and outcome forms, and doing follow-up. In all cases, we provide an interpretation of the results of the trial and are anxious to learn how the trial was used in clinical decision making and practice.

In summary, single-patient clinical trials can be used to improve the efficacy of treatment—especially long-term treatments and treatments with uncertain efficacy or a risk of serious toxic effects. Examples of suitable conditions for study are numerous, including common problems such as chronic obstructive lung disease, osteoarthritis, recurrent headache and other chronic pain syndromes, "fibrositis" or fibromyalgia, and agitation in demented patients. We have done trials in these common conditions and have also investigated more unusual and complex problems such as progestational drug side effects, treatment of the "restless" leg syndrome, and treatments of orthostatic hypotension. The principal benefits are an increased certainty for patients and their physicians that a treatment is worth pursuing because it is effective or should be abandoned because of an absence of a net benefit.

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The *n*-of-1 Randomized Controlled Trial: Clinical Usefulness

Our Three-Year Experience

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Objective: To review the feasibility and effectiveness of *n*-of-1 randomized controlled trials (*n*-of-1 trials) in clinical practice.

Design: Individual trials were double-blind, randomized, multiple crossover trials. The impact of *n*-of-1 trials was determined by eliciting physicians' plans of management and confidence in those plans before and after each trial.

Setting: Referral service doing *n*-of-1 trials at the requests of community and academic physicians.

Object of Analysis: All trials were planned, started, and completed by the *n*-of-1 service.

Measures of Outcome: The proportion of planned *n*-of-1 trials that were completed and the proportion that provided a definite clinical or statistical answer. A definite clinical answer was achieved if an *n*-of-1 trial resulted in a high level of physician's confidence in the management plan. Specific criteria were developed for classifying an *n*-of-1 trial as providing a definite statistical answer.

Main Results: Seventy-three *n*-of-1 trials were planned in various clinical situations. Of 70 *n*-of-1 trials begun, 57 were completed. The reasons for not completing *n*-of-1 trials were patients' or physicians' noncompliance or patients' concurrent illness. Of 57 *n*-of-1 trials completed, 50 provided a definite clinical or statistical answer. In 15 trials (39% of trials in which appropriate data were available), the results prompted physicians to change their "prior to the trial" plan of management (in 11 trials, the physicians stopped the drug therapy that they had planned to continue indefinitely).

Conclusion: We interpret the results as supporting the feasibility and usefulness of *n*-of-1 trials in clinical practice.

Annals of Internal Medicine. 1990;112:293-299.

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Randomized controlled trials are usually required to establish valid evidence of drug efficacy (1-3). However, there remain a number of clinical situations in which treatment decisions cannot be based on such trials. For example, guidance is unavailable for treating conditions that have not been investigated with randomized controlled trials; some conditions are so rare that even multicenter collaborative trials are not feasible. Further, even when a relevant randomized controlled trial generates a definite answer, its result may not apply to an individual patient. First, if the patient does not meet the eligibility criteria, extrapolation may not be appropriate; second, regardless of the overall trial results, some patients appear to benefit from the experimental therapy and some do not (4). To maintain the methodologic safeguards provided by randomized controlled trials and avoid the disadvantages of large-sample multicenter studies, we have developed a corresponding methodology for examining the intervention effect in individual patients.

Experimental studies (5-7) of single subjects have long been part of psychologic research. The methodology is known as single case or single subject research, $n = 1$, or, *n*-of-1 randomized controlled trials (hereafter referred to as *n*-of-1 trials). We have previously described how *n*-of-1 trials may be used in medical practice to determine the optimum treatment of an individual patient (4). More recently, we have provided detailed guidelines (8) for clinicians interested in conducting their own *n*-of-1 trials. Results pertaining directly to the patient involved are available immediately after the patient has completed the trial.

In 1985, we designed an *n*-of-1 service to facilitate clinicians' involvement with *n*-of-1 studies in our community (9). We have a formal referral service for *n*-of-1 studies and a tutorial service that teaches clinicians how to run their own trials. We describe our 3-year experience with providing the *n*-of-1 service in our community. We examined a spectrum of conditions and interventions in which *n*-of-1 trials were done and studied the outcome of each trial. The questions we asked were as follows: Are *n*-of-1 trials able to provide clinically useful information? Do clinicians change their management plans as a result of *n*-of-1 trials? Does physicians' confidence in management decisions change as a result of *n*-of-1 trials?

Methods

Criteria for Doing an *n*-of-1 Trial

After a clinician and a patient expressed interest in conducting an *n*-of-1 trial, we assessed the suitability of the underly-

ing condition and potential therapeutic intervention. We have previously reported a set of criteria (8) that should be satisfied before an *n*-of-1 trial is attempted; these criteria were applied to patients' presentation to the *n*-of-1 service. In short, in addition to the effectiveness of treatment being in doubt, the disorder should be chronic and relatively stable. The treatment, if effective, should be continued long-term, and the patient should be eager to collaborate in designing and participating in the *n*-of-1 trial. In addition, the treatment or treatments must have a rapid onset and termination of action, and an optimal treatment duration should be known and practical. In each case, the choice of medication and the dosage were selected on the basis of the attending physician's clinical judgment.

Conduct of Individual *n*-of-1 Trials

If our initial assessment of the clinical situation indicated that an *n*-of-1 trial was indicated, we prepared an individualized trial package. To assess drug efficacy, we administered individualized questionnaires that examined the severity of symptoms that were identified by patients as part of their disease and important in their daily life. These questionnaires consisted of four to seven items (symptoms), and severity of symptoms was usually measured on a 7-point scale. For example, if shortness of breath while shopping was a symptom identified as part of the illness and important in daily life, the patient was asked: Please indicate how short of breath you have been while shopping during the previous 2 or 3 days, by choosing one of the options from the scale below:

1. Extremely short of breath
2. Very short of breath
3. Quite a bit short of breath
4. Moderately short of breath
5. Mildly short of breath
6. A little short of breath
7. Not at all short of breath

Either the referring physician or a physician-member of the *n*-of-1 service saw the patient after each treatment period. The trial design was based on pairs of active drug and placebo, high dose and low dose, or first drug and alternate drug combinations; the order of administration within each pair was determined by random allocation. We recommended that at least three pairs of treatments be completed. Medication was prepared by one of the participating pharmacies. If active medication and matching placebo were available from the manufacturer, they were used; if not, the medication was crushed and put in capsules, and matching placebo capsules were prepared. The pharmacy held the code, and all other members of the team were blind to allocation. Treatment targets were monitored on a regular, predetermined schedule throughout the trial. If a patient felt much worse at any time during the trial, the current treatment period was terminated and, without breaking the code, the next treatment period was begun. The trial continued as long as the clinician and patient agreed that they needed more information to get a definite answer about the efficacy of the treatment or until the patient or clinician decided for any other reason to end the trial.

At the study's conclusion, the results were reported to the patient's physician. Mean values for all measures for each treatment period, the mean differences between treatment and control periods, the 90% confidence interval (CI) around the differences, and the probability of differences seen being due to chance (using a one-sided paired *t*-test of the difference in score) were reported (8). We also examined each treatment's magnitude of effect. Our previous experience with the symptom questionnaires that used a 7-point scale suggested that an improvement of 0.5 points per question corresponds to a noticeable improvement in the patient's well-being (10). For instance, if there were six questions, a total change of 3 or more points was considered clinically important.

To assess the impact of the *n*-of-1 trial on the physician's management plan, we asked each physician how he or she would treat the patient without an *n*-of-1 trial and, when *n*-of-1 trial results became available, how he or she intended to treat the patient. Management plan options included continuing the drug therapy, withdrawing the drug, or "other." We also investigated the level of the physician's confidence in his or her management plan, both before and after the *n*-of-1 trial, again using a 7-point scale. The physicians were asked the following: How comfortable do you feel now about your treatment plan?

1. Totally comfortable, certain it's the right thing for the patient
2. Almost totally comfortable, very likely it's the right thing for the patient
3. Quite comfortable, likely that the treatment plan is best for the patient
4. Not totally comfortable, but treatment plan is very likely to be as good as alternatives
5. Mildly uncomfortable, some uncertainty whether treatment plan is best for the patient
6. Moderately uncomfortable, feeling that the treatment plan may not be the best for the patient
7. Extremely uncomfortable, uncertain about treatment plan and, if wrong, patient may suffer

Review of 73 *n*-of-1 Trials

Between October and December of 1988, we reviewed the files of all *n*-of-1 trials done in cooperation with our *n*-of-1 service. Trials were classified as complete when three pairs of treatment periods were completed or the trial was interrupted before completing three treatment pairs because of the clinician's and patient's belief that drug effectiveness had been established or refuted. The reasons for interruption were occurrence of intolerable symptoms compatible with side effects, perceived large treatment effect of the active medication, and such a low frequency of symptoms that the medication was judged not to be needed.

Trials not in either of these categories were classified as incomplete (interrupted before completing three pairs with no clinical conclusion reached before trial termination). Among completed trials, we examined the proportion that provided a definite clinical answer. These included trials that resulted in a high level of clinicians' confidence in their management decisions after an *n*-of-1 trial (1 or 2 on a 7-point scale); and trials that were interrupted before completing three treatment pairs because of the clinician's and patient's belief that drug effectiveness had been established or refuted. To classify such trials as providing definite answers, the clinical impression of drug efficacy (or its side effect) had to be confirmed after breaking the code.

For trials in which the primary outcome measure was the symptom questionnaire that used a 7-point scale, we have developed a set of statistical criteria to classify individual *n*-of-1 trials. Categories include providing a definite answer (either confirming drug or placebo superiority or indicating no difference), showing a trend in favor of active drug or placebo, or leaving the question of intervention efficacy unanswered (indefinite). These criteria use a combination of the clinical importance cut-off (0.5 points per question mean difference [D] in symptoms score) and statistical evaluation of the difference observed (one-tailed $P \leq 0.05$, narrow CI around the difference between active drug and placebo). The complete set of criteria is presented in Appendix 1.

Examples of *n*-of-1 Trials

To show what is involved in doing an *n*-of-1 trial, we will describe a case in detail. A 23-year-old woman

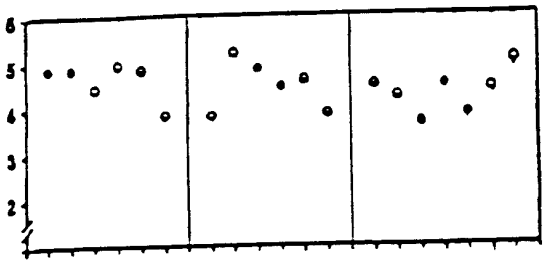

Figure 1. Results of *n*-of-1 trial, propranolol therapy for vasovagal syncope. Half-open circles represent weekly mean scores while receiving propranolol, 40 mg four times daily; open circles represent weekly mean scores while receiving propranolol, 20 mg four times daily; and closed circles represent weekly mean scores while receiving placebo.

presented in the autumn of 1987 with a history of recurrent vasovagal syncope of a year's duration. Associated symptoms included presyncope, nausea and vomiting, migrainous headaches, and flushing episodes. There was no obvious trigger to these symptoms. The syncopal episodes occurred as frequently as twice a week, the other symptoms on a more frequent basis, and the constellation of symptoms was adversely affecting the patient's quality of life. Extensive investigation showed no hormonal or autonomic nervous system abnormality. The patient was given nifedipine (for headaches) and amitriptyline as a vagolytic agent and her condition was initially judged to have improved somewhat; however, symptoms remained a major problem.

It has been hypothesized that a vasodepressor reaction (or common faint) can follow sympathetic nervous system stimulation, resulting in decreased left ventricular volume and stimulation of intracardiac receptors (11). This mechanism was thought to be playing a role in this patient's problems. A "tilt-table isoproterenol" test was abnormal; the patient developed significant bradycardia and hypotension when tilted to 60 deg and infused with 8 μg of isoproterenol (11). The patient's physician thought that propranolol might benefit (11) and contacted our *n*-of-1 service to conduct a trial.

The physician was uncertain of the optimal dosage, so the trial was set up with triplets of treatment periods instead of pairs. Each period lasted 2 weeks and, in each triplet, the patient received either placebo, 20 mg of propranolol four times daily, or 40 mg of propranolol four times daily. Treatment targets included daily rating of symptoms of lightheadedness and syncope, headaches, nausea or vomiting, feeling warm or sweating, and fatigue. Each symptom was rated on a 7-point scale. For instance, the patient was asked the following: How much trouble or distress as a result of lightheadedness or loss of consciousness have you had during the last day?

1. A very great deal of trouble or distress
2. A great deal of trouble or distress
3. A good deal of trouble or distress
4. A moderate amount of trouble or distress
5. Some trouble or distress
6. Very little trouble or distress
7. No trouble or distress

The results of the three triplets of treatment periods are summarized in Figure 1. Each data point in Figure 1 represents the mean of seven ratings of the five symptoms over a period of 1 week. The patient felt that there were no significant differences in how she felt over the 19 weeks of the trial, and this was confirmed by the symptom scores. It was concluded that propranolol was not effective.

Now uncertain about the benefit of amitriptyline in relieving symptoms, the attending physician wished to conduct a second trial before restarting the therapy. This trial was to have 4-week treatment periods, with the patient receiving placebo or 100 mg of amitriptyline at bedtime during each period. The same five symptoms were monitored, again on a daily basis. Before starting the trial, the physician replied to our questionnaire, stating that his a priori estimate of effectiveness was that the amitriptyline was of no benefit and that he was very confident of this assessment.

The patient felt much worse during the second period of the first pair than she had during the first period and, after 2 weeks of the second period, was convinced that she was receiving placebo. Without breaking the code, the period was terminated and the next pair begun. During the second period of the second pair, the patient again felt much worse and the period was terminated after the first week. After 1 week of the third pair, the patient again became convinced that she was receiving placebo and the second period of the third pair was begun early. The results are presented in Figure 2. The patient had been correct in each case about when she received placebo, and the large differences in symptom score reflect the magnitude of the differences she experienced between taking active drug and taking placebo. The mean differences in symptom score per question between active drug and placebo periods for the three pairs were 1.88, 1.81, and 2.08. A paired *t*-test with two degrees of freedom suggests that these results are very unlikely to have occurred by chance ($P < 0.001$). It was concluded that amitriptyline was effective, and the drug treatment has been continued to the present.

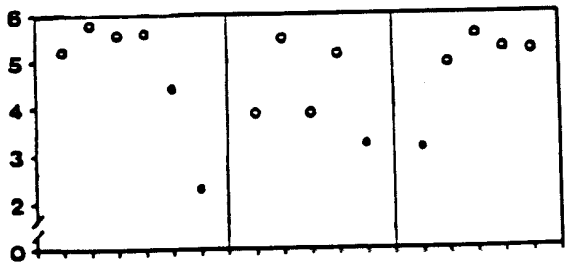

Figure 2. Results of *n*-of-1 trial, amitriptyline therapy for vasovagal syncope. Open circles represent weekly mean scores while receiving amitriptyline, and closed circles indicate weekly mean scores while receiving placebo.

Table 1. *Outcome of 73 n-of-1 Randomized Controlled Trials*

Planned *n*-of-1 trials, $n = 73$
Three *n*-of-1 trials never started (1 because of death; 1, concurrent illness; and 1, consent withdrawn)
n-of-1 trials begun, $n = 70$
Thirteen *n*-of-1 trials not completed (7 because of patients' noncompliance; 5, concurrent illness; and 1, physician noncompliance)
Completed *n*-of-1 trials, $n = 57$
Nine *n*-of-1 trials with 3 pairs completed did not provide a definite clinical answer; 2 of the 9 provided a definite statistical answer
Definite *n*-of-1 trials, $n = 50$
Forty-eight trials were clinically definite; 19, statistically definite

Results

Spectrum of Use

We have not kept systematic track of inquiries about *n*-of-1 trials that were planned but deemed infeasible after preliminary discussion. Some examples include trials with patients with inflammatory bowel disease (in whom exacerbations occur too infrequently to make a trial feasible) and major changes in prednisone in patients with obstructive airway disease (in whom functional adrenal deficiency is likely to have developed). On several occasions, an open trial resulted in obvious benefit or obvious side effects before a formal trial was begun. In several instances, we were approached about patients with many unstable medical problems that made reliable ascertainment of the effect of a single medication impossible. Finally, *n*-of-1 trials were sometimes infeasible because of reservations about the patient's ability to keep a valid symptom diary.

Overall, our service participated directly in preparing 73 *n*-of-1 trials. Some results from 5 of these trials have been reported elsewhere (4, 8, 9, 12). Most of the trials tested a specific form of therapy in patients whose underlying condition was clearly defined (for example, amitriptyline therapy for fibrositis, ipratropium or theophylline for chronic airflow limitation). In three instances, the trial was used as a diagnostic tool: In a patient with inconclusive laboratory test results, the clinician investigated the efficacy of hydrocortisone in relieving symptoms possibly caused by Addison disease; in two trials, the clinician tested the efficacy of pyridostigmine bromide in ameliorating symptoms possibly caused by myasthenia gravis. In two other cases, different dose regimens of the same medication were used to determine the balance between the drug's efficacy and its side effects (prednisone therapy for chronic airflow limitation and propranolol for syncope).

The results of the 73 *n*-of-1 trials are presented in Table 1. Three trials were planned, but never started (1 because of concurrent illness; 1, consent withdrawn; and 1, patient's death). Of the 70 *n*-of-1 trials that began, 57 were completed. The reasons for suspension of 13 trials were patients' concurrent illness (5 trials) and lack of patients' (7 trials) or physicians' (1 trial) compliance with the study protocol. Among the 57 completed *n*-of-1 trials, the number of pairs were as follows: eight pairs, 1 trial; six pairs, 1; five pairs, 2; four pairs, 9; three pairs, 31; two pairs, 11; and one pair, 2. The duration of treatment periods varied widely, from 1.5 days to 6 weeks. The majority of trials lasted 1 to 4 weeks. Appendix 2 presents the spectrum of clinical conditions in which *n*-of-1 trials were done. One physician was involved in 19 trials; another, in 8. An additional four physicians participated in more than 1 completed trial.

Results of Completed Trials

Forty-eight of 57 completed *n*-of-1 trials (84% of all completed and 66% of all planned) provided a definite clinical answer. These 48 trials included 39 that resulted in a high level of clinicians' confidence in the appropriateness of their management decisions after three pairs of treatment had been completed. An additional 9 *n*-of-1 trials were classified as complete despite trial interruption before completing three pairs. In 4 trials, differences between two treatment periods were so dramatic, the physician and patient decided to end the trial (ipratropium therapy for chronic airflow limitation on three occasions and haloperidol for psychosis on one). In each of these 4 trials, the clinical impression was confirmed after breaking the code; the clinician had guessed correctly when the patient was receiving active drug. On two additional occasions, occurrence of clinically important deleterious effects led to the termination of *n*-of-1 trials (theophylline therapy for chronic airflow limitation and clonidine for rheumatoid arthritis). Again, the clinical decision was substantiated after the code was broken. During 3 trials, the symptoms chosen as treatment targets did not occur within the first few treatment periods and the trial was terminated (propranolol therapy for syncope, dilantin for Meniere disease, and propantheline for abdominal pain). In each of the 9 *n*-of-1 trials classified as complete despite less than three pairs being done, active drug was compared with placebo.

Results of complete trials that used symptom questionnaires with responses on a 7-point scale as a primary outcome measure were reviewed according to criteria presented in Appendix 2. We had the data necessary to do this analysis in 44 *n*-of-1 trials. In 19 of 44 cases, the trial provided a definite statistical answer. In 15 trials, the beneficial role of the drug was confirmed; in 4, there was no difference between investigated therapy and placebo. None of the trials analyzed using these criteria indicated a harmful effect of a drug. All but 2 *n*-of-1 trials providing a definite statistical answer were classified as definite according to clinical criteria. In 1 of these 2 *n*-of-1 trials, the physician tested the efficacy of amitriptyline therapy for fibrositis—the impression of drug efficacy obtained during an earlier open trial was so strong that the results of the initial *n*-of-1 trial excluding drug benefit were questioned. A subsequent *n*-of-1 trial, with the same patient using a higher dosage of amitriptyline, confirmed the results of the first trial, and the physician discontinued the medication. In the second case, the physi-

cian questioned a patient's claim that pyridostigmine provided an improvement in weakness that was possibly related to myasthenia gravis. Despite a clearly positive *n*-of-1 result, failure by a neurologist to confirm the diagnosis of myasthenia led the attending physician to speculate that the patient might somehow have broken the blind, thus invalidating the results. The total number of *n*-of-1 trials providing definite clinical or statistical answer was, therefore, 50. Five *n*-of-1 trials had trends suggesting drug benefit, and, in two cases, trends favored placebo. Results of 18 completed trials were classified according to the statistical criteria as indefinite.

Management Plans and Clinicians' Confidence

In 38 trials, the data on management decisions were available both before and after the trial. In 23 cases, the original decision was unchanged after the trial result became available. In the remaining 15 trials (39%), results of the *n*-of-1 trial prompted physicians to change the original decision (in 11 cases, to stop the drug treatment completely rather than continue; in 3 cases, to continue drug therapy indefinitely rather than stop; and, in 1 case, to conduct an additional *n*-of-1 trial). The level of confidence in the new management decision, measured on a 7-point scale, was 1.82 ± 1.05 (mean ± SD). Confidence in the original decision was 4.62 ± 1.36. This change in management confidence was similar to the increase seen in the *n*-of-1 trials that supported the original decision (from 4.53 ± 1.62 to 1.82 ± 1.07). The complete spectrum of changes in physicians' confidence after the 38 *n*-of-1 trials for which data are available for both before and after the trial is depicted in Figure 3. In most cases, physicians clearly were far more confident in their management after the *n*-of-1 trial.

In 44 *n*-of-1 trials, three pairs of treatment were completed. In 39 of these trials, physicians expressed total or very high confidence in their management decision (1 or 2 on a 7-point scale). In no case was this degree of confidence present before the *n*-of-1 trial. After these 44 *n*-of-1 trials, the average score on a 7-point management confidence scale was 1.77 ± 0.99.

In most of the trials we report, the attending clinicians had already conducted their own open trials and remained uncertain about treatment efficacy. In these instances, they would have managed the patients as described in the questionnaires we administered. In a few trials, physicians preferred to have the first exposure of patients to the experimental treatment as part of an *n*-of-1 trial. Although physicians may have considered options such as continuing the medication for a period and then testing response to withdrawal or conducting open trials of withdrawal and reinstitution, such plans were made explicit on only a few occasions.

Discussion

We present our initial, 3-year experience in conducting *n*-of-1 trials and offering the *n*-of-1 service to community physicians. We tested this method of solving difficult therapeutic dilemmas in a broad spectrum of conditions and using different interventions. The clinical problem was most commonly clarification of the efficacy of a medication, generally recognized as useful, in an individual patient. In some cases, trials were used for the clarification of an optimal dosage of a medication or as an aid to diagnosis.

We were able to complete 81% of trials that were begun. The commonest reasons for not completing a trial were patients' noncompliance with the study protocol or emergence of a concurrent illness. In each trial, we tried to complete three pairs of treatments; achieving this goal was the commonest reason to categorize a trial as complete. Some trials were also categorized as complete despite the fact that three pairs of treatments had not been achieved. In all of these *n*-of-1 trials, the clinically relevant answer was reached at an earlier point. On three occasions, target end points occurred with an unexpectedly low frequency regardless of the treatment used. These *n*-of-1 trials were interrupted and classified not only as complete but also as providing a definite clinical answer: Indication for the use of a drug was refuted. These three *n*-of-1 trials dramatically show the necessity of assessing drug efficacy in a blind manner. Had the drug been tested in an open trial, the results would have been interpreted as showing the striking efficacy of the intervention.

To judge the clinical usefulness of *n*-of-1 trials, we developed a set of both clinical and statistical criteria. We felt that because the goal of an *n*-of-1 trial is to clarify a management decision, an *n*-of-1 trial can be considered definite only if this goal is achieved. A definite answer was obtained in 71% of all attempted *n*-of-1 trials. Clinicians were more liberal in their conclusions that a definite answer had been reached. When using rigorous statistical criteria for a definite answer, such an answer was attained in only 27% of trials that were begun (43% of the trials in which data required to make this assessment were present). On two occasions, physicians did not believe the statistical results; in both cases, two separate *n*-of-1 trials yielded the same results.

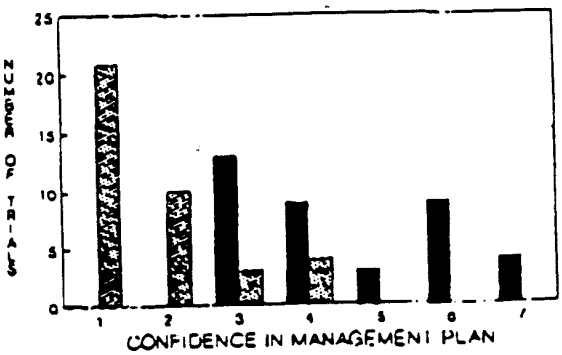

Figure 3. Impact of *n*-of-1 trials on clinicians' confidence in their management plans, data from 38 *n*-of-1 trials. The *y*-axis represents number of trials, and the *x*-axis indicates confidence in management plan. Closed bars represent confidence in management plan before trial, and open bars represent confidence in management plan after trial.

The relatively small proportion of trials in which statistical criteria for a definite result were obtained reflects to some extent the limited power of statistical tests when only three pairs have been conducted. The extent to which the clinicians were convinced of the results when statistical criteria were not met attests to the value of the method even without statistical analysis. Another limitation of statistical analysis is that the decision to continue with additional pairs can be driven by the results, potentially invalidating the nominal *P*-value obtained. Because of these limitations, we view the statistical analysis as an adjunct (but often very useful adjunct) for the interpretation of the results of *n*-of-1 trials.

The expense incurred by conducting *n*-of-1 trials will be an issue. Until now, our trials have been paid for by research funds. We have not, therefore, established a standard fee for the referral nor decided on how fees should be modified depending on the nature and length of the study. Although, in our experience, the research assistant time per trial was considerable, much of this time was spent on activities (such as administering questionnaires to physicians) that would not be part of *n*-of-1 trials once they are established in clinical practice. We believe that even without detailed information on costs, conducting *n*-of-1 trials is likely to be cost-effective. In our experience, a substantial proportion of trials result in discontinuation of medication that would otherwise have been continued for months or years. The cost savings from discontinuing medication and from reducing physician time spent in medication review and in treating adverse reactions to medication is likely to be considerable. Third-party payers may wish to consider these potential savings when developing policies on reimbursement of costs associated with *n*-of-1 trials.

We believe that our results show that *n*-of-1 trials are feasible to conduct in clinical practice and often result in clinically important changes in clinicians' confidence in their management decisions and in the management decisions themselves. We believe that most physicians try to be scientific in their approach to medication prescription and use some of the principles of the *n*-of-1 trial (such as observation of patients on and off medication) in their day-to-day practice. The methodology of the *n*-of-1 trial provides physicians with a set of tools that can further increase the scientific rigor of their clinical practice and increase the likelihood that the treatments they prescribe are indeed those that are best for the patient.

Acknowledgments. The authors thank Drs. Christopher Allen, Jennifer Blake, Dody Bienenstock, Ramona Carbotte, Clive Davis, Judah Denburg, Susan Denburg, Brian Hutchison, Jan Irvine, David Martin, Christopher Patterson, Michel Rathbone, Peter Rosenbaum, William Walsh, Robin Whyte, and the many other physicians who helped in the planning and conduct of individual trials; Professor Robin Roberts and Wil Boyce and Drs. Dave Sackett, Murray Enkin, Stewart Pugsley, and John Chong, who contributed to the conceptual development of the *n*-of-1 approach; the pharmacy staff at McMaster University Medical Centre, particularly Ina Laschuck and Kathy Susanna, and at St. Joseph's Hospital, Hamilton, Ontario, particularly Doris Thompson, Betty Wong, and Nancy Ottaviano for their help with preparation and management of medications.

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Dr. Adachi: 25 Charlton Avenue East, Hamilton, Ontario, L8N 1Y2 Canada.
Dr. Newhouse: Firestone Chest/Allergy Services, St. Joseph's Hospital, 50 Charlton Avenue East, Hamilton, Ontario, L8N 1Y2 Canada.

Appendix 1. Criteria for Assessing the Results of an *n*-of-1 Randomized Controlled Trial

Statistical criteria

Definite answer

Beneficial	$P \leq 0.05$ and $D \geq 0.5$
Harmful	$P \leq 0.05$ and $D \leq -0.5$
Neutral	$P > 0.05$ and $0.25 > D > -0.25$ and $\lvert CI \rvert$ not ≥ 0.5 or $P > 0.05$ and $0.25 > D > -0.25$ and $\lvert D \rvert$ for each pair ≤ 0.5

No definite answer but trend seen

Beneficial trend	$0.3 \leq D < 0.5$ and $P \leq 0.05$ and CI includes 0.5 or $D \geq 0.5$ and $P > 0.05$
Harmful trend	$-0.3 > D > -0.5$ and $P < 0.05$ and CI includes -0.5 or $D \leq 0.5$ and $P > 0.05$

No definite answer

Not meeting criteria for either of the above categories.

Clinical criteria for definite trial

1. The clinician's high level of confidence in the appropriateness of the management decision after the *n*-of-1 trial (1 or 2 on a 7-point scale).
2. *n*-of-1 trial interruption before completing three treatment pairs because of the clinician's belief that drug effectiveness had been established or refuted (perceived large treatment effect or severe side effects, both confirmed after breaking the code, or low frequency of treatment endpoints).

Appendix 2. Spectrum of Clinical Conditions in Which *n*-of-1 Randomized Controlled Trials Were Used

Fifty-seven trials were completed. Twenty trials were done with 19 patients with fibrositis. In 18 of these trials, amitriptyline was tested; nitrazepam was tested in 2 trials. Sixteen trials were completed in patients with chronic airflow limitation. In 10 trials, inhaled ipratropium was tested; in 6, oral theophylline; and, in 3, inhaled salbutamol. Two other patients participated in 2 trials each. In a patient with suspected myasthenia

gravis, pyridostigmine was tested in 2 different trials. A patient with recurrent syncope participated in 1 trial testing propranolol, and 1 trial testing amitriptyline. Single trials were done in the following conditions, with the associated medication: chronic pain, maprotiline; anxiety, lorazepam; insomnia, lorazepam; suspected Addison disease, hydrocortisone; cryptosporidiosis, spiramycin; Raynaud disease, ketanserine; syncope, propranolol; coronary disease, diltiazem; familial, Mediterranean fever, colchicine; rheumatoid arthritis, clonidine; myositis, prednisone; abdominal pain, propantheline; Meniere disease, phenytoin; psychosis, haloperidol; and suspected polymyalgia rheumatica, prednisone.

Thirteen trials were begun but not completed. Eight of these trials involved patients with chronic airflow limitation. Five tested inhaled ipratropium; two, inhaled salbutamol; and one, oral theophylline. Single trials were started but not completed in the following conditions, with the associated medication: premenstrual syndrome, pyridoxine; spasticity in a paraplegic, clonidine; irritable bowel syndrome, trimebutine; idiopathic edema, captopril; and temporal lobe epilepsy, carbamazepine.

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ER1338

IN THE UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

UNITED STATES OF AMERICA, Plaintiff, v. CANNABIS CULTIVATOR'S CLUB, et al., Defendants. AND RELATED ACTIONS.	No. C 98-00085 CRB C 98-00086 CRB C 98-00087 CRB C 98-00088 CRB C 98 00089 CRB C 98 00245 CRB **DECLARATION OF JAMES D. MCCLELLAND**

ER1339

I, JAMES D. McCLELLAND, declare:

1. I am the Chief Financial Officer ("CFO") of the Oakland Cannabis Buyers' Cooperative (the "Cooperative" or "OCBC"). I am also a board member. As a board member and CFO of the Cooperative, I am familiar with the policies and procedures of the OCBC. I have personal knowledge of the facts stated herein, and if called as a witness, I could and would testify competently as to them.

2. I graduated from Arkansas Technical College in 1985. After graduation, I was an account manager at Electronic Data Systems Corporation for approximately eleven years. During this time I was in charge of implementing computer systems in banks and other financial institutions. I became a board member and Chief Financial Officer of the Oakland Cannabis Buyers' Cooperative in 1997.

3. The goal of the Cooperative is to provide seriously ill patients with a safe and reliable source of medical cannabis products and plants. Our cooperative is open to all patients with a verifiable letter of diagnosis and recommendation or approval from a doctor for medical cannabis use. A complete Mission Statement is attached hereto as Exhibit 1.

4. The Cooperative consists of one class of patient-members. According to the Cooperative's Bylaws, to qualify for membership an applicant must comply with the Protocols of the Oakland Cannabis Buyers' Cooperative. A copy of the OCBC Bylaws and Articles of Incorporation is attached hereto as Exhibit 2.

5. Before a patient is accepted for membership into the Cooperative, he or she must complete an extensive screening process. This process is described in detail in the Oakland Cannabis Buyers' Cooperative Protocols ("Protocols"), a copy of which is attached hereto as Exhibit 3.

6. First, all applicants must satisfy the threshold requirement of providing authorization from a treating physician assenting to cannabis therapy for one or more medical conditions listed on the Medicinal Cannabis User Initial Questionnaire (Exhibit C to the Protocols). Upon acceptance of the doctor's note by Intake staff, the prospective member undergoes an extensive screening process to determine whether the applicant meets the Medical Admissions Criteria (Exhibit D to the Protocols).

Each applicant must fill out and submit the Cooperative Information Form (Exhibit E to the Protocols).

7. If, upon screening by the Cooperative Intake staff member the applicant does not qualify for membership, he or she will be denied membership to the Cooperative.

8. If the applicant does appear to qualify for membership, a staff nurse must independently verify the physician's approval of cannabis use. It is the OCBC's policy and practice that an applicant not be admitted to membership in the Cooperative unless and until the applicant's physician's approval is verified by the staff nurse.

9. The Cooperative schedules a staff nurse to be on duty throughout every weekday business hour of the Cooperative. No new applicants are admitted on weekends.

10. Soon after an applicant is admitted to membership in the Cooperative, he or she is issued a laminated membership card. A copy of a membership card is attached as Exhibit J to the Protocols. Each time a patient-member comes to the Cooperative he or she must present this membership card along with secondary valid photo identification.

11. Each time a patient-member comes to the Cooperative to receive medicine, the patient-member must pass three separate security check-points. At each of the check-points the member must present two forms of identification described in paragraph 10. First, the member must present identification to a security guard at the front door to the Cooperative. Second, a second security guard examines the member's identification at the member room door leading into the sales area of the Cooperative. Finally, a Cooperative staff member always checks the patient-member's identification again at the point of sale.

12. As a board member and CFO of the Cooperative, I have reviewed and am generally familiar with the medical circumstances that have led Cooperative members to seek medical cannabis. Many patient-members of the Cooperative have no reasonable legal alternative to obtaining medical cannabis through the Cooperative. Although every patient's experience is unique, some general comments apply to many patients. Some Cooperative members have tried other legal medications and treatments to alleviate their conditions but these other medications and treatments do not work for them. For other members, other medications have intolerable negative side effects they

have chosen not to endure. Some members' experiences with other legal drugs is that, while they are somewhat effective, they are not nearly as effective at relieving their symptoms as medical cannabis.

13. Patient-members of the Cooperative suffer from debilitating and often deadly diseases, including HIV and/or AIDS, cancer, arthritis, multiple sclerosis, and glaucoma. Medical cannabis provides relief to patient-members as a pain reliever, an appetite stimulant, an anti-nauseant, and an anti-convulsant. Medical cannabis relieves intraocular eye pressure in patient-members who suffer from glaucoma.

14. Some of the patient-members who suffer from AIDS-related "wasting syndrome" or who have cancer and are undergoing chemotherapy may need medical cannabis in order to survive. Supplying medical cannabis to these patient-members is necessary to avert imminent and often life-threatening harm. Other drugs either do not work for these patients at all (or they are not nearly as effective as medical cannabis) or they cause severe adverse side effects that medical cannabis does not cause. Many of these patient-members have no reasonable alternative to medical cannabis.

15. The patient-members who suffer from multiple sclerosis or quadriplegia experience debilitating spasticity and/or constant pain. Other drugs either do not work for these patients at all (or they are not nearly as effective as medical cannabis) or they cause severe adverse side effects that medical cannabis does not cause. Many of these patient-members have no reasonable alternative to medical cannabis.

16. Some of the patient-members who suffer from glaucoma risk going blind if they are prevented from receiving medical cannabis.

17. Many patient-members' lives may be endangered if they were forced to try to obtain cannabis from criminal street dealers. This is because both the act of purchasing from street dealers is inherently dangerous and because impurities in marijuana purchased on the street may be harmful to their fragile health. In fact, some patient-members may choose to forego their medication if they have no choice but to turn to street dealers for cannabis.

18. The patient-members of the Cooperative are joint participants in a cooperative effort to obtain and share medical cannabis. Patient-members of the Cooperative jointly acquire marijuana for medical purposes to be shared among themselves and not with anyone else. No third persons are

involved other than "primary caregivers" who are responsible for the housing, health, or safety of the patient. Any payment made to the Cooperative constitutes reimbursement for administrative expenses and operations which all patient-members who utilize the services of the Cooperative agree to share. Attached hereto as Exhibit 4 is a true and correct copy of the Oakland Cannabis Buyers' Cooperative Statement Of Conditions under which each and every member agrees to receive their medicine.

19. The Cooperative prohibits the smoking of cannabis on its premises; therefore, patient-members who smoke medical cannabis cannot immediately consume their medicine in the presence of other patient-members.

20. Last month, the City of Oakland designated the Oakland Cannabis Buyers' Cooperative to administer the City's Medical Cannabis Distribution Program. Attached hereto as Exhibit 5 is a true and correct copy of this designation along with supporting documents which helped satisfy the City of Oakland that the Cooperative is a bona fide corporation safely and lawfully engaged in activities benefiting the citizens of Oakland.

21. I understand and believe that currently the federal government will not enroll any additional patients in any federal program studying the medical use of cannabis.

22. I understand and believe that currently pending are petitions to reschedule medical cannabis from Schedule I to Schedule II of the Controlled Substances Act, but that none of these petitions have yet been granted.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct.

Executed this 11th day of September at Oakland, California.

James D. McClelland

EXHIBIT 1

Oakland Cannabis Buyers' Cooperative

Compassion

Mission Statement

The goal of the Oakland Cannabis Buyers' Cooperative (OCBC) is to provide seriously ill patients with a safe and reliable source of medical cannabis products and plants. Our cooperative is open to all patients with a verifiable letter of diagnosis and recommendation or approval for medical cannabis use.

The City of Oakland has enacted an Ordinance to provide immunity for medical cannabis provider associations so that patients can safely obtain their medicine. The Cooperative is dedicated to reducing the harm these patients encounter due to the prohibition of cannabis. This includes alleviating the fear of arrest, as well as negating problems associated with purchasing cannabis on the illicit market.

OCBC's headquarters is a multi-faceted facility, accessible to people with disabilities. We provide a professional atmosphere for patients to procure cannabis, with trained member advocates on hand to offer advice and assistance. We also offer self-help services such as support groups for a wide variety of medical conditions, massage therapy and cultivation meetings to teach Members how to grow their own medicine. The Cooperative once a month has a buffet dinner for all Members and caregivers. Seasonally the Cooperative is involved with activities such as Softball and Bowling. In addition, OCBC provides information on a variety of topics, including AIDS prevention and treatment, safe sex, and cannabis reform in general.

The Oakland CBC currently operates under the auspices of California Proposition 215 now Health and Safety Code Section 11362.5 and Oakland City Council Resolution Numbered 72379 C.M.S. and 72516 C.M.S.

Resolution 72516, passed in March 1996, makes the enforcement of medical cannabis laws the lowest priority for the City of Oakland. Furthermore, the City has appointed a working group to oversee OCBC functions and to determine the most effective means to protect and assist seriously ill patients. Most recently the City has enacted Ordinance Number 12076 setting up a medical cannabis distribution program, which the Oakland Cannabis Buyers' Cooperative hopes to fulfill.

OAKLAND CANNABIS BUYERS' COOPERATIVE, P.O. Box 70401 Oakland, CA 94612-0401
Phone (510) 832-5346 Fax (510) 986-0534 Email ocbc@rxcbc.org Web www.rxcbc.org

JWJ

MAN

EXHIBIT 2

AAS

State of California

2000456

SECRETARY OF STATE

I, *BILL JONES*, Secretary of State of the State of California, hereby certify:

That the annexed transcript has been compared with the corporate record on file in this office, of which it purports to be a copy, and that same is full, true and correct.

IN WITNESS WHEREOF, I execute this certificate and affix the Great Seal of the State of California this

FEB 5 1997

Bill Jones

Secretary of State

ER1347

SEC/STATE FORM CE-107 (REV. 11/96)

2000456

ENDORSED-FILED
in the office of the Secretary of State
of the State of California

FEB - 1997

BILL JONES, Secretary of State

ARTICLES OF INCORPORATION
OF
OCB COOPERATIVE INC.

Article 1. The name of this Corporation is: OCB Cooperative Inc.

Article 2. This Cooperative is a cooperative corporation organized under the California Consumer Cooperative Corporation Law. The purpose of this Cooperative is to engage in any lawful act or activity for which a Cooperative may he organized under such law.

Article 3. The name and address in the state of California of this Cooperative initial agent for service of process is Jeff W. Jones
1755 Broadway, Oakland CA 94612

Article 4. The voting rights of each Member of the Cooperative are equal, and each Member is entitled to one vote. The proprietary interests of each Member of the Corporation are unequal, and the rules by which the proprietary interests are determined shall be prescribed in the Bylaws of the Corporation.

Article 5. The names and post office addresses of Directors who shall serve until the first annual meeting are:

Name	Address
Jeff Jones	1755 Broadway, Oakland CA., 94612
Matt Quirk	P.O. Box 70401, Oakland CA., 94612
J. D. Mc Clelland	P.O. Box 70401, Oakland CA., 94612
Tim Sidwell	375 Van Buren, Oakland CA., 94610
Helen Reading	P.O. Box 70401, Oakland CA., 94612
Barbara Johnson	P.O. Box 70401, Oakland CA., 94612
Paul Scott	P.O. Box 70401,Oakland CA., 94612

IN WITNESS WHEREOF, the undersigned, being the incorporators and the initial Directors of this Cooperative, have executed those Articles of Incorporation on February 4, 1997.

Tim Sidwell
Director

Matthew T Quirk
Director

J. D. McClelland
Director

Paul Scott
Director

Barbara Johnson
Director

Helen Reading
Director

Jeffrey W. Jones
Director

DECLARATION

We are the persons whose names are subscribed below. We collectively are all of the incorporators of this Cooperative and all of the initial Directors named In the Articles of Incorporation. and we have executed these Articles of Incorporation. The foregoing Articles of Incorporation are our act and deed. jointly and severally.

Executed February 4, 1997. at Oakland. California. We. and each of us. declare that the foregoing is true and correct.

Tim Sidwell
Director

Tom D. McClure
Director

Barbara Gutierrez
Director

Director

Matthew T. Davis
Director

Director

Helen Reading
Director

BYLAWS
OF
OCB COOPERATIVE, INC. d/b/a
OAKLAND CANNABIS BUYERS' COOPERATIVE

ARTICLE I.

MEMBERSHIP

Section 1.01. Classification of Members.

The Cooperative shall have one (1) class of Members.

Section 1.02 Membership Qualifications.

Any individual, may become and remain a Member of this Cooperative by:

(a) Complying with Protocols of the Oakland Cannabis Buyers' Cooperative;

(b) Complying with such uniform conditions as may be prescribed by the Board of Directors; and

(c) Making full payment of any non-refundable Membership fee as set forth in Section 1.06;

Section 1.03. Membership Application.

Any individual eligible for and desiring admission to Membership in the Cooperative shall file a written application for admission in whatever form and containing whatever information the Board of Directors shall prescribe.

Section 1.04. Acceptance of Members.

Applications for Membership shall be reviewed by the Membership Committee duly authorized by resolution to admit Members. The application shall be accepted unless rejected in writing within thirty (30) days for reasons satisfactory to the Committee. If accepted, the applicant shall be admitted to membership and shall be allowed to vote and hold office. If rejected, the applicant shall be entitled to a refund of any amounts paid for Membership fees. There shall be no discrimination of any kind.

Section 1.05. Transfers Prohibited.
No Member may transfer his or her Membership or any right arising therefrom.

Section 1.06. Membership Fee
A one time non-refundable Membership card fee, in an amount set from time to time by the Committee, may be charged to and collected from each Member upon qualifying for the Cooperative. This fee may be waived in case of financial need and on approval from the Membership Committee.

Section 1.07. Bylaws and Articles to Prospective Members.

Each prospective member, upon request for membership, shall upon request receive a copy of the Articles of Incorporation, Bylaws and Disclosure Document of the Cooperative.

Section 1.08 Shareholders and Members.

"Shareholder" and " Member" and their plurals shall be synonymous terms throughout these Bylaws.

ARTICLE II.

SHARES

Section 2.01. Share Issuance.

Shares may be issued for money paid in an amount as is determined from time to time by the Board and as share dividends, patronage refunds, or other changes affecting outstanding shares.

Section 2.02. Share Ownership

Share ownership entitles a Member to only one (1) vote in the affairs of the Cooperative, irrespective of the total number of shares a Member owns, and to all the rights of the Membership as described by stature, the Articles, and these Bylaws. Pursuant to subsection (b) of Bylaw Section 9.03, the Directors may declare noncumulative dividends on shares not to exceed any maximum rate established by statute.

Section 2.03. Share Certificates and Disclosure Document.

(a) The Cooperative may issue, but is not required to issue, share certificates. In the event that share certificates are issued, the certificates shall state the information required to be contained in the Disclosure Document described in subsection (b). Nothing in this section shall restrict the Cooperative from issuing identity cards or similar devices to Members which serve to identify Members qualifying to use facilities or services of the Cooperative

(b) Except as provided in subsection (e), prior to issuing a share, the Cooperative shall provide the purchaser of a share with a Disclosure Document. The Disclosure Document may be a prospectus, offering circular, brochure, or similar document, a specimen copy of the share certificate, or a receipt which the Cooperative proposes to issue. The Disclosure Document shall contain the information required by Section 12401 of the California Corporations Code.

(c) If the Articles of Incorporation or Bylaws are amended so that any statement required by subsection

(a) of this Bylaws Section on outstanding share certificates is no longer accurate, the Board may cancel the outstanding certificates and issue in their place new certificates conforming to the Articles of Incorporation or Bylaws amendments.

(d) When new share certificates are issued in accordance with subsection (c) of this Bylaw Section, the Board may order holders of outstanding certificates within a reasonable time fixed by the Board. The Board may further provide that the holder of the certificate to be surrendered shall not be entitled to exercise any of the rights of Membership until the certificate is surrendered, but such rights shall be suspended only after notice of the order is given to the holder of the certificate and only until the certificate is surrendered.

(e) The Cooperative shall issue a share certificate, receipt, or written advice of purchase to anyone purchasing a share upon the Member's first purchase of a share. No Disclosure Document need be provided to an existing Member prior to the purchase of additional shares if the Member has previously been provided with a Disclosure Document which is accurate and correct as of the date of the purchase of additional shares

Section 2.04. Prohibition on Transfer of Shares

No shares of this Cooperative may be assigned or transferred. Any attempted assignment or transfer shall be wholly void and shall confer no rights on the intended assignee of transferee.

Section 2.05 Partial Withdrawal.

A Member having a monetary amount in his or her share account in excess of a monetary amount to be determined from time to time by the board may cause the Cooperative to purchase his or her excess share amount upon written request to the Directors. Subject to Bylaw Section 2.06, the Directors must, within one (1) year of such request, pay the amount the Member requests in cash or other property or both. The exact form of payment is within the discretion of the Directors.

Section 2.06 Insolvency Delay.

The Cooperative shall delay the purchase of shares as described in Bylaw Sections 2.05 and 3.04 if the Cooperative, in making such purchase is, or as a result thereof would be, likely to be unable to meet its liabilities (except those whose payment is otherwise adequately provided for) as they mature.

Section 2.07 Unclaimed Equity Interests

Any share of a Member, together with any accrued and unpaid dividends and patronage distributions related to that Member, that would otherwise escheat to the State of California as unclaimed personal property shall instead become property of the Cooperative if the Cooperative gives at least 60 days prior notice of the proposed transfer to the affected Member by (1) first-class or second-class mail to the last address of the Member shown on the Corporation's records, and (2) by publication in a newsletter of general circulation in the county in which the Cooperative has its principal office. No shares or amounts shall become the property of the Cooperative under this section if written notice objecting to the transfer is received by the Cooperative from the affected Member prior to the date of the proposed transfer.

ARTICLE III.

TERMINATION OF MEMBERSHIP

Section 3.01 Voluntary Withdrawal

A member shall have the right to resign from the Cooperative and terminate his or her Membership by filing with the Secretary of the Cooperative a written notice of resignation. The resignation shall become effective immediately without any action on the part of the Cooperative.

Section 3.02 Death or Dissolution

A Membership shall immediately terminate upon the death of a Member or the dissolution of a Member which is an organization .

Section 3.03 Expulsion

(a) A Member may for failure to comply with the Bylaws, rules or regulations of the Cooperative, for failure to patronize the Cooperative during the immediately preceding fiscal year of the Cooperative in the amount of at least $1.00, or for any other justifiable reason, be expelled from the Cooperative by resolution adopted by a two-thirds (2/3) vote of all the Directors. Expulsion shall become effective immediately unless the Board shall, in the resolution, fix another time. On expulsion, the name of the Member expelled shall be stricken from the Membership register and all of his of her rights shall cease except as provided in Section 3.04.

(b) Prior to expulsion of a Member, the Board shall give such Member at least fifteen (15) days notice prior thereto and the reasons therefor. Such Member shall have the opportunity to be heard, orally or in writing, not less than five (5) days before the effective date of expulsion by the Board.

(c) The notice required pursuant to subsection (b) of this Bylaw Section may be given by any method reasonably calculated to provide actual notice. Any notice given by mail must be given by first-class or registered mail sent to the last known address of the Member shown on the Cooperative's records.

Section 3.04 Settlement of Share Interest

If a Membership is terminated for any reason set forth in this Article of the Bylaws, the share interest held by the Member shall be purchased by the Cooperative, subject to Section 2.06 of these Bylaws, within one (1) year of the date of termination of the extent of the paid-up value of the Member's shares on such date. The Board, in so settling the Member's share interest, shall have the right to set off any and all indebtedness of the Member to the Cooperative. The paid-up value of the Member's share interest is the monetary amount of such interest (including fractional shares) that the Member has been issued in accordance with Bylaw Section 2.01.

ARTICLE IV.

MEMBERSHIP MEETINGS AND MEMBERS

Section 4.01. Location.

Meetings of Members shall be held at the principal office of the Cooperative, or at such other place that may be designated by the Board of Directors, with notice as provided in this article.

Section 4.02. Regular Annual Meetings.

A regular meeting of Members shall be held annually on the first Saturday in June at 1:00 p.m. for the purpose of transacting any proper business, including the election of Directors, that may come before the meeting.

Section 4.03. Special Meetings.

Special meetings of Members for any purpose may be called by the Board of Directors, Executive Director, Coordinator, Chief of Finance, Financial Secretary, Secretary, the or by five percent or more of the Members.

Section 4.04. Time for Notice of Meetings.

Whenever members are required or permitted to take action at a meeting, a written notice of the meeting shall be given not less than 10 nor more than 90 days before the date of the meeting to each member who is entitled to vote on the record date for notice of the meeting. In the case of a specially called meeting of members, within 20 days after receipt of a written request, the Secretary shall cause notice to be given to the members entitled to vote that a meeting will be held at a time fixed by the Committee not less than 15 nor more than 90 days after receipt of the request

Section 4.05. Method of Giving Notice.

Notice shall be given either personally, or by mail or other written communication to the address of a member appearing on the books of the Cooperative or provided by the member. If no address appears or is given, notice shall be given at the principal office of the Cooperative.

Section 4.06. Record Date for Notice.

The record date for determining the members entitled to notice of any meeting of Members is 30 days before the date of the meeting.

Section 4.07. Contents of Notice.

The notice shall state the place, date, and time of the meeting. The notice of a regular meeting shall state any matters that the Board, at the time of giving notice, intends to present for action by the Members. The notice of a special meeting shall state the general nature of the business to be transacted. The notice of any meeting at which Directors are to be elected shall include the names of all nominees at the time of giving notice.

Section 4.08. Waivers, Consents, and Approvals.

The transactions of a meeting, whether or not validly called and noticed, are valid if a quorum is present and each of the absent Members who is entitled to vote, either before or after the meeting, signs a written waiver of notice, a consent to the holding of the meeting, or an approval of the minutes of the meeting. All waivers, consents, and approvals shall be filed with the Cooperative records or made a part of the minutes of the meeting.

A Member's attendance at a meeting shall constitute a waiver of notice of and presence at the meeting, unless the member objects at the beginning of the meeting. However, attendance at a meeting is not a waiver of any right to object to the consideration of matters required to be included in the notice but not included, if an objection is made at the meeting.

Section 4.09. Quorum at Meeting.

The lesser of 250 Members or members representing 5 percent of the voting power shall constitute a quorum at a meeting of members. Any Bylaws amendment to increase the quorum may be adopted only by approval of the Members. When a quorum is present, the affirmative vote of the majority of the voting power represented at the meeting and entitled to vote shall be the act of the Members, unless provided otherwise by these Bylaws or the law. The only matters that may be voted upon at any regular meeting actually attended by less than one-third of the voting power are matters notice of the general nature of which was given pursuant to Section 4.04 of these Bylaws.

Section 4.10. Loss of Quorum at Meeting.

The Members present at a duly called or held meeting at which a quorum is present may continue to transact business until adjournment, notwithstanding the withdrawal of enough Members to leave less than a quorum, if the action taken, other than adjournment, is approved by at least a majority of the Members required to constitute a quorum.

Section 4.11. Adjournment for Lack of Quorum.

In the absence of a quorum, any meeting of Members may be adjourned by the vote of a majority of the votes represented in person, but no other business may be transacted except as provided in Section 4.10 of these Bylaws.

Section 4.12. Adjourned Meetings.

The Cooperative may, transact any business at an adjourned meeting that could have been transacted at the original meeting. When a meeting is adjourned to another time or place, no notice is required if the time and place are announced at the original

meeting. If the adjournment is for more than 45 days or if a new record date is fixed, a notice of the adjourned meeting shall be given to each Member of record entitled to vote at the meeting.

Section 4.13. Voting of Memberships.

(a) Each member of the Cooperative is entitled to one vote on each matter submitted to a vote of the Members.

(b) If a Membership stands of record in the names of two or more persons, whether fiduciaries, Members of a partnership, joint tenants, tenants in common, husband and wife as community property, tenants by the entirety, persons entitled to vote under a agreement, or otherwise, or if two or more persons have the same fiduciary relationship respecting the same Membership, unless the Secretary is given written notice to the contrary and furnished with a copy of the instrument or order appointing them or creating the relationship, the vote of one joint holder will bind all, when only one votes, and the vote of the majority will bind all, when more than on joint holder votes

(c) The record date for determining the Members entitled to vote at a meeting or cast written ballots is 20 days before the date of the meeting or the day on which the first ballot is mailed or solicited.

(d) Cumulative voting shall not be permitted for any purpose

(e) Voting by proxy shall not be permitted for any purpose.

Section 4.14. Use of Written Ballots at Meetings.

A combination of written ballot and personal voting may be used at any regular or special meeting of Members, and may be used for the election of Directors. Prior to the meeting, the Board may authorize distribution of a written ballot to every Member entitled to vote The ballots shall be distributed in a manner consistent with the provisions of Section 4.05, 4.17(b), and 4.19 of these Bylaws. When ballots are distributed, the number of Members voting at the meeting by written ballot shall be deemed present at the meeting for purposes of determining a quorum but only with respect to the proposed actions referred to in the ballots.

Section 4.15. Contents of Written Ballot Used at Meeting.

Any written ballot used at a meeting shall set forth the proposed action to be taken, provide an opportunity to specify approval or disapproval of the proposed action, and state that unless revoked by the Member voting in person, the ballot will be counted if received by the Cooperative on or before the time of the meeting.

Section 4.16. Action by Ballot Without Meeting.

Any action that may be taken at any regular or special meeting, including election of Directors, may be taken without a meeting through distribution of a written ballot to every member entitled to vote on the matter. The Secretary shall cause a vote to be taken by written ballot on any action or recommendation so requested in writing by at least 5% of the Members.

Section 4.17. Written Ballot Used Without Meeting.

(a) Any ballot used without a meeting shall set forth the proposed action, provide an opportunity to specify approval or disapproval of any proposal, and provide a reasonable time within which to return the ballot to the Cooperative.

(b) The form of written ballot distributed shall afford an opportunity to specify a choice between approval and disapproval of each matter or group of related matters intended, at the time of distribution, to be acted on by the ballot. The form must also provide that whenever the person solicited specifies choice with respect to any matter, the vote will be cast in accordance with that choice.

(c) Approval by written ballot shall be valid only when the number of votes cast by ballot within the time period specified equals or exceeds the quorum required to be present at a meeting authorizing the action, and the number of approvals equals or exceeds the number of votes that would be required to approve at a meeting at which the total number of votes cast was the same as the number of votes cast by ballot.

Section 4.18. Solicitation of Written Ballots.

Ballots shall be solicited in a manner consistent with Sections 4.05, 4.17(b), and 4.19 of these Bylaws. The solicitations shall indicate the number of responses needed to meet the quorum requirement and specify the time by which the ballot must be received to be counted. Ballots other than for the election of Directors shall state the percentage of approvals necessary to pass the measure.

Section 4.19. Withholding Vote.

Any written ballot on which the Member has marked "withhold" (or otherwise indicated that the authority to vote in the Directors is withheld) shall not be used for voting in that election.

Section 4.20. Appointment of Inspectors of Election.

In advance of any meeting of Members, the Board may appoint inspectors of election to act at the meeting and any adjournment. If inspectors are not appointed or if any appointed persons fail to appear or reuse to act, the chairperson of the meeting may, and, on the request of any Member, shall, appoint inspectors at the meeting.

Section 4.21. Duties of Inspectors of Election.

The inspectors shall determine the number of Memberships outstanding and the voting power of each, the number represented at the meeting, and the existence of a quorum. They shall receive votes, ballots, and consents, hear and determine all challenges and questions regarding the right to vote, count and tabulate all votes and consents, determine when the polls will close, and determine the result. They may do those acts which are proper to conduct the election or vote with fairness to all Members. The inspectors shall perform these duties impartially in good faith, to the best of their ability; and as expeditiously as is practical.

ARTICLE V.

DIRECTORS

Section 5.01. Number.

The Cooperative shall have Seven (7) Directors, collectively known as the Board of Directors.

Section 5.02 Qualification

The Directors of the Cooperative shall be shall be Members of the Cooperative and residents of California.

Section 5.03. Nomination.

(a) The Board of Directors shall prescribe reasonable nomination and election procedures for the election procedures for the election of Directors given the nature, size, and operations of the Cooperative. The procedures shall include: (1) a reasonable means of nominating persons for election as Directors, (2) a reasonable opportunity for a nominee to communicate the nominee's qualifications and the reasons for the nominee's candidacy to the Members, (3) a reasonable opportunity for all nominees to solicit votes, (4) a reasonable opportunity for all the Members to choose among the nominees.

(b) When the Cooperative distributes any material soliciting a vote for any nominee for director in any publication owned or controlled by the Cooperative, it shall make available to each other nominee, in the same material, an equal amount of space with equal prominence to be used by the nominee for a purpose reasonably related to the election

Section 5.04. Election.

The Directors shall be elected at the annual meetings or by written ballot in accordance with Sections 4.16-4.19 of these Bylaws. The candidates receiving the highest number of votes up to the number of Directors to be elected shall be elected.

Section 5.05. Terms of Office.

The terms of office for Directors shall be one (1) year. Each Director shall hold office until the expiration of the term for which elected and until the election and qualification of a successor.

Section 5.06. Compensation.

The Directors shall serve without compensation except that they shall be paid their actual and necessary expenses incurred in serving the Cooperative.

Section 5.07. Call of Meetings.

Meetings of the Board may be called by the any officer, or any two Directors.

Section 5.08. Place of Meetings.

Meetings of the Board may be held at any place designated in the notice of the meeting, or, if not stated in a notice, by resolution of the Board.

Section 5.09. Presence at Meetings.

Directors may participate at meetings of the Board through the use of conference telephone or other communications equipment, as long as all participating Directors can hear one another. Participation by communications equipment constitutes presence at the meeting.

Section 5.10. Regular Meetings.

Regular meetings of the Board shall be held, without call or notice, immediately following the annual meeting of Members, as set forth in Section 4.02 of these Bylaws, and one regular meeting shall be held during each calendar quarter of the year.

Section 5.11. Special Meetings; Notice.

Special meetings shall be held on four day's notice by first-class mail or 48 hours notice delivered personally or by telephone or telegraph. Notice of regular or special meetings need not be given to any Director who signs a waiver of notice, a written consent to holding the meeting, or an approval of the minutes (either before or after the meeting), or who attends the meeting without protesting, prior thereto or at its commencement, the lack of notice to that Director. All waivers consents, and approvals shall be filed with the corporate records or made a part of the minutes of the meeting.

Section 5.12. Quorum at Meetings.

A majority of the authorized number of Directors constitutes a quorum for the transaction of business.

Section 5.13. Acts of Board at Meetings.

Unless provided otherwise in the Articles of Incorporation, these Bylaws, or by law every act or decision done or made by a majority of the Directors present at a duly held meeting at which a quorum is present is the act of the Board. A meeting at which a quorum is initially present may continue to transact business notwithstanding the withdrawal of Directors, if any action taken is approved by at least a majority of the required quorum for the meeting or a greater number required by the Articles, Bylaws, or by-law.

Section 5.14. Adjournment of Meetings.

A majority of the Directors present, whether or not a quorum is present, may adjourn to another time and place. If the meeting is adjourned for more than 24 hours, notice of the adjournment shall be given prior to the time of the adjourned meeting to the Directors who were not present at the time of adjournment.

Section 5.15. Action Without Meeting.

Any action required or permitted to be taken by the Board may be taken without a meeting if all Directors individually or collectively consent in writing to the action. The consents shall be fled with the minutes of the proceedings of the Board Action by written consent has the same force and effect as a unanimous vote of the Directors.

Section 5.16. Executive Committees.

(a)The Board may create one or more committees to serve at its pleasure by resolution adopted by a majority of the number of Directors then in office when a quorum is present. Each committee shall consist of two or more Directors, appointed by a majority vote of the Directors then in office.

(b)Any committee, to the extent provided in the resolution of the Board, shall have all the authority of the Board, except with respect to the following actions:

(1) The approval of any action for which the approval of the Members or a majority of all Members is required by law;

(2) The filling of vacancies on the Board or in any committee that has the authority of the Board;

(3) The amendment or repeal of Bylaws or the adoption of new Bylaws;

(4) The amendment or repeal of any resolution of the Board;

(5) The appointment of committees of the Board or their Members;

(6) The expenditure of corporate funds to support a nominee for Director after there are more people nominated for Director than can be elected.

Section 5.17. Resignation of Directors.

Any Director may resign effective upon written notice to the Executive Director, the Secretary, or the Board of Directors, unless the notice specifies a later time for the effectiveness of the resignation. If a resignation is effective at a future time, a successor may be elected to take office when the resignation becomes effective.

Section 5.18. Removal of Directors.

Any or all Directors may be removed without cause by the Members. The removal shall be approved or ratified by the affirmative vote of a majority of all the votes represented and voting at a duly held meeting at which a quorum is present or by written ballot, or by the affirmative vote or written ballot of any greater proportion of the votes as required in these Bylaws or by law.

Section 5.19. Cause of Vacancies on Board.

Vacancies on the Board of Directors shall exist on the death, resignation, or removal of any Director, whenever the authorized number of Directors is increased; whenever the Board declares an office vacant pursuant to Section 5.20 of these Bylaws; and on the failure of the Members to elect the full number of Directors authorized.

Section 5.20. Declaration of Vacancies.

The Board may declare vacant the office of any Director whose eligibility for election has ceased, who has been declared of unsound mind by a final order of court, or who has not attended 2 or more consecutive regular or special meetings of the Board.

Section 5.21. Filling Vacancies on Board.

Except for vacancies created by removal of a Director pursuant to Section 5.18 of these Bylaws, vacancies may be filled by a majority of the Directors then in office, whether or not less than a quorum, or by a sole remaining Director. Vacancies created by the removal of a Director may be approved only by approval of the Members pursuant to Section 12224 of the Corporations Code. The Members may elect a Director at any time to fill any vacancy not filled by the Directors.

ARTICLE VI.

OFFICERS

Section 6.01. Titles.

The officers of the Cooperative shall be a Executive Director, Coordinator, a Secretary, Chief Operating Officer, a Chief Financial Officer, and any other officer with the titles and duties as determined by the Board and as may be necessary to enable it to sign instruments. The same person may hold any number of offices.

Section 6.02. Appointment and Resignation.

The officers shall be chosen by the Board and serve at the pleasure of the Board, Any officer may resign at any time on written notice to the Cooperative.

ARTICLE VII.

CORPORATE RECORDS AND REPORTS

Section 7.01. Required Records.

The Cooperative shall keep adequate and correct books and records of account and minutes of the proceedings of its members, Board, and committees of the Board. It shall also keep a record of the members, including the names, addresses. The minutes shall be kept in written form. Other books and records shall be kept either in written form or in any other form capable of being converted into written form.

Section 7.02. **Annual Report**

(a) For fiscal years in which the Cooperative has, at any time, more than 25 Members, the Cooperative shall notify each Member yearly of the Member right to inspect the annual financial report. The annual report shall be prepared no later than 120 days after the close of the Cooperative fiscal year.

(b) The annual report shall contain in appropriate detail all of the following: (1) a balance sheet as of the end of the fiscal year, an income statement, and statement of changes in financial position for the fiscal year; and (2) the statement required by Section 7.03 of these Bylaws.

(c) The annual report shall be accompanied by any pertinent report by independent accountants, or, if there is no such report, by the certificate of an authorized officer of the Cooperative that the statements were prepared without audit from the books and records of the Cooperative.

Section 7.03. **Annual Statement of Transactions and Indemnifications.**

In addition to the annual report described in Section 7.02, the Cooperative shall furnish annually to its Members and Directors a statement of the transactions and indemnifications to interested persons as required by law. If the Cooperative does not issue an annual report pursuant to Section 7.02 of these Bylaws, the statement shall be mailed or delivered to Members within 120 days after the close of the fiscal year.

ARTICLE VIII.

INSPECTION RIGHTS

Section 8.01. **Articles and Bylaws.**

The Cooperative shall keep at its principal office the original or a copy of its Articles and Bylaws as amended to date, which shall be open to inspection by the Members at all reasonable times during office hours.

Section 8.02. **Books and Records.**

The accounting books and records and minutes of proceedings of the Members, the Board, and committees of the Board shall be open to inspection on the written demand of any Member at any reasonable time, for a purpose reasonably related to that person's interests as a Member.

Every Director has the absolute right at any reasonable time to inspect and copy all books, records, and documents of every kind, and to inspect the physical properties of the Cooperative.

Section 8.03. **Inspection of Membership List.**

(a) The Cooperative's Membership list shall remain confidential.

(b) Subject to the Cooperative's right to set aside a Member's demand for inspection pursuant to Section 12601 of the Corporations Code and the power of the court

to limit inspection rights pursuant to Section 12602 of the Corporations code, and unless the Corporation provides a reasonable alternative pursuant to Section 8.03 (d) of these Bylaws, a Member may do either or both of the following:

(1) Inspect and copy the record of all the Members' names, addresses, and voting rights, at reasonable times, on making a written demand five business days in advance which states the purpose for which the inspection rights are requested;

(2) Obtain from the Secretary, upon written demand and tender of a reasonable charge, a list of names, addresses, and voting rights of those Members entitled to vote for the election of Directors, as of the most recent record date for which it has been compiled, or as of a date specified by the member subsequent to the date of demand. The demand shall state the purpose for which the list is requested. The Member list shall be made available on or before the later of 10 business days after the demand is received or after the date specified as the date as of which the list is to be compile.

(c) Any Member or Members possessing 5 percent or more of the voting power may demand the list for a purpose reasonably related to the Members interests as Members. The Cooperative may deny access if it reasonably believes that the information shall be used for another purpose or if it provides a reasonable alternative to Section 8.03(d) of these Bylaws.

(d) The Cooperative may within ten days after receiving a demand, deliver a written offer of an alternative method of achieving the purpose identified in the demand without providing access to or a copy of the membership list. An alternative method which reasonably and in a timely manner accomplishes the proper purpose set forth in a demand made pursuant to Section 8.03(b) of these Bylaws shall be a reasonable alternative, unless the Cooperative fails to do the things which it offered to do within a reasonable time after acceptance of the offer. Any rejection of the offer shall be in writing and indicate the reasons the purposed alternative does not meet the proper purpose of the demand

ARTICLE IX.

SURPLUS ALLOCATIONS AND DISTRIBUTIONS

Section 9.01. Fiscal Year.

The fiscal year of the Cooperative shall end at the close of the business day on the last day of December of each year.

Section 9.02. Surplus Defined.

"Surplus" shall be defined as the excess of revenues and gains over expenses and losses for a fiscal year. Such surplus shall be determined in accordance with generally accepted accounting principles and shall be computed without regard to any patronage refunds, capital allocations, or income taxes. All surplus shall be reinvested in the Cooperative.

Section 9.03 Allocations and Distributions of Surplus.

(a) Before any dividends or patronage refunds are distributed, any surplus should first be allocated to any deficit in Retained Earnings

(b) After any deficit in Retained Earnings has been eliminated, the Directors may declare a dividend upon shares at a yearly rate not to exceed any maximum rate established by statute. No such dividends shall be cumulated.

(c) The Directors may then uniformly distribute all the remaining surplus attributed to patronage of the Members of the Cooperative to such Members as described in the following paragraphs of this subsection of the Bylaws. For the purposes of this subsection of the Bylaws, the remaining patronage surplus shall be computed without regard to any gains or losses on the sale or other disposition of assets

1) Any remaining patronage surplus attributed to the Members and to be distributed to them shall be distributed to them shall be the total remaining patronage surplus attributed to both Member and non-Member business (but reduced by dividends on shares and any allocations to eliminate a deficit in Retained Earnings) multiplied by the ratio of member patronage to total patronage.

2) A member is entitled to patronage refund, if such is distributed, in the amount of the remaining patronage surplus, as determined by paragraph (1) of this subsection of the Bylaws, multiplied by the ratio of such Member's patronage with the Cooperative to the patronage of all Members.

(d) Any dividends or patronage refunds declared under this bylaw Section may be in the form of shares, in whole or in part, subject to subsections (e) and (f) of the Bylaw Section.

(e) If a member owns $300.00 or more in shares as of the end of the fiscal year for which a distribution is made, such Member shall receive all of his or her dividends and patronage refunds in cash. The $300.00 amount shall be known as a Member's "Fair Share".

(f) If the cash payment to a Member for such Member's dividends and patronage refunds together would total less than on dollar ($1.00), the Directors shall distribute such dividends and patronage refunds wholly in shares.

(g) Each person who becomes a Member of this Cooperative consents to include in his or her gross income for federal income tax purposes the amount of any patronage refund paid to him or her by this Cooperative in money or by written notice of allocation (as defined in the Internal Revenue Code), except to the extent that such a patronage refund in not income to the Member because (i) it is attributable to the purchase of personal, living, or family items, or (ii) it should properly be treated as an adjustment to the tax basis of property previously purchased. The term "patronage refund," as used herein, shall have the same meaning as the term "patronage dividend," as used in the Internal Revenue Code.

(h) For the purpose of allocating and distributing the surplus, the entire operations of the Cooperative shall be considered as a unit; provided that by resolution of the Board of Directors, the Cooperative may distribute patronage refunds on the basis of the business transacted by each of the departments or divisions into which the operations of the Cooperative shall be divided by the Board for the purpose of such allocations.

ARTICLE X.

BYLAW CHANGES

Section 10.01. **Bylaw Changes by the Board.**

These Bylaws shall initially be adopted by the Board. Thereafter, these Bylaws may be amended, or repealed by the Board unless the action would:

(a) Materially and adversely affect the rights or obligations of Members as to voting, dissolution, distributions, property rights, or rights to repayment of contributed capital;

(b)Increase or decrease the number of Members authorized in total or for any class;

(c) Effect an exchange, reclassification or cancellation of all or part of the Memberships;

(d) Authorize a new class of Memberships;

(e) Change the number of Directors or establish a variable number of Directors;

(f) Extend the term of a Director beyond that for which the Director was elected or increase the terms of the Directors;

(g) Allow up to one-third (1/3) of the Directors to hold office by virtue of designation or selection rather than by election by the Members; and

(h) Allow the Board to fill vacancies occurring in the Board by reason of the removal of Directors.

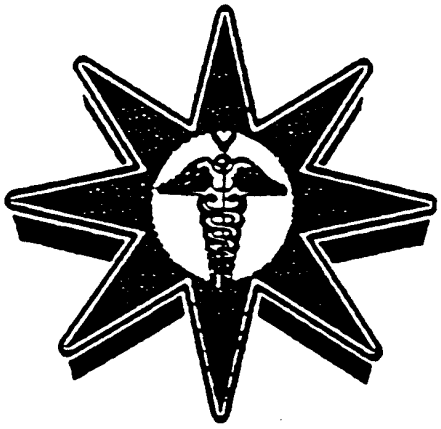
Section 10.02. **Bylaw Changes by the Members.**

Where the Board is denied the right to, amend or repeal the Bylaws pursuant to subsections (a) through (h) of Section 10.01 of these Bylaws, the Bylaws shall be amended or repealed by approval of the Members.

EXHIBIT 3

Oakland Cannabis Buyers' Cooperative

Protocols



Compassion

Oakland Cannabis Buyers' Cooperative
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March, 30 1998

Oakland Cannabis Buyers' Cooperative

Protocols

The Oakland Cannabis Buyers' Cooperative operates pursuant to and in accordance with the statewide mandate of Proposition 215 (Exhibit A) and Resolutions passed unanimously by the Oakland City Council and an Administrative Memorandum promulgated by the Chief of Police (Exhibit B). Its operating procedures have been consolidated as these Protocols.

I. Admission and Membership Requirements

A person seeking membership of the Oakland Cannabis Buyers' Cooperative must at the threshold provide a note from a treating physician assenting to cannabis therapy for a medical condition listed on the Medicinal Cannabis User Initial Questionnaire (Exhibit C). Upon acceptance of the note by Intake staff, the prospective member will undergo an extensive screening and such questioning as shall establish that the candidate meets the Medical Admissions Criteria (Exhibit D) including, without being limited to, the Oakland Cannabis Buyers' Cooperative Information Form (Exhibit E). If, upon the screening by Cooperative staff the candidate does not appear to qualify for membership, he or she will be denied membership with a statement of reasons for his/her being screened out. If the candidate appears to qualify for membership, Intake staff will give the candidate the Authorization for Release of Patient Status form (Exhibit F) and the Physician Statement (Exhibit G), with a request that the candidate's treating physician sign it. When the form is returned, the Intake staff will verify the physician's approval by independent telephone verification. Medical cannabis cultivators and manufactures are issued cultivation and manufacturing Certificates (Exhibit H), which the City Council has approved to aid the Police in recognizing agents of the Cooperative.

No person under the age of eighteen shall be admitted to membership without the written consent of parents, in addition to meeting all other requirements.

II. Responsibilities of Membership

All members must sign a Membership Agreement (Exhibit I), whereupon they will receive a Membership Card (Exhibit J). Members agree to conduct themselves discreetly, in accordance with the Statement of Safe Use of Cannabis (Exhibit K) and the Principles of Responsible Cannabis Use (Exhibit L).

III. Other Provisions

A. Purpose. The purpose of the Oakland Cannabis Buyers' Cooperative is to help provide medicine for people who need it. Accordingly, it shall be operated as a not for profit organization.

B. Privacy of members. The staff of the Cooperative shall take steps to protect the privacy and identity of members. However, neither the Cooperative nor its staff shall be liable for any breach thereof

C. Changes. These Protocols, and all medical protocols, are subject to change without notice from time to time in the sole discretion of management.

D. Cooperative operation.

a. No smoking of anything on premises.
b. Members shall observe additional house rules as same maybe posted by management.
c. Management may eject any person at any time.

Exhibits

A. Proposition 215

B. Oakland City Council Resolutions and Police Memorandum

C. Medicinal Cannabis User Initial Questionnaire

D. Medical Admissions Criteria

E. Information Form

F. Authorization for Release of Patient Status

G. Physician Statement

H. Cultivation and Manufacturing Certificates

I. Membership Agreement

J. Membership Card

K. Statement of Safe Use of Cannabis

L. Principles of Responsible Cannabis Use

Ex. A

THE CALIFORNIA MEDICAL MARIJUANA INITIATIVE

This initiative to permit medical use of marijuana will appear on the ballot November 5, 1996. The Attorney General of California has prepared the following title and summary of the chief purpose and points of the initiative.

MEDICAL USE OF MARIJUANA. INITIATIVE STATUTE. Provides that patients or defined caregivers, who possess or cultivate marijuana for medical treatment recommended by a physician, are exempt from general provisions of law which otherwise prohibit possession or cultivation of marijuana. Provides physicians shall not be punished or denied any right or privilege for recommending marijuana to a patient for medical purposes. Declares that the measure not be construed to supersede prohibitions of conduct endangering others nor to condone diversion of marijuana for nonmedical purposes. Contains severability clause. Summary of estimate by Legislative Analyst and Director of Finance of fiscal impact on state and local government: Because this measure restricts the use of marijuana to only those persons for whom it is prescribed by a licensed physician, it would probably have no significant state or local fiscal impact.

Initiative text:

SECTION 1. Section 11362.5 is added to the Health and Safety Code, to read:

11362.5. (a) This section shall be known and may be cited as the Compassionate Use Act of 1996.

(b)(1) The people of the State of California hereby find and declare that the purposes of the Compassionate Use Act of 1996 are as follows:

(A) To ensure that seriously ill Californians have the right to obtain and use marijuana for medical purposes where that medical use is deemed appropriate and has been recommended by a physician who has determined that the person's health would benefit from the use of marijuana in the treatment of cancer, anorexia, AIDS, chronic pain, spasticity, glaucoma, arthritis, migraine, or any other illness for which marijuana provides relief.

(B) To ensure that patients and their primary caregivers who obtain and use marijuana for medical purposes upon the recommendation of a physician are not subject to criminal prosecution or sanction.

(C) To encourage the federal and state governments to implement a plan to provide for the safe and affordable distribution of marijuana to all patients in medical need of marijuana.

(2) Nothing in this act shall be construed to supersede legislation prohibiting persons from engaging in conduct that endangers others, nor to condone the diversion of marijuana for nonmedical purposes.

(c) Notwithstanding any other provision of law, no physician in this state shall be punished, or denied any right or privilege, for having recommended marijuana to a patient for medical purposes.

(d) Section 11357, relating to the possession of marijuana, and Section 11358, relating to the cultivation of marijuana, shall not apply to a patient, or to a patient's primary caregiver, who possesses or cultivates marijuana for the personal medical purposes of the patient upon the written or oral recommendation or approval of a physician.

(e) For the purposes of this section, "primary caregiver" means the individual designated by the person exempted under this act who has consistently assumed responsibility for the housing, health, or safety of that person.

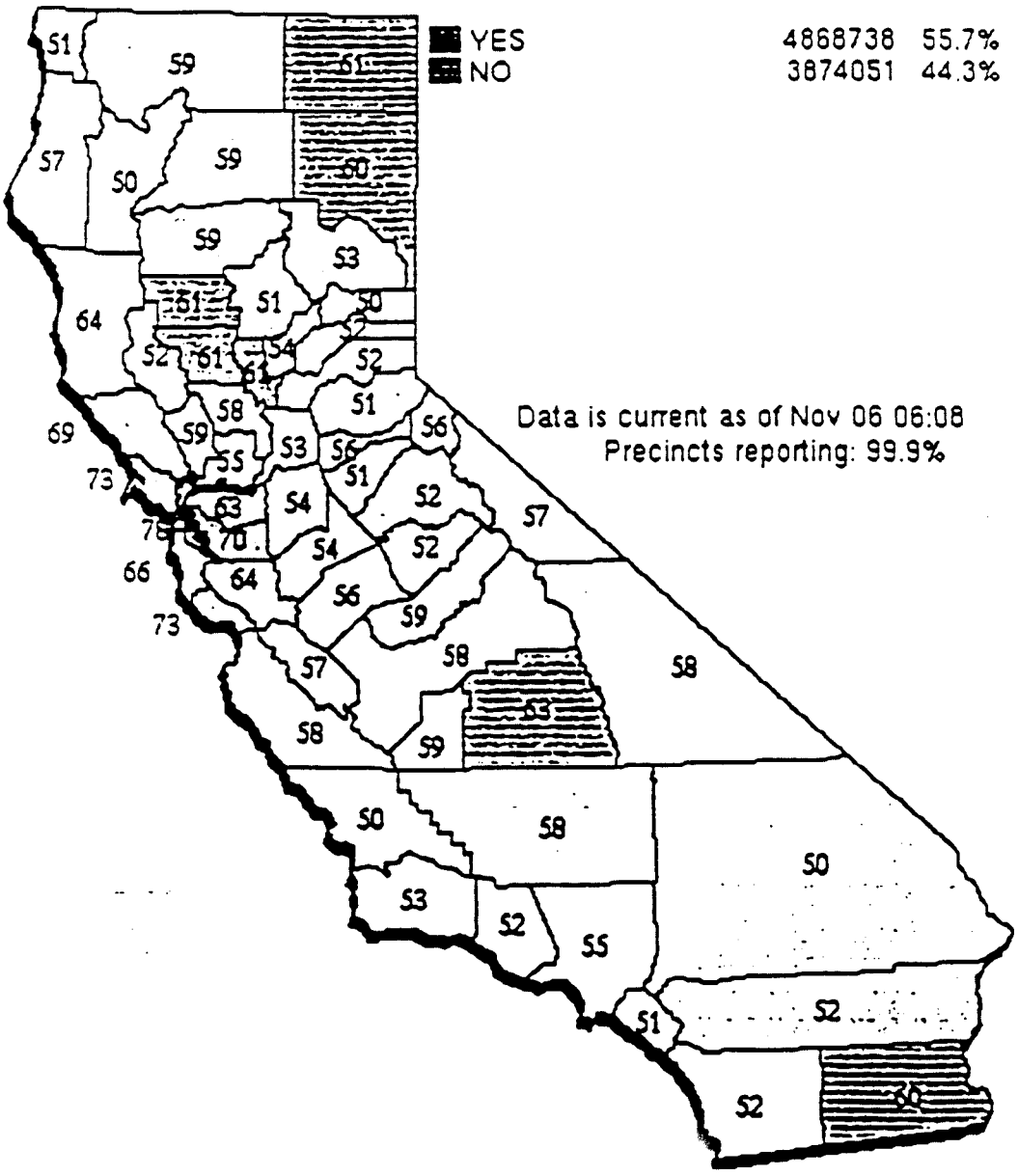
SECTION 2. If any provision of this measure or the application thereof to any person or circumstance is held invalid, that invalidity shall not affect other provisions or applications of the measure which can be given effect without the invalid provision or application, and to this end the provisions of this measure are severable.

For more information, contact: Californians for Medical Rights
1250 Sixth St., Suite 202, Santa Monica, CA 90401
(310) 394-2952 fax: (310) 451-7494

1996 General Election Returns for

Proposition 215 - Marijuana

The number in each county indicates the percentage of the vote cast as indicated by the color.



ER1373

OAKLAND CITY COUNCIL

RESOLUTION NO. 72379 C. M. S.

Ex. B

RESOLUTION ENDORSING AB - 1529, "THE MEDICAL MARIJUANA BILL" and the "COMPASSIONATE USE INITIATIVE OF 1996"

WHEREAS, marijuana has been shown to alleviate nausea and pain associated with cancer and;

WHEREAS, marijuana has been shown to helped people with AIDS to relieve stress and depression, eliminate nausea, reduce and manage pain and fight the "wasting away" syndrome by stimulating the appetite and;

WHEREAS, marijuana has been shown to control spasticity from multiple sclerosis and paralysis and;

WHEREAS, marijuana has been shown to arrest the advance of glaucoma and:

WHEREAS, marijuana has been shown to relieve the pain of arthritis and rheumatism and;

WHEREAS, marijuana has been shown to block epileptic seizures and help migraine headaches and;

WHEREAS, AB - 1529 and the "Compassionate Use Initiative of 1996" will not legalize the personal use of marijuana;

LET IT BE RESOLVED that the Oakland City Council endorses the passage of AB - 1529, "THE MEDICAL MARIJUANA BILL"; and let it be

FURTHER RESOLVED that the Oakland City Council endorses the "Compassionate Use Initiative of 1996".

I certify that the foregoing is a full, true and correct copy of a Resolution passed by the City Council of the City of Oakland, California on December 12, 1995

CEDA FLOYD
City Clerk and Clerk of the Council

Per Margie Sosa *Deputy*

C AKLAND CITY COUNCIL

RESOLUTION NO. 72516 C. M. S.

INTRODUCED BY COUNCILMEMBER _____

RESOLUTION ENDORSING H.R. 2618, SUPPORTING THE ACTIVITIES OF THE OAKLAND CANNABIS BUYER'S CLUB AND DECLARING THAT THE INVESTIGATION AND ARREST OF INDIVIDUALS INVOLVED WITH THE MEDICAL USE OF MARIJUANA SHALL BE A LOW PRIORITY FOR THE CITY OF OAKLAND

WHEREAS, marijuana has been shown to help alleviate pain and discomfort in people suffering from a variety of illnesses including AIDS, cancer, glaucoma, and multiple sclerosis; and,

WHEREAS, marijuana has alleviated the suffering of people with chronic illnesses when no other medications have been effective; and,

WHEREAS, the use of marijuana is presently unlawful even under the supervision of physician; and

WHEREAS, the illegal purchase of marijuana by people already suffering with chronic illnesses subjects them to further suffering in the form of potential arrest and prosecution; and

WHEREAS, Representative Barney Frank (MA) and local co-sponsors Representative Ronald Dellums and Pete Stark have introduced H.R. 2618 which would allow physicians to prescribe marijuana for medical purposes and would insure the production of marijuana to meet the need for medical use; and

WHEREAS, the Oakland Cannabis Buyer's Club provides a way for patients needing to purchase marijuana for medical use to do so with greater ease and less risk of arrest and prosecution; and

WHEREAS, the City of Oakland wishes to declare its desire not to expend City resources in any investigation, detention, arrest or prosecution arising out of alleged violations of state and federal law regarding the distribution of marijuana for compassionate medical use; and

WHEREAS, the Oakland City Council passed Resolution 72379 C.M.S. endorsing state legislation AB 1529, "The Medical Marijuana Bill" and the "Compassionate Use Initiative of 1996;" now, therefore, be it

RESOLVED: That the Oakland City Council endorses of the passage of H.R. 2618: and be it further

RESOLVED: That the Oakland City Council authorizes the City Manager to instruct the City's federal lobbyists to work in support of H.R. 2618; and be it further

RESOLVED: That, the Mayor and City Council hereby declare that it shall be the policy of the City of Oakland that the investigation and arrest of members of the Oakland Cannabis Buyers' Club for purchasing, selling and distributing marijuana for medical purposes shall be a low priority; and be it further

RESOLVED: That, the Mayor and City Council hereby declare that it shall be the policy of the City of Oakland that the investigation and arrest of persons for planting, cultivating, purchasing, and/or possessing marijuana shall be a low priority for the City of Oakland if such persons have been medically diagnosed as suffering from an illness or injury, the symptoms of which may be alleviated by the medicinal use of marijuana; and be it further

RESOLVED: That, the Mayor and City Council hereby declare that it shall be the policy of the City of Oakland that the investigation and arrest of persons for cultivating, purchasing, possessing and/or distributing marijuana shall be a low priority for the City of Oakland if such persons purchase or possess marijuana for, and/or distribute marijuana to patients, whose physicians have determined that they are suffering physical pain that may be alleviated by the medicinal use of marijuana; and be it further

RESOLVED: That, the Mayor and City Council call upon the Alameda County District Attorney to cease prosecution of persons involved in the medical use of marijuana; and be it further

RESOLVED: That if any provision of this resolution is declared by a court of competent jurisdiction to be contrary to any statute, regulation or judicial decision, or its applicability to any agency, person or circumstances is held invalid, the validity of the remainder of this resolution and it applicability to any other agency, person or circumstance shall not be affected.

IN COUNCIL, OAKLAND, CALIFORNIA, MAR 12 1996, 19 _____

PASSED BY THE FOLLOWING VOTE:

AYES- BAYTON, CHANG, DE LA FUENTE, ~~JORDAN~~, MILEY, RUSSO, SPEES, ~~WOODS-JONES~~, and PRESIDENT HARRIS — 7

NOES-NONE

ABSENT-NONE

ABSTENTION-NONE

Excused - Jordan/Woods-Jones-2

ATTEST: Ceda Floyd
CEDA FLOYD
City Clerk and Clerk of the Council
of the City of Oakland, California

O KLAND CITY COUN IL

RESOLUTION NO. 72881 C. M. S.

INTRODUCED BY COUNCILMEMBER _____

BJP:trc

RESOLUTION ESTABLISHING A WORKING GROUP TO DISCUSS AND MAKE RECOMMENDATIONS TO THE CITY COUNCIL REGARDING THE MEDICAL MARIJUANA POLICY OF THE CITY OF OAKLAND

WHEREAS, marijuana has been shown to help alleviate pain and discomfort in people suffering from a variety of illnesses including AIDS, cancer, glaucoma, and multiple sclerosis; and

WHEREAS, marijuana has alleviated the suffering of people with chronic illnesses when no other medications have been effective; and

WHEREAS, the use of marijuana is currently unlawful even under the supervision of a physician, and

WHEREAS, the illegal purchase of marijuana by people already suffering chronic illnesses subjects them to further suffering in the form of potential arrest and prosecution; and

WHEREAS, the Oakland Cannabis Buyers Club provides a way for patients needing to purchase marijuana for medical use to do so with greater ease and less risk of arrest and prosecution; and

WHEREAS, the Oakland City Council passed Resolution 72516 C.M.S., supporting the activities of the Oakland Cannabis Buyers Club and declaring it to be the policy of the City of Oakland that the arrest of individuals involved with the medical use of marijuana shall be a "low priority" for the City of Oakland; and

WHEREAS, to the extent permitted by applicable law, the City of Oakland wishes not to expend any City resources, including but not limited to those of the Oakland Police Department, in any investigation, detention, arrest, and/or prosecution arising out of alleged violations of state or federal law regarding the cultivation, distribution, sale, purchase, and/or possession of marijuana for medicinal purposes; now therefore, be it

RESOLVED: that a Working Group be established to discuss and make recommendation to the City Council regarding refinement of the City's medical marijuana policy; and be it

FURTHER RESOLVED: that said Working Group shall consist of representatives designated by the City Manager and interested members of the public; and be it

FURTHER RESOLVED: that said Working Group shall consider legislative and administrative methods to insure enforcement of and compliance with the City's medical marijuana policy; and be it

FURTHER RESOLVED: that said Working Group shall consider the feasibility of any other matters pertaining to the City's medical marijuana policy; and be it

FURTHER RESOLVED: that said Working Group shall report to the Public Safety, Health, Human Services and the Family Committee no later than October 1, 1996, concerning the results of its discussions and any recommendations regarding the refinement of the City's medical marijuana policy.

I certify that the foregoing is a full, true and correct copy of a Resolution passed by the City Council of the City of Oakland, California on July 30, 1996.

CEDA FLOYD
City Clerk and Clerk of the Council

Per Margie Sosa *Deputy*

C .KLAND CITY COUNC

RESOLUTION NO. 73555 C.M.S.

RESOLUTION SUPPORTING MEDICAL MARIJUANA ACTIVITIES IN THE CITY OF OAKLAND AND DECLARING THAT THE INVESTIGATION AND/OR ARREST OF INDIVIDUALS INVOLVED WITH THE CULTIVATION, MANUFACTURE, AND/OR TRANSPORTATION OF MEDICAL MARIJUANA PRODUCTS SHALL BE A LOW PRIORITY FOR THE CITY OF OAKLAND

WHEREAS, on November 5, 1996, the voters of California passed Proposition 215, the Compassionate Use Act of 1996, by a YES vote of 55.7 percent, and the residents of Oakland voted YES for Proposition 215 by an overwhelming 79.3 percent; and

WHEREAS, marijuana had been shown to help alleviate pain and discomfort in people suffering from a variety of illnesses including AIDS, cancer, glaucoma, and multiple sclerosis when no other medications have been effective; and

WHEREAS, cultivation of medicinal strains of marijuana, the manufacture of medical cannabis products such as oral preparations, and the transportation of marijuana and cannabis products for medical purposes may remain illegal notwithstanding the passage of Proposition 215; and

WHEREAS, there is a need to ensure that patients have access to a safe and affordable supply of medical grade marijuana and cannabis products; and

WHEREAS, the Oakland City Council passed Resolution 72379 C.M.S. endorsing the Compassionate Use Act of 1996 and similar measures; and

WHEREAS, the Oakland City Council passed Resolution 72516 C.M.S. supporting the activities of the Oakland Cannabis Buyers Club and declaring it to be the policy of the City of Oakland that the investigation and arrest of certain individuals involved with the medical use of marijuana shall be a low priority for the City of Oakland; and

WHEREAS, the Oakland City Council passed Resolution 72881 C.M.S. establishing a Working Group to make recommendations regarding the City's medical marijuana policy; and

WHEREAS, to the extent permitted by applicable law, the City of Oakland wishes not to expend any City resources, including but not limited to those of the Oakland Police Department, in any investigation, detention, arrest, and/or prosecution arising out of alleged violations of state or federal law regarding the cultivation, manufacture, or transportation of marijuana or cannabis products for medical purposes; now therefore, be it

RESOLVED: that the Mayor and City Council hereby declare that it shall be the policy of the City of Oakland that the investigation, detention, arrest, or prosecution of a person and/or that person's primary caregiver for the cultivation, manufacture, or transportation of marijuana or cannabis products shall be a low priority for the City of Oakland if such person has been medically diagnosed as suffering from a serious illness or injury, the symptoms of which may be alleviated by the medicinal use of marijuana and such cultivation, manufacture and/or transportation of marijuana or cannabis products is for the personal medical use of such person upon the written or oral recommendation or approval of a physician; and, be it further

RESOLVED: that the Mayor and City Council hereby declare that it shall be the policy of the City of Oakland that investigation, detention, arrest, and/or prosecution of persons for the cultivation, manufacture or transportation of marijuana or cannabis products shall be a low priority for the City of Oakland if such persons cultivate, manufacture, or transport marijuana or cannabis products for patients whose physicians have determined that they are suffering from a serious illness or injury, the symptoms of which may be alleviated by the medicinal use of marijuana and have recommended or approved medical marijuana use for such patients; and be it further

RESOLVED: that the Mayor and City Council call upon the Alameda County District Attorney not to prosecute persons involved with the possession, purchase, distribution, cultivation, manufacture or transportation of marijuana or cannabis products for medical use; and be it further

RESOLVED: that if any provision of this Resolution is declared by a court of competent jurisdiction to be contrary to any statute, regulation, or judicial decision, or its applicability to any agency, person, or circumstance is held invalid, the validity of the remainder of this resolution and its applicability to any other agency, person, or circumstances shall not be affected.

IN COUNCIL, OAKLAND, CALIFORNIA, JUN 03 1997 19___

PASSED BY THE FOLLOWING VOTE:

AYES- BRUNNER, CHANG, DE LA FUENTE, MILEY, NADEL, REID, RUSSO, SPEES, and PRESIDENT HARRIS — 9

NOES- None

ABSENT- None

ABSTENTION- None

ATTEST: Ceda Floyd
CEDA FLOYD
City Clerk and Clerk of the Council
of the City of Oakland, California

C^KLAND CITY COUNCI'

RESOLUTION NO. 74039 C.M.S.

RESOLUTION CALLING UPON FEDERAL AUTHORITIES TO DESIST THEIR EFFORTS TO TERMINATE THE OPERATIONS OF THE OAKLAND CANNABIS BUYERS' COOPERATIVE

WHEREAS, in November 1996 the voters of the State of California passed Proposition 215, the Compassionate Use Act of 1996, to "ensure that seriously ill Californians have the right to obtain and use marijuana for medical purposes" by a YES vote of 55.7 percent, and the residents of Oakland voted YES for Proposition 215 by an overwhelming 79.3 percent; and

WHEREAS, the City Council of the City of Oakland finds that many of its City residents are suffering from life-threatening or serious illnesses whose painful symptoms are alleviated by the ingestion of cannabis; and

WHEREAS, the City of Oakland has repeatedly expressed its support for access to a safe and affordable supply of marijuana for medicinal purposes and the operations of the Oakland Cannabis Buyers' Cooperative in Resolution Nos. 72379 C.M.S., 72516 C.M.S., 72881 C.M.S., and 73555 C.M.S.; and

WHEREAS, the City Council finds that the Oakland Cannabis Buyers' Cooperative has served the aforementioned residents with a well-organized, safe, and responsible opportunity to obtain cannabis in furtherance of a course of medical treatment; and

WHEREAS, federal law enforcement authorities have threatened to disrupt and prevent ill Oakland residents' access to cannabis by filing suit to enjoin the Oakland Cannabis Buyers' Cooperative from supplying medical marijuana and to shut down its operations; and

WHEREAS, the federal law enforcement policy impairs public safety by encouraging a market for street narcotic peddlers to sell cannabis to Oakland's ill citizens; now therefore be it

RESOLVED: the Mayor and the Oakland City Council urge the federal government to desist from any and all actions that pose obstacles to access to cannabis for Oakland residents whose physicians have determined that their health will benefit from the use of marijuana and recommended medical marijuana use for such residents; and be it

FURTHER RESOLVED: the Mayor and the Oakland City Council endorse Senator John Vasconcello's call for a statewide summit on the distribution of medical marijuana; and be it

FURTHER RESOLVED: the Mayor and the Oakland City Council urge the Alameda County Board of Supervisors to declare a state of medical emergency; and be it

FURTHER RESOLVED: the Mayor and the Oakland City Council express their support of the furtherance of medical marijuana research; and be it

FURTHER RESOLVED: copies of this resolution shall be forwarded to Senators Boxer and Feinstein and Congressman Ron Dellums urging the federal policy-makers to dismiss current lawsuits impacting California's cannabis buyers' clubs and cooperatives.

I certify that the foregoing is a full, true and correct copy of a Resolution passed by the City Council of the City of Oakland, California on January 27, 1998

CEDA FLOYD
City Clerk and Clerk of the Council

Per _____ *Deputy*

ADMINISTRATIVE MEMO
Oakland Police Department

TO	DATE	NUMBER	DUE DATE
BUREAU COMMANDERS (BFO)	11 Dec 96	-	-
SUBJECT: MEDICINAL USE OF MARIJUANA			

The City Council has adopted a resolution in support of the medicinal use of marijuana as a means of alleviating pain and discomfort for individuals suffering from medical illnesses.

In accordance with the subsequent directive of the City Manager to handle medicinal marijuana activity (in violation of Health and Safety Code 11357, relating to the possession of marijuana, and 11358, relating to the cultivation of marijuana) as a low priority, the following procedures will be implemented immediately:

- Citizen calls for service requesting police intervention at sites where such activity is occurring shall be assigned a "D" priority by Communications Division staff.

- At both field and dispatch levels, every effort shall be made to obtain and record the identity of the reporting citizen(s).

- Field units receiving a dispatched assignment or initiating a contact with persons purportedly involved in the use of marijuana for medicinal purposes shall summon a command-level officer to the scene if an enforcement action (citation or arrest) for the 11357 H&S or 11358 H&S violation is intended.

- The command officer shall evaluate the facts and exercise the discretion and decision-making required to resolve the incident, in accordance with the low-priority policy.

- If an enforcement action is to be taken, the command officer shall promptly notify his/her Bureau Commander and provide him with a written summary of the incident and a copy of all pertinent documents.

- Incidents involving persons who wish to make citizen arrests for the law violation shall be handled in the normal manner.

- Discretion to arrest will be left with the officer and commander at the scene, based upon the facts presented to them at the time. The marijuana should be turned in as evidence for follow-up investigation by the Vice/Narcotics Section.

There are varied and opposing views--professional, legal and medical in nature--regarding the practice of medicinal use of marijuana as a means of alleviating symptoms and controlling chronic pain of patients with specific medical conditions.

Nevertheless, the recent passage of Proposition 215 by California voters has now created law. Federal and state officials are reviewing the initiative and may issue guidelines in the near future. In the interim, the Department will continue its participation on a City working group to identify and resolve local implementation issues. As agreements are reached or decisions made, additional procedural guidelines will be set forth in Departmental publications or communications.

Interim training to all commanders in general and BFO commanders in particular shall be provided over the next 3-4 weeks by Lieutenant Peterson.

Joseph Samuels, Jr.
Chief of Police

CITY OF OAKLAND

Memorandum

TO: Bureau of Field Operations
ATTN: Command Staff
FROM: Vice/Narcotics Section
DATE: 12 Dec 96

RE: Medicinal Marijuana Enforcement

Attached is a copy of an administrative memorandum you will be receiving shortly outlining Chief's Samuels' guidelines for the enforcement of Proposition 215. It is similar to the guidelines dealing with the needle exchange issue. The primary people you will come into contact with will be members of the Oakland Cannabis Buyer's Club (CBC) who are working with us (to the extent they can) to find a way to make this thing work until the issue is settled in the courts.

Clients of the CBC are being issued new photo identification cards with a 24-hour number to contact to verify they are medicinal members. The City's working group has agreed to accept these new cards as a legitimate means of verifying identification if the person has no driver's license, etc. You may come into contact with older ID cards until the transition is complete; these more than likely will be valid.. I would assume non-CBC members will claim in some fashion to be medicinal marijuana users; they may, or may not, have some form of doctor verification.

In evaluating whether an arrest should be made, you should consider the intent of Proposition 215 and the City Council's resolution supporting it and setting a low priority on enforcement. Each case should be decided on its own merits.

It is requested the identification cards not be seized without a valid need. All information on the card should be listed on the report. The marijuana should be seized and turned into criminalistics. All such incidents require a report in addition to any citation which may be issued. Follow-up responsibility for verifying the medicinal use will rest with the Vice/Narcotics charging officers. The DA will make charging decisions. Ultimately, a court order will have to be initiated by the patient/suspect if no charges are filed.

I realize this is confusing; feel free to call me anytime, day or night. I will try to provide some guidance based upon what I know about the issue.

Peter A. Peterson
Lieutenant of Police
Vice/Narcotics Section

Ex. C

Medicinal Cannabis User Initial Questionnaire

Today's Date _____

Identifying Data

Last name_____, First name _____ Middle Initial __
Address _____ City _____ State ____ Zip _____
Res Ph _____-_____-_____ Work Ph _____-_____-_____ ext____ Fax _____-_____-____
Birthdate (MMDDYY)_____ SS#___-__-____ Sex M_ F_ Ethnic Wh_B_Hisp_Or_ NatAm_
Other _____ Education _____Occupation(s)_____ Unemployed_ Disabled_
Marital Status: Single_ Mar_ Sep_ Div_ W_ Living situation:_ Alone _ Couple_ Group_ Apartment_
House_ Institution_ Homeless_
Health Insurance None_ Medicaid_ Medicare_ Workers Compensation_ Other health plan._
(specify)_____ ID Number _____ GroupNumber_____
Address _____ City _____ State ___ Zip _____ Phone ___-___-____x _____
Referred by: Self _ Name_____ Institution _____
Address _____ City _____ State __ Zip_____
Phone ___-___-____x _____ Fax ___-___-____ Pager ___-___-____

Chief Complaint(s) circle and rank in importance: example: AIDS related illness 1 anorexia 2

1. Alcoholism
2. Alcohol Abuse
3. Sedative/Opiate Habit
4. Cocaine or Speed Habit
5. Nicotine Habit
6. AIDS related illness
7. Cancer & cancer Rx
8. Anorexia
9. Nausea
10. Vomiting
11. Diarrhea
12. Irritable bowel
13. Colitis
14. Cron's disease
15. Gastritis
16. Pancreatitis
17. Hepatitis
18. Peptic Ulcer
19. Antibiotic
20. Asthma
21. Sinusitis
22. Cough
23. Anxiety
24. Panic attacks
25. Insomnia
26. Mania
27. Depression
28. Lethargy
29. Weakness
30. Chronic Fatigue Syndrome
31. Epilepsy
32. Delirium Tremens
33. Dementia
34. Multiple Sclerosis
35. Huntington's Chorea
36. Cerebral Palsy
37. Brain Trauma
38. Spinal Cord Injury
39. Muscle spasm
40. Parkinson's disease
41. Tremor
42. Peripheal neuropathy
43. Tic doloroux
44. Tourette's syndrome
45. Glaucoma
46. Menstrual cramps
47. Labor pains
48. Migraine
49. Meniere's Disease
50. Hypertension
51. Itching
52. Hiccough
53. Arthritis
54. Carpal Tunnel Syndrome
55. Lupus, scleroderma
56. Amyloidosis
57. Conjunctivitis
58. Other Pain (specify source)____
59. External Use ___
60. Drug Side Effect control (specify)___
61. Decrease Use of Other Drugs (specify)_____
62. Substitute for Other Drugs (specify) _____
63. Other _____

Chief Complaint _____ ICD9-CM Diagnoses _____ _____ _____
History ofPresent Illness: (date of onset, course) _____
PastMedicalHistory: (Allergies & adverse drug reactions):_____
Family Medical History:_____
Social History: _____ Drug law arrests/convictions: None_ Yes (specify) _____
Cannabis type preferred: Sinsemilla_ Mexican_ Hashish_ No preference Other_____
Age or date Use Begun:_____ Marinol ®(dronabinol) 2.5 mg _ 5 mg _ 10 mg _ result (+)_ (0)_ (-)_
Route: Oral_ Inhaled: Joint_ Pipe_ Water Pipe_ Vaporizer_ Other (specify):_____
Frequency: Monthly_ Weekly_ Semiweekly_ Daily_ Twice a day_ 3 x a day _ 4 x a day _more _
Other drugs using- Rx and Over the Counter_____
Has your physician discussed your use of cannabis with you? Yes _ No _ Discussed any non prescribed psychoactive drugs? (including alcohol and tobacco) Yes _ No _ Remarks _____
Completed by:_____

Ex. D

Medical Admissions Criteria
to Cannabis Buyers' Cooperative
Tod H. Mikuriya, M.D.
Medical Coordinator

Because of the vacuum of clinical knowledge about the therapeutic applications of cannabis caused by cannabis prohibition a widespread condition of ignorance exists. While it is acknowledged that there exists a range of illnesses on the dimension of seriousness objectively, there is none to the person afflicted who is seeking relief. Exclusion because the condition does not appear on a list developed by a group of non-medical politicians or bureaucrats merely perpetuate this clinical ignorance. Therefore the medical criteria are to be inclusive limited only by contemporary classifications of illness.

Medical Criteria

Persons shall have a verified specific diagnosis by a licensed physician that is included within the latest revision of the International Classification of Diseases ICD-9. Or the Diagnostic Statistical Manual DSM-IV vague statements about conditions, disorders, or syndromes without specific information or not recognized by either ICD-9 or DSM-IV are not acceptable.

Mental Disorders Admissions Protocol

Since the inception of Cannabis Buyers' Cooperatives some have expressed concern about the possibility of adverse effects on individuals suffering from emotional or mental disorders.

In clinical interviews I have conducted with members and patients in my psychiatric practice it is my impression that while many definitely benefit from cannabis there are others for whom use of cannabis is contraindicated.

The Cannabis Buyers' Cooperative Protocols seek to both address these concerns and study more fully the effects of cannabis on emotional and mental disorders.

All persons seeking membership in the Cooperative for treatment of conditions listed in DSM-IV or emotional or mental conditions listed in ICD-9 shall be reviewed by mental health professional after verification by intake staff.

Individuals in whom the use of cannabis is or has been problematic shall be excluded. This group includes persons suffering from cannabis related disorders.

Additionally, other emotional and mental conditions may be worsened by the use of cannabis. Some persons are involved in treatment requiring abstinence from cannabis especially those involved in twelve step recovery programs.

Cases where verification or suitability for the program is in dispute shall be reviewed by a panel of volunteer psychiatrists who will make final determination.

Adverse Effects of Cannabis

As with any drug, cannabis is a tool. There will always be individuals that experience adverse consequences from any drug use. The abuse of cannabis had been recognized for millennia. These problems were described by O'Shaughnessey during his observations in India in 1839 which included references in the Persian medical literature. With widespread non medical use of the drug for the past thirty years, psychiatrists have developed classifications of cannabis presented in the latest Diagnostic and Statistical Manual, Revision IV (DSM-IV).

Intoxication/Overdose

Overdose is most common by the oral route since the time from taking the drug until the experience of effects begin is from one to three or more hours. Inexperienced and ignorant first time users will have an unforgettable experience.

The effects of overdose have been numerously described in general, clinical, and scientific literature. Cannabis overdose comprises the majority of listings in the Surgeon General's list, 19th century precursor of the Indicus Medicus. American literary accounts in books: FizHugh Ludlows Hashish Eater and an essay on Hashish by Victor Robinson M.D are expressly devoted to cannabis. Descriptions of experience with the drug as part of travel to areas of indigenous use may be found in English and European literature over the past three centuries. Scientific and medical descriptions of effects of cannabis overdose have been numerous extensive. Before and after its removal in 1937.
The effects of overdose are from the stimulation and sedation of the central nervous system. Stimulation with a flooding of ideas and images that are vivid and rapidly changing. Attention and concentration are markedly impaired. Time perception is significantly altered with minutes seeming like hours. There may be distortion of spatial perception. Secondary physical effects, aside from a speeding up of the heart rate is generally no more than that associated with mild to moderate exercise.

Cannabis-Induced Disorders
292.89 Cannabis Intoxication

A. Recent use of cannabis.
B. Clinically significant maladaptive behavior or psychological changes (e.g. impaired motor coordination, euphoria, anxiety, sensation of slowed time, impaired judgment, social withdrawal) that developed during, or shortly after, cannabis use.
C. Two (or more) of the following signs, developing within 2 hours of cannabis use: (1) conjunctivae injection (2) increased appetite (3) dry mouth (4) tachycardia.
D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.

E. Specify if:
With Perceptual Disturbances: This specifier may be noted when hallucinations with intact reality testing or auditory, visual, or tactile illusions occur in the absence of delirium. Intact reality testing means that the person knows that the hallucinations are induced by the substance and do not represent external reality. When hallucinations occur in the absence of intact reality testing, a diagnosis of Substance-Induced Psychotic Disorder, with Hallucinations should be considered.

292.81 Cannabis Intoxication Delirium
292.11 Cannabis-Induced Psychotic Disorder, With Delusions Specify if with onset during intoxication.
292.89 Cannabis-Induced Anxiety Disorder, Specify if: with onset during Intoxication.

Continuing or chronic use.
Use or abuse? Cannabis, like any other drug, is a tool. Properly utilized with realistic expectations and awareness of its properties, cannabis is a safe and effective medicine. Improperly used with unrealistic expectations and ignorance, adverse effects may result. The onset of unwanted effects may be obvious or insidious. The general etiology is some emotional discomfort for which cannabis is taken to relieve producing undesirable consequences from using the drug itself.
Paranoia and delusional thinking are not uncommon effects of cannabis both acute and chronically. In the acute experience it appears to be from the perceptual distortions of space, time and feelings of detachment.
In chronic use paranoid and delusional thinking appear to be the consequences of the suppression of feelings, the dulling of feelings may alienate the cannabis users from others by diminishing empathetic capabilities. This emotional insensitivity then results in conflict through misperception. Misperception results from the dulling of affect that is important contextual collateral information source. An effective relief of emotional distress then becomes an impediment to relationships with the cannabis user. Feelings are an integral dimension of social perception that convey important contextual information. Cannabis, as an effective sedative and antidepressant, has this undesirable side effect when misused. The relief afforded by the drug may be paid for by complications caused by avoiding dealing with the causes of the emotional pain as well as diminished functioning while under its influence.
Cognitive impairment by continuing or overuse of cannabis creates a form of mild dementia that may persist for up to several weeks after discontinuing the drug.

Individuals sensitive to the drug report a persistent " hangover" that diminishes the ability to pay attention and concentrate. The onset may be insidious, subtle, and gradual. This condition is reversible with abstinence from cannabis.

304.30 Cannabis Dependence

A maladaptive pattern of cannabis use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the same 12 month period:

(1) tolerance, as defined by either of the following;
   (a) a need for markedly increased amounts of the substance to achieve intoxication or desired effect.
   (b) markedly diminished by either of the following;
(2) withdrawal, as manifested by either of the following:
   (a) the characteristic withdrawal syndrome for the substance.
   (b) the same (or a closely related) substance is take to relieve or avoid withdrawal symptoms.
(3) cannabis is often taken in larger amounts or over a longer period than was intended.
(4) there is a persistent desire or unsuccessful efforts to cut down or control cannabis use.
(5) a great deal of time is spent in activities necessary to obtain cannabis (e.g. visiting multiple dealers or driving long distances), use the substance (e.g. chain smoking) or recover from its effects
(6) important social, occupational, or recreational activities are given up or reduced because of cannabis use
(7) cannabis use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been cause or exacerbated by the substance.

305.20 Cannabis Abuse

A. Maladaptive pattern of cannabis use leading to clinically significant impairment or distress, as manifested by one (or more) of the following, occurring within a 12 month period:

1) recurrent cannabis use resulting in a failure to fulfill major role obligations at work, school, or home (e.g. repeated absences or poor work performance related to substance use; cannabis related absences, suspensions, or expulsions from school; neglect of children or household)
2) recurrent cannabis use in situations in which it is physically hazardous (e.g. driving an automobile or operating a machine when impaired by cannabis use)
3) recurrent cannabis related legal problems (e.g. arrests for cannabis relate disorderly conduct)

4) continued cannabis use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance (e.g. arguments with spouse about consequences of intoxication, forgotten promises)

B. The symptoms have never met the criteria for Cannabis Dependence for this class of substance.

232.9 Cannabis Related Disorder not Otherwise Specified

The Cannabis Related not Otherwise Specified category is for disorders associated with the use of cannabis that are not classifiable as one of the disorders listed above.

Ex. E

OAKLAND CANNABIS BUYERS' COOPERATIVE

Compassion

INFORMATION FORM
(Please print clearly)

Name_____

Street Address _____Apt. Number_____

City _____, State_____ Zip Code_____

Phone Number (_____)_____Date of Birth_____

Driver License #_____State_____ Gender (M or F)____

Caregiver_____DL#_____DOB_____

Physician's Name _____DX #_____

Address, City, State _____PHD#_____

Phone (_____)_____

Specific Diagnosis _____

_____ ICD9 CODE_____

Medication(s)_____

_____

How do you use cannabis? Smoke hi grade___smoke lo grade___edibles___tisture__

Are you politically active?_____

_____ _____

Member Signature Date

_____ _____

Intake By Member #

OAKLAND CANNABIS BUYERS' COOPERATIVE, P.O. Box 70401 Oakland, CA 94612-0401
Phone (510) 832-5346 Fax (510) 986-0534 Email ocbc@ocbc.org Web www.ocbc.org

Ex. F

OAKLAND CANNABIS BUYERS' COOPERATIVE

Authorization for Release of Patient Status
(Please print clearly)

I,_____ hereby authorize my treating physician,
print patient name

Dr._____ to release to the Oakland Cannabis
print physician name
Buyers' Cooperative, my current patient status.

_____ Date _____
Member/ patient signature

Membership number_____

OAKLAND CANNABIS BUYERS' COOPERATIVE, P.O. Box 70401 Oakland, CA 94612-0401
Phone (510) 832-5346 Fax (510) 986-0534 Email ocbc@rocbc.org Web www.rocbc.org

Ex. G

Health and Safety Code 11362.5
PHYSICIAN'S STATEMENT

This certifies that _____ is a patient under my
print patient's name

medical care and supervision for the treatment of _____.
Diagnosis

I have discussed the medical benefits and risks of cannabis use with the patient as a treatment for these medical conditions. I recommend cannabis use for my patient.

If my patient chooses to use cannabis therapeutically, I will continue to monitor his/her medical condition and to provide advice on his/her progress.

I understand that I may be contacted to verify the information in this letter. My patient authorizes me to discuss their medical condition and the contents of this letter, for verification purposes only. I am a physician licensed to practice medicine in the state of California.

_____
Patient's Signature

_____ _____
Physician's Signature Date

_____ _____
Physician's Name (print) N.P./P.A. Signature (optional)

_____ _____
Physician CA License No. N.P./P.A. Name (optional-print)

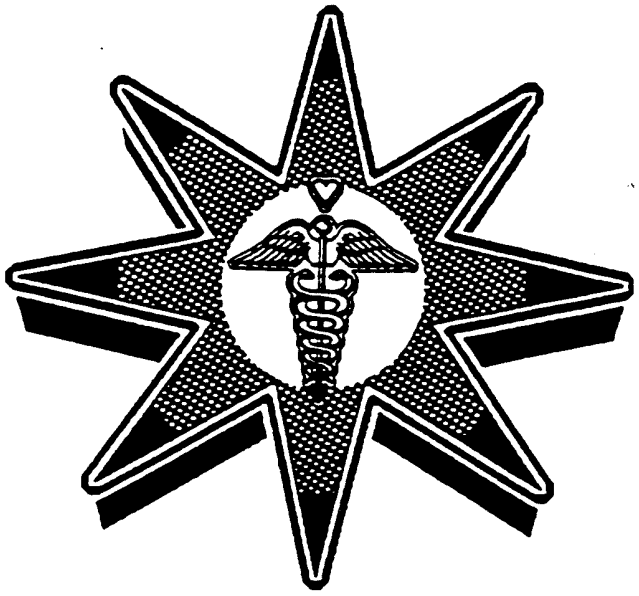
_____
(street)

_____
(City)

( )_____
Phone Number

Oakland Cannabis buyers' Cooperative

Ex. H



Compassion

Officer- This crop of medical herb is being grown in its entirety for my personal medical use, and is intended to be free of toxic chemical, fungus, and mold contamination. This crop is safe for use by people with HIV/AIDS and other patients. Any excess will be given to the Oakland Cannabis Buyers' Cooperative. Thank you for your courage and care. If there are any questions regarding this garden please call 1-888-304-1260 (law enforcement use only).

_____

Name, Grower
Oakland Cannabis Buyers' Cooperative

_____

Jeffrey W. Jones
Agent of Oakland Cannabis Buyers' Cooperative

OAKLAND CANNABIS BUYERS' COOPERATIVE, P.O. Box 70401 Oakland, CA 94612-0401
Phone (510) 832-5346 Fax (510) 986-0534 Email ocbc@rvcbc.org Web www.rvcbc.org

Ex. I

OAKLAND CANNABIS BUYERS' COOPERATIVE

Membership and Informed Consent

Compassion

I, (print clearly)_____, hereby consent to the benefits provided by the Oakland Cannabis Buyers' Co-op (OCBC).

I understand that the OCBC has made no efforts in encouraging me to produce or use any substances for my medical condition. I have been informed by an authorized representative of OCBC that I should continue to seek professional medical advice prior to and during my use of any cannabis product I may acquire through OCBC.

I understand that the OCBC was organized to fill the necessity of medical cannabis. Prompting the passing of the Oakland City Council Resolution Number 72516 C.M.S. which supports the OCBC operations. I further understand that circumstances may require defense of authorization in a court of law and agree to participate in such defense to the extent necessary and practicable.

I understand that the OCBC reserves the right to refuse service(s) to members.

I affirm that I am above eighteen (18) years of age or have the consent of my parent/guardian, and that I have a medical condition(s) as attested to on my information form.

I understand that my contributions to OCBC, through products I may acquire from the organization, are used to insure continued operation of the OCBC and that this transaction, in no way, constitutes commercial promotion.

I understand that medical marijuana, while being a well-known effective therapeutic agent, is still illegal in this country. Therefore, by signing this form, all members of OCBC are committing an act of collective Federal civil resistance.

I authorize the OCBC to acknowledge the fact of my membership, when needed, for the preservation of my medical rights under the Oakland Resolution # 72516 and the Compassionate use Act of 1996.

_____ _____

Member Signature Date

_____ _____

Intake By Member #

OAKLAND CANNABIS BUYERS' COOPERATIVE, P.O. Box 70401 Oakland, CA 94612-0401
Phone (510) 832-5346 Fax (510) 986-0534 Email ocbc@ocbc.org Web www.ocbc.org

Ex. J

Oakland Cannabis Buyers' Cooperative

Compassion

Shawn Malvo

222 Anyplace

Oakland CA 94612

CDL: XXXXXXXXXXX

DOB: 12/05/65

ISSUE DATE:10/24/97 Member # 167

Certificate of Membership

This is to certify that on file with the undersigned officer of the Oakland Cannabis Buyers' Cooperative is a signed statement of a licensed Physician ackowledging and assenting to cannabis therapy for the patient identified on the reverse hereof, who, having satisfied all conditions of membership, is recognized as a Member in good standing of the

Oakland Cannabis Buyers' Cooperative

with all benefits and subject to all conditions as same shall from time to time be established by the Oakland CBC in accordance with its rules and Protocols. Presentation of this card shall be evidence that said patient's Physician would consider prescribing cannabis if he/she were legally able to do so, assents to the theraputic use, and has agreed to monitor and provide medical advice on the patient's progress.

Hours: M & F 11am - 7pm T, W, TH 11am - 1pm, 5pm - 7pm

Office # (510) 832-5346

24 hr Emergency voicemail/pager service (for Law Enforcement use only) 1-888-340-1260.

[redacted]

Jeffrey W. Jones
Executive Director

ER1398

Ex. K

Safe Use of Cannabis
1996 Tod H. Mikuriva, M.D.

Dosage and Route of Administration

Starting with a small amount and gradually increasing the dose is the key to avoiding unwanted mental side effects. This is called titration- self-titration if adjusted by the user.

Mental Effect Impatience and overdosing with oral cannabis is the most frequent mention of the drug in medical literature of the 1800's. Oral cannabis over-dosage is much more intense and longer lasting than from the inhaled route. Because of the two to three hours before onset of effects, a common mistake of the inexperienced is to repeat the oral dose with the consequence of overdosing.

Over-dosage

Should you take too much cannabis you may expect the mental effects of time distortion, racing thoughts, disorientation, speeding heart rate, dry mouth, and reddened eyes. The greater the dose, the greater intensity and longer these stimulant effects will last before sinking into a deep sleep. No lasting harm will result but the experience will not be forgotten.

Other Adverse Effects

Other adverse mental effects are a prolonged dullness after use of paranoia and a fear of loss of control. Cannabis, an effective relaxant, can cause an alienation or detachment. The price of relief of tension may be a dulling or suppression of feelings. Insensitivity to feelings of other or situations may result.

Set and Setting

The result of the drug is a combination of set (expectations), setting, personality, and the drug.

Best case: Enjoying a puff or two sitting at home with a friend at the end of the day.
Worst case: Taking a puff driving down the freeway, then looking sideways into the eyes of a cop.

Personality and Individual Difference

Individuals with personalities that are prone to substance abuse, allergy, sensitivity, or adverse reactions to other medicines should exert greater caution and try the drug only if absolutely necessary

Dependence and Withdrawal

Because cannabis is such an effective medicine for the relief of many uncomfortable conditions, using the
drug on a continuing basis is not uncommon. One must decide issues of personal risks/benefits of continuing using cannabis.

Withdrawal from chronic cannabis use produces several nights of more intense dreaming and possibly some slightly increased nervousness during the day. Some increased nervousness during the day. Some increase in exercise, if possible, and/or small amounts of other sedatives will ease the transition from cannabis dependence.

Ex. L

Principals of Responsible Cannabis Use

I. No Driving

The responsible consumer of cannabis does not operate a motor vehicle or other dangerous machinery while impaired by cannabis or - like other responsible citizens-any other substance or condition, including some medicines and fatigue. Although cannabis is said by most experts to be safer than many prescription drugs, responsible cannabis users never operate motor vehicles in an impaired condition. Public safety demands not only that impaired drivers be taken off the road, but also that objective measures of impairment other than chemical testing be developed and used.

II. Set and Setting

The responsible cannabis user will carefully consider his or her set and setting, regulating use accordingly. "Set" refers to the consumer's values, attitudes, experience and personality. "Setting" means the consumer's physical and social circumstances. The responsible cannabis consumer will be vigilant as to conditions-time, place, mood, etc- and should not hesitate to say no when those conditions are not conducive to a safe, pleasant and/or productive experience.

III. Resist Abuse

Use of cannabis to the extent that it impairs health, personal development or achievement is abuse, is resisted by responsible cannabis users. Abuse means harm. Some cannabis use is harmful; most is not. That which is harmful should be discouraged; that which is not, need not be. Wars have been waged in the name of eradicating "drug abuse," but instead of focusing on abuse, enforcement measures have been diluted by targeting all drug use, whether abusive or not. If Marijuana abuse is to be targeted, it is essential that clear standards be developed to identify it.

IV. Respect Other's Rights

The responsible cannabis user does not violate the rights of others, observes accepted standards of courtesy and propriety and respects the preferences of those who wish to avoid cannabis entirely. No one may violate the rights of others, and no substance use excuses any such violation. Regardless of the cannabis' legal status, responsible users will adhere to emerging tobacco smoking protocols in public and private places.

EXHIBIT 4

OAKLAND CANNABIS BUYERS' COOPERATIVE
STATEMENT OF CONDITIONS

On May 19, 1998, United States District Judge Charles R. Breyer issued a preliminary injunction enjoining the Oakland Cannabis Buyers' Cooperative from engaging in the distribution of marijuana in violation of federal law. The Oakland Cannabis Buyers' Cooperative would like to assure all Members that the Cooperative will continue to operate in the good faith belief that it is not engaging in the distribution of cannabis in violation of law. Federal law excludes from the definition of "distribution" the joint purchase and sharing of controlled substances by users. As a Member of the Oakland Cannabis Buyers' Cooperative, you are a joint participant in a cooperative effort to obtain and share medical cannabis. Each transaction in which you participate is not a "sale" or "distribution," but a sharing of jointly obtained medical cannabis. If you make a payment to the Cooperative such payment is a reimbursement for administrative expenses and operations, which all Members who utilize the services of the Cooperative agree to share.

The medical cannabis, shared among the Members of the Cooperative may only be used by you for the medical purposes approved or recomended by your physician. Federal law recognizes that the sharing and use of cannabis is justified by medical necessity when reasonable alternatives are not available. At the present time, federal authorities refuse to enroll any additional patients in the federal program for the medical use of cannabis.

EXHIBIT 5

CITY OF OAKLAND

CITY HALL · ONE CITY HALL PLAZA · OAKLAND, CALIFORNIA 94612

Office of City Manager
Robert C. Bobb
City Manager

(510) 238-3301
FAX (510) 238-2223
TTY/TDD (510) 238-3724

August 11, 1998

Mr. Jeff Jones
Executive Director
Oakland Cannabis Buyers' Cooperative
1755 Broadway, Suite 300
Oakland, CA 94612

Dear Mr. Jones:

Pursuant to Chapter 8.42 of the Oakland Municipal Code, the City hereby designates the Oakland Cannabis Buyers Club to administer the City's Medical Cannabis Distribution Program. The designation is subject to the cooperative's agreement to comply with the terms and conditions attached hereto as Exhibit A which hereby are incorporated by reference in this letter as if set forth in full herein.

The designation shall be effective upon the Oakland Cannabis Buyers' Cooperative's acceptance and agreement to the terms and conditions in Exhibit A. Please confirm the Oakland Cannabis Buyers' Cooperative's agreement to comply with the terms and conditions in Exhibit A by signing below.

Very truly yours,

for Robert C. Bobb
City Manager

SO AGREED:

Jeff Jones Date: 8/12/98
Jeff Jones
Executive Director
Oakland Cannabis Buyers' Cooperative

ER1406

EXHIBIT A[1]

"WHEREAS, on July 28, 1998 the City of Oakland ("City") added Chapter 8.42 of the Oakland Municipal Code entitled, "Medical Cannabis" ("Chapter 8.42); and

WHEREAS, Chapter 8.42 establishes a City Medical Cannabis Distribution Program to be administered by medical cannabis provider associations designated by the City Manager; and

WHEREAS, consistent with the intent of Proposition 215 (the Compassionate Use Act of 1996, Health and Safety Code section 11362.5), the purpose of the City's program is to ensure that seriously ill Californians have the right to obtain and use marijuana for medical purposes when such medical use is recommended by a physician; and

WHEREAS, designation of one or more medical cannabis provider associations to administer a well-organized, safe medical cannabis distribution program in accordance with the requirements of Health and Safety Code section 11362.5 will preserve public health and safety by discouraging a market of street narcotic peddlers who desire to prey upon Oakland's ill residents whose painful symptoms are alleviated by ingestion of cannabis; and

WHEREAS, the City has designated the Oakland Cannabis Buyers' Cooperative ("Medical Cannabis Provider Association") to distribute cannabis to patients and primary caregivers who satisfy the requirements of Health and Safety Code section 11362.5

NOW THEREFORE, in consideration of the City's designation of Medical Cannabis Provider Association by the City Manager to administer the City's medical cannabis distribution program, the association agrees to comply with the following terms and conditions:

1. Compliance with Applicable Laws and Administrative Procedures

Medical Cannabis Provider Association agrees to comply with the requirements of Health and Safety Code section 11362.5, Chapter 8.42 of the Oakland Municipal Code and to comply with the administrative procedures and requirements established by the City as they may be amended from time to time.

2. Indemnification

The Medical Cannabis Provider Association agrees to save, indemnify, defend and hold harmless, City, its Councilmembers, directors, officers, agents and employees from any and all claims, losses and expenses (including reasonable attorney's fees) or liability on account of damage of property or injury to or death of persons accruing or resulting to Medical Cannabis Provider Association, Medical Cannabis Provider Association's directors, agents, employees, contractors, material persons, laborers and any other person, firm or corporation furnishing or supplying work, services, materials or supplies in connection with the Medical Cannabis Provider Association's designation as the City's agent to administer and the Medical Cannabis Provider Association's administration of the City's Medical Cannabis Distribution Program; and from any and all claims and losses accruing or resulting to any person, firm or corporation who may be injured or damaged in connection with the Medical Cannabis Provider Association's administration of the City's Medical Cannabis Distribution Program as the City's designee.

[1] This document is Exhibit A to the August 11, 1998 letter from the City Manager designating Oakland Cannabis Buyers' Cooperative to administer the City's Medical Cannabis Distribution Program.

JWJ

MAN

3. Insurance

Medical Cannabis Provider Association shall procure and keep in force for the duration of its designation as a Medical Cannabis Provider Association, at Medical Cannabis Provider Association's own cost and expense, such policies of insurance or certificates or binders as required by the City's Risk Manager to represent that coverage is in place with companies doing business in California and acceptable to City. Medical Cannabis Provider Association shall provide City with copies of all insurance policies. Medical Cannabis Provider Association shall, "pending acceptance" of insurance, supply and furnish City with information, such as certificates or binders, showing such insurance policies are in force with the written undertaking of each insurer shall give City thirty (30) days prior written notice of any cancellation, termination or material change of such insurance coverage. The insurance shall at a minimum include all that is required by the City's Risk Manager in accordance with Section 4 of Chapter 8.42 of the Oakland Municipal Code.

In the case of the breach of any of the insurance provisions of this Agreement, City may, at City's option, take out and maintain at the expense of Medical Cannabis Provider Association, such insurance in the name of Medical Cannabis Provider Association as is required pursuant to this Agreement, and may deduct the cost of taking out and maintaining such insurance from any sums which may be found or become due to Medical Cannabis Provider Association under this Agreement.

4. Audit

Medical Cannabis Provider Association shall permit City and its authorized representatives to have access to Medical Cannabis Provider Association's books, records, accounts and any and all data relevant to this Agreement and/or the association's administration of the City's Medical Cannabis Distribution Program, for the purpose of making an audit or examination for the period commencing on the date the Medical Cannabis Provider Association was designated by the City Manager to administer the City's Medical Cannabis Distribution Program and ending four years after the designation is revoked. Any audit or examination under this section shall be deemed privileged and confidential in accordance with Section 6 of Chapter 8.42 of the Oakland Municipal Code. All such audits or examinations shall be carried out by appropriate personnel (e.g. physicians, nurses, accountants, bookkeepers and auditors) for the sole purpose of determining designee's compliance with the provisions of this exhibit.

5. Revocation of Designation

The Medical Cannabis Provider Association understands and agrees that the City may revoke the designation of the association to administer the City's Medical Cannabis Distribution Program at any time based on the City's sole judgment and discretion.

6. Reports, Information

Medical Cannabis Provider Association shall provide all reports and information reasonably requested by the City and shall immediately advise the City Manager of any complaints communicated to Medical Cannabis Provider Association, its directors, agents and/or employees and of any contacts by law enforcement personnel or agencies.

7. Standard of Performance

Medical Cannabis Provider Association shall administer the City's Medical Cannabis Distribution Program in accordance with the requirements of Health and Safety Code section 11362.5, the City's administrative procedures and requirements as they may be amended from time to time, the protocols, uniform conditions, rules and regulations and procedures appended hereto as Appendix 1.

8. Access to Premises, Inventory, Supplies, etc.

Medical Cannabis Provider Association shall provide the City Manager, or a member of his staff, access to the premises of its operations for the purpose of inspections, quality control investigations and monitoring with or without notice during normal hours of operation. Nothing in this section shall be construed to substitute for the requirements of reasonable suspicion and or probable cause for law enforcement action.

9. Effective Date

The terms and conditions set forth herein shall be effective and binding upon the Medical Cannabis Provider Association as of the date that the Medical Cannabis Provider Association is designated by the City as its agent to administer the City's Medical Cannabis Distribution Program and shall remain in full force and effect until such designation is revoked by the City or by operation of law.

10. Payment of Income Taxes

Medical Cannabis Provider Association shall be responsible for paying, when due, all income taxes, including estimated taxes, incurred as a result of the administration of the City's Medical Cannabis Distribution Program. Medical Marijuana Provider Association agrees to indemnify City for any claims, costs, losses, fees, penalties, interest or damages suffered by City resulting from its failure to comply with this provision.

11. Non-discrimination

Medical Cannabis Provider Association shall not discriminate or permit discrimination against any person or group of persons in any manner prohibited by federal, state or local laws. Medical Cannabis Provider Association shall not discriminate against any employee, applicant, patient, primary caregiver, contractor, supplier or other person supplying goods or services because of gender, sexual orientation, race, creed, color, national origin, Acquired-immune Deficiency Syndrome, (AIDS), AIDS-Related Complex, or disability.

12. Business Tax Certificate

Medical Cannabis Provider Association shall obtain and provide proof of a valid City business tax certificate. Said certificate must remain valid for the period during which the association is designated by the City Manager to administer the City's Medical Cannabis Distribution Program.

13. Independent Contractor

It is expressly agreed that in administering the City's Medical Cannabis Distribution Program pursuant to the City's designation under Chapter 8.42 of the Oakland Municipal Code, the Medical Cannabis Provider Association is not an employee of the City and is an independent contractor. Medical Cannabis Provider Association has and shall retain the right to exercise full control and supervision over the employment, direction, compensation and discharge of all persons assisting Medical Cannabis Provider Association in administering the City's Medical Cannabis Distribution Program and shall be solely responsible for all matters relating to the payment of its employees, including compliance with social security, withholding and all other regulations governing such matters, and shall be solely responsible for its own acts and those of its subordinates and employees.

JWT 213307v1

MAN

14. Notice to the City

Medical Cannabis Provider Association acknowledges and understands that the City's designation of the association is based on its adherence to the protocols, quality control procedures and uniform conditions appended hereto as Appendix 1. Further, Medical Cannabis Provider Association acknowledges and understands that the City's designation of the association is based in part on the City's knowledge of the current officers and directors of the association. Medical Cannabis Provider Association agrees that it will not change its protocols, procedures, rules and regulations and/or uniform conditions, appended hereto as Appendix 1, without obtaining the prior written consent of the City. Further the Medical Cannabis Provider Association agrees that it will immediately notify the City of any change in the officers and/or directors of the association, its articles of incorporation, bylaws and/or membership fees.

15. Assignment

Medical Cannabis Provider Association shall not assign or otherwise transfer any rights, duties, obligations or interest in this agreement or arising hereunder to any person, person, entity or entities whatsoever without the prior written consent of the City and any attempt to assign or transfer without such prior written consent shall be void. Consent to any single assignment or transfer shall not constitute consent to any further assignment or transfer.

16. Entire Agreement

The terms and conditions of this agreement represent the entire agreement of the parties and supersede any prior agreements of the parties.

- end-

JWJ 213307v1

MAH

APPENDIX 1

MISSION STATEMENT

OAKLAND CANNABIS BUYERS' COOPERATIVE JOB DESCRIPTIONS

1. ADMINISTRATIVE DEPARTMENT
2. INTAKE DEPARTMENT
3. GREEN ROOM AND MEMBER ROOM DEPARTMENT

OAKLAND CANNABIS BUYERS' COOPERATIVE CAREGIVER POLICY

OAKLAND CANNABIS BUYERS' COOPERATIVE QUALITY ASSURANCE PROGRAM

OAKLAND CANNABIS BUYERS' COOPERATIVE SUPPLIER INITIAL QUESTIONNAIRE

1. QUESTIONNAIRE
2. NOT ACCEPTABLE CHEMICALS AND PESTICIDES
3. ACCEPTABLE CHEMICALS AND PESTICIDES

OAKLAND CANNABIS BUYERS' COOPERATIVE QUALITY ASSURANCE CONTRACT

OAKLAND CANNABIS BUYERS' COOPERATIVE PEST CONTROL MEASURES

OAKLAND CANNABIS BUYERS' COOPERATIVE RULES AND POLICIES FOR MEMBERS

OAKLAND CANNABIS BUYERS' COOPERATIVE MEMBER ROOM PROCEDURES

1. OPENING PROCEDURES
2. MEMBER TRANSACTIONS
3. CLOSING PROCEDURES

WEIGHING ROOM STANDARD PROCEDURES

JWJ

MAL

Oakland Cannabis Buyers' Cooperative

Compassion

Mission Statement

The goal of the Oakland Cannabis Buyers' Cooperative (OCBC) is to provide seriously ill patients with a safe and reliable source of medical cannabis products and plants. Our cooperative is open to all patients with a verifiable letter of diagnosis and recommendation or approval for medical cannabis use.

The City of Oakland has enacted an Ordinance to provide immunity for medical cannabis provider associations so that patients can safely obtain their medicine. The Cooperative is dedicated to reducing the harm these patients encounter due to the prohibition of cannabis. This includes alleviating the fear of arrest, as well as negating problems associated with purchasing cannabis on the illicit market.

OCBC's headquarters is a multi-faceted facility, accessible to people with disabilities. We provide a professional atmosphere for patients to procure cannabis, with trained member advocates on hand to offer advice and assistance. We also offer self-help services such as support groups for a wide variety of medical conditions, massage therapy and cultivation meetings to teach Members how to grow their own medicine. The Cooperative once a month has a buffet dinner for all Members and caregivers. Seasonally the Cooperative is involved with activities such as Softball and Bowling. In addition, OCBC provides information on a variety of topics, including AIDS prevention and treatment, safe sex, and cannabis reform in general.

The Oakland CBC currently operates under the auspices of California Proposition 215 now Health and Safety Code Section 11362.5 and Oakland City Council Resolution Numbered 72379 C.M.S. and 72516 C.M.S.

Resolution 72516, passed in March 1996, makes the enforcement of medical cannabis laws the lowest priority for the City of Oakland. Furthermore, the City has appointed a working group to oversee OCBC functions and to determine the most effective means to protect and assist seriously ill patients. Most recently the City has enacted Ordinance Number 12076 setting up a medical cannabis distribution program, which the Oakland Cannabis Buyers' Cooperative hopes to fulfill.

ER1412

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MAN

Oakland Cannabis Buyers' Cooperative

Compassion

Oakland Cannabis Buyers' Cooperative
Job Descriptions

The Oakland Cannabis Buyers' Cooperative has three main departments: Administrative, Intake, Green Room and Member Room.

1. Administrative Department
   A. Executive Director is responsible for all issues and responsibilities to allow the Cooperative to operate on a day to day basis.
   B. Chief Financial Officer is responsible for all financial issues relating to the operation of the Cooperative.
   C. Chief Operating Officer is responsible for the managing of the Green Room and Member Room.
   D. Secretary keeps track of Board minutes and handles other correspondence, and manages security.
   E. Cleaning crew is responsible for making sure the Cooperative office stays clean.

2. Intake Department
   A. Head Nurse is responsible for making sure all intake information is correct and all potential Member's recommendations and approvals have been verified with their doctor's offices.
   B. Assisting Nurse makes sure that all work has been done and has been verified correctly.

3. Green Room and Member Room Department
   A. Managers keep track of inventory and handle staff and Member issues.
   B. Budtenders assist Members in procuring cannabis from the OCBC.
   C. Weighers are responsible for accurately weighing and accounting for all cannabis that is checked in and made available to Members.

ER1413

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Oakland Cannabis Buyers' Cooperative Caregiver Policy

The Cooperative currently has a limited caregiver policy for patients who are bedridden and wheelchair bound or has mobility problems and need assistance with their daily living. The staff nurse approves of caregivers by talking with the Member and reviewing their file to see if in each instance it is needed.

Each caregiver at the threshold of being approved has to provide us with valid form of California ID or License. The caregiver also has to complete a caregiver certificate form. Then the Member will sign it certifying the caregiver to provide care for them.

In order for the caregiver to access our facility the Member will have to:

*Place a phone call to the Cooperative verifying with the receptionist that they are sending in their caregiver. The Member needs to send in a note stating the specific nature of their needs and how much medicine they will need.

*Give their Member ID to the Caregiver or the caregiver has to have Caregiver ID from the Cooperative. In addition to this, we need to have a valid form of ID from the caregiver.

*The caregiver must stop at the front desk to turn in the Member's note and receive pass to be allowed into the Member only room.

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Oakland Cannabis Buyers' Cooperative

Oakland Cannabis Buyers' Cooperative
Quality Assurance Program

The Oakland Cannabis Buyers' Cooperative ensures to the best of its ability that its medical cannabis products are free from molds, fungus, and pesticides. This is because only medical patients who are seriously ill or disabled and have qualified under Health and Safety Code Section 11362.5 have access to the Cooperative's service.

Our Cooperative develops trusting relationships with all the medical cannabis cultivators from whom we receive medicine. This secures that we are not receiving cannabis contaminated by the cultivators spraying with dangerous pesticides or using other chemicals that are not approved for horticultural food purpose.

We have an initial interview with all cultivators and ask questions about how the cannabis was grown and what methods are being used to control bugs. We also ask what other chemicals the cultivators are using to grow with and point out if any are unsafe for human consumption. If the cultivator doesn't qualify by our standards during the initial interview we communicate which cultivation practice must be corrected in order to cultivate cannabis for us.

We try to inspect every facility from which we get cannabis. The things we look for are as follows:

1. What type of insecticide is being used for pest control measures.
2. Other chemicals being used for growing plants.
3. How clean the facility is and if there are any fire, health or safety hazardous.

There are assigned staff members who are allowed to procure medical cannabis for the Members of the Cooperative. Experienced horticulturists that know what to look for and how to identify potentially contaminated cannabis flowers, which could have molds, fungus, or other problems, have trained the assigned staff members. Our policy is that if any of these problems are found we do not accept the product.

We inspect cannabis flowers that are brought into the Cooperative office by three methods:

1. We ask every cultivator a series of questions pertaining to the methods and chemicals used during cultivation.
2. We use a visual inspection, first by eye, throughout the whole sample in question and then look into the midsection of random cannabis flowers in search of molds and abnormal growth. Then, a high magnification jeweler's loupe is used to inspect random cannabis flowers for spores, molds, or abnormal growth.
3. We use a method of smelling the container or bag of cannabis for hints of abnormal smells. This method helps to identify any smell of potentially harmful molds and fungus.

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If the Cooperative staff member finds or is notified of any problems with any medical cannabis product, the product is rejected.

The Cooperative inspects manufacturing facilities where medical cannabis preparations are manufactured. We look for fire, health or safety concerns and cleanliness of the facility. If any issues come up we communicate to the manufacturer that corrections must be made.

Manufactures of medical cannabis edibles and concentrations use standard recipes for preparing each product. Our policy is that if the manufacturer changes or alters this standard they notify us and we test the products before they can be made available at the Cooperative.

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Oakland Cannabis Buyers' Cooperative

Compassion

Oakland Cannabis Buyers' Cooperative
Supplier initial Questionnaire

The list of questions we ask each cultivator and supplier of the Cooperative helps us to identify if the medical cannabis is suitable for medical use. The questions have been designed in a way that we can assure our members safe and quality medical cannabis.

1. What kind of insects or pests have you seen in or around your garden?

2. What kind of pesticides do you use to control pest problems?

3. Have you seen molds or spores on your flowers, if so what is the description?

4. What kind of nutrients or chemicals have you used to complete your harvest?

5. Have you noticed abnormalities in your garden?

6. What kind of water do you use?

Not Acceptable Chemicals and Pesticides:

Avid, Malithion, Only Ornamental approved chemicals, DDT, No Pest-Strip or similar type products.
Absolutely NO systemic type pesticides, this means pesticides that stay in the plant and do not biodegrade readily.

Acceptable Chemicals and Pesticides:

Safer Brand Soap, Pyrethrums, Pepper Spray, Tobacco mixes, Food grade approved chemicals by the State Department of Agriculture.

ER1417

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Oakland Cannabis Buyers' Cooperative

Compassion

Oakland Cannabis Buyers' Cooperative
Quality Assurance Contract

I agree that I have answered all of the questions in the 'Supplier Initial Questionnaire' truthfully and to the best of my knowledge. I understand if I change my current practices in providing medical cannabis products to the Oakland Cannabis Buyers' Cooperative I will notify them of these changes and address any questions at that time.

Supplier	Date	OCBC Staff	Date

ER1418

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MAN

Oakland Cannabis Buyers' Cooperative

Compassion

Oakland Cannabis Buyers' Cooperative

Pest Control Measures

The Oakland Cannabis Buyers Cooperative has an inspection process that is used for new cannabis clones and seedlings brought into the Cooperative for Members. We use a high magnification jeweler's loupe to inspect leaves and other areas of the plants before they are allowed to be checked into the Cooperative Member area. If bugs are found we ask the provider what pest control methods are being used and try to assist them in nontoxic and horticulture approved methods of pest control.

The Cooperative has a weekly, and as needed insect control program for cannabis plants. When bugs are found, all affected leaves are removed and properly disposed of. All remaining leaves are then treated with insecticide and are clearly marked. This means that we do not use the plant in manufacturing for three weeks or we destroy them. We have a policy not to use pyrethrum foggers on flowers. Safer Brand Insecticidal Soap Spray on a weekly basis and as needed to control and eliminate pests from Cooperative gardens. This soap is potassium salt and pyrethrum based and is approved for horticulture food crops by the State Department of Agriculture. Our main insecticide, pyrethrum, breaks down when exposed to light and oxygen. We never use chemicals that have not been horticulture food approved, because all the cannabis we are in contact with is used by seriously ill and disabled patients.

If we have an infestation of bugs we use pyrethrum foggers in closed rooms only after we have closed for business and all employees have left the building. These foggers have the ability to eliminate all insects in the areas that need attention by filling the air with tiny droplets of biodegradable pyrethrum. Early the next day we completely ventilate the area where the insecticide was used.

All methods of insect control using sprays and chemicals are discontinued two to three weeks prior to harvest of cannabis. This ensures the product will be free of insecticides prior to use by patients.

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Oakland Cannabis Buyers' Cooperative

Compassion

Oakland Cannabis Buyers' Cooperative
Rules and policies for Members

If prospective Members are unable to read these rules for any reason, the Cooperative will provide persons to read and explain them; we will assist non-English speaking Members by appointment.

- No in and out privileges allowed; one visit per day per Member / Caregiver.
- Purchases for people other than Cooperative Members are strictly prohibited.
- Members who wish to have their Caregiver pick-up medicine for them must make arrangements in advance.
- Please have Member ID card out and available until cannabis is received, this is for Members' safety and to keep the medicine secure.
- Being under the influence of illicit drugs or alcohol will NOT be tolerated in the Cooperative.
- The procurement of cannabis is limited to ¼ oz (7 grams) per day, unless the member lives outside of the Bay Area and makes not more than one visit to the cooperative per week. We are able to monitor these Members by our purchase tracking system.
- The Oakland Cannabis Buyers' Cooperative reserves the right to refuse service to any Member or Caregiver.
- No rude behavior will be tolerated towards staff or other Members.
- We operate in a smoke free building.
- Members should discourage friends from waiting for them immediately outside the front door of the Oakland CBC, as congestion on the sidewalk could be objectionable to some of our neighbors.
- Complaint Process Form:
  The Cooperative will institute a complaint form in duplicate with one copy going to the complainant and one copy going to the Cooperative.

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Oakland Cannabis Buyers' Cooperative
Member Room Procedures

Opening Procedures

Turn Computer on
-Set up computer

Open windows and turn ventilation units on.

Retrieve inventory from safe and distribute into proper bins at the budbar.
-Verify counts of inventory
-Check what additions to inventory need to be made.

Arrange samples according to price and selection.

Retrieve baked goods from cooler.

Check sundry stock for needed additions.

Clean glass on cases.

Put verified starting till in cash tray and into drawer.

Each morning the manager checks out medical cannabis to the individual weighers and bud inventory for bar from safe.

He then counts and places all cannabis to be used for that day in storage locker until it is ready for use at the restock of the bar.

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Member Transactions

As Members enter the member room and budbar area they must provide their membership card and California identification card to the guard at the door as well as to the budtender.

Members are then invited to smell and visually inspect the various grades of medical cannabis available that day.

After the visual inspection Members will request to see 3.5 or 1.0-gram packages of medicine. Members will then have a selection of 1 or 2 packages to select from.

> *It is a policy at OCBC that Members may only purchase 1/4 ounce (7 grams) per day and only visit the Cooperative one time per day. If a Member lives in a outlying area he or she may purchase up to one and half ounces, provided that the next visit is not within a weeks time.*
>
> *OCBC provides 1.5 grams of cannabis sativa as no cost medicine for Members who are unable to pay. Members may not purchase on the same day as receiving no cost medicine.*

The budtender enters transaction into the computer tracking system, identifying the transaction with the membership number. The transaction is then completed with cash, ATM, or VISA/MC/Discover.

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Closing Procedures

Our hours of operation are:

Monday and Fridays 11am - 7pm
Tuesday, Wednesday, and Thursdays 11am - 1pm and 5pm - 7pm
Saturdays 1pm - 4pm

At the close of each shift the budtender counts and verifies the inventory of medical cannabis and logs it on the shift inventory in and out form.

The ATM and VISA/MC/Discover batch reports, that give a total of all electronic receipts, are printed out. Next a sum query report is printed to show the totals of all goods dispensed that day in dollar amounts. Then a form is printed showing the totals of of all cannabis that was dispensed during that shift. This form designates the type and amount of medical cannabis each member has purchased and allows for accurate tracking and balance of inventory.

All cash and electronic receipts are counted and recorded on proper forms for reconciliation.

All forms are then verified by the shift manager and budtender(s). Forms, cash, and all receipts are then delivered to business office manager, who verifies all revenue counts and submits General Ledger tickets for posting.

All inventory that was checked out is then verified and secured by the manager and placed back into a locked safe.

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Oakland Cannabis Buyers' Cooperative

Compassion

Weighing Room Standard Procedures

1. Receive bulk cannabis from bar manager
   A. Remove paperwork labeled Bud Inventory Sheet.
   B. Weigh bulk on triple beam balance and subtract bag weight, write number on second line of breakdown section of bud inventory sheet (bulk weight quantity/grams). Write date on line one (date given to weigher), Initial line three (weighers signature).
   C. Have staff member check weight and Initial line four (verifier's signature), Notify manager if weight differs significantly from first bulk weight figure. Manager will then research further to find the source of the differing amount.

2. Break down bulk cannabis into small quantities
   A. Turn on electric scale and set mode to grams. Rezero scale with cannabis container on plate. Periodically rezero scale throughout weighing process.
   B. Place bulk cannabis in metal tray. To prevent weight loss due to evaporation only remove small amounts of cannabis from bulk container at one time.
   C. Using ziplock bags that have been prestickered with OCBC labels, weigh cannabis. We use two kinds of bags, sandwich and snack size. The sandwich baggies are used for eighths of an ounce (3.5 grams) and the snack baggies are used for single grams (1.0 grams). Once cannabis has been put into bags they are rolled up to remove excess air and then are sealed.
   D. Unless otherwise specified by manager, make ten-gram bags for every 100 grams of bulk weight. The rest of remaining bulk is made into 3.5-gram bags.
   E. When weighers have to the leave weighing area, they secure cannabis currently checked out to them in a locked cabinet. If the weighing area is empty the room is also locked.
   F. Weighers periodically check cannabis for mold, fungus and other contaminants. If anything abnormal is found the manager is notified. Manager will then eliminate any contaminated product.
   G. Remove obvious unusable material (stems and seeds), set aside until paperwork is reconciled.
   H. Any remaining bulk material left that weighs less than one gram should go into container marked "gratus"(no cost medicine).

3. Repackaging for bar use.
   A. Count individual bags according to size. Place in one-gallon storage bags, fifteen units per bag for mid to high grade, twenty-five for sativas.
   B. Label bags with appropriately colored labels for separating the different varieties of cannabis. Green is for most potent (high grade), white is for mild potency

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(midgrade), orange is for sativa. Labels are filled out completely (bud description, date, quantity of units, and unit weight) and Initialed.

4. Reconcile Bud Inventory Sheet (B.I.S.).
   A. Add up number of grams from labels of sealed one-gallon bags marked grams, and then note on B.I.S. Do the same for eighths and any amounts for procurement or for transfer in bulk between start and finish of weighing process.
   B. Add together bulk remaining figure (Care Packages) to weight of unusable material (stems and seeds). Verify this with staff member and note on B.I.S. in space titled bulk remaining.
   C. Convert number of eight bags to grams (number of units times 3.5), add to number of grams and bulk remaining figures to come up with total grams accounted for figure. Note on B.I.S.
   D. Subtract total grams accounted for from total grams to start. Note this figure as total grams lost in bagging. Inform manager if this figure is excessive. Manager will then research and find the source of the differing amount.
   E. Initial line marked "who weighed the bags."

5. Verifying cannabis packaged for Member procurement.
   A. Once steps one through four are completed, another staff member must verify the count. Weigh room personal will assist each other with this task.
   B. Count number of units in one-gallon bags, check against number on label. If figures agree squeeze excess air out of bag and seal with OCBC labels. Initial label. Repeat until all bags are verified and sealed.
   C. Check number of bags against figures on B.I.S. If figures agree initial line marked "who verified the counts." If figures do not agree, refer to weigher for relabeling and/or correction of paperwork.

6. General Weigh Room Protocol
   A. Clean up workstation after every shift.
   B. Turn off all electrical devices (scales, air purifier, radio)
   C. Lock and secure all doors to weigh room when leaving.

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IN THE UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

UNITED STATES OF AMERICA, Plaintiff, v. CANNABIS CULTIVATOR'S CLUB, et al., Defendants. AND RELATED ACTIONS.	No. C 98-0085 CRB C 98-0086 CRB C 98-0087 CRB C 98-0088 CRB C 98-0089 CRB C 98-0245 CRB **DECLARATION OF JOHN P. MORGAN, M.D.**

I, JOHN P. MORGAN, declare:

1. I am a medical doctor and Professor of Pharmacology at the City University of New York Medical School. I have personal knowledge of the facts stated herein, and if called as a witness, I could and would testify competently as to them.

2. I am co-author of the book entitled "Marijuana Myths, Marijuana Facts—A Review of the Scientific Evidence," published in 1997.

3. Marijuana, also known as cannabis, has many proven medical uses. Medical cannabis reduces nausea and vomiting induced by cancer chemotherapy, stimulates appetite and promotes weight gain in AIDS patients, reduces intraocular pressure in people suffering from glaucoma, reduces muscle spasticity in patients with neurological disorders, spinal cord injuries, and multiple sclerosis. Furthermore, patients and physicians have reported that smoked marijuana also provides relief from migraine headaches, depression, seizures, and pain.

4. Recent studies have shown that cannabinoids may also be useful for other neurological disorders, such as stroke.

5. There are no reasonable legal alternatives to medical cannabis for many patients. Delta-9-THC is the main active ingredient in marijuana. While synthetic THC is available in capsule form, it is not nearly as effective as smoked marijuana for many patients. For people suffering from nausea and vomiting, who are unable to swallow and hold down a pill, smoking marijuana is often the only reliable way to deliver THC to the body. Smoking marijuana delivers THC quickly, providing relief in a few minutes, compared to an hour or more when THC is swallowed.

6. Smoking marijuana not only delivers THC to the bloodstream more quickly than swallowing synthetic THC, but smoking delivers most of the THC inhaled. When synthetic THC is swallowed, 90 percent or more of it never reaches sites of activity in the body as a result of the body's extensive metabolism of swallowed THC.

7. Another problem with swallowed THC is that its effects vary considerably, both from one person to another and in the same person from one episode of use to another. Further, because the onset of effect is an hour or more, patients using synthetic THC have difficulty achieving just the effective dose. Moreover, when THC is swallowed, the effects last longer (up to six hours) compared

to one or two hours when marijuana is smoked. Thus, smoking marijuana is a more flexible route of administration than swallowing because smoking allows patients to adjust their dose to coincide with the rise and fall of symptoms. For people suffering from nausea and vomiting from AIDS or cancer chemotherapy, smoked marijuana provides rapid relief with lower overall doses of THC.

8. The psychoactive side effects of swallowed synthetic THC may be more intense than those that occur from smoking, thereby increasing the likelihood of adverse psychological reactions. This occurs because the liver actually produces, in high concentration, an active metabolite.

9. Smoking is a highly unusual way to administer a drug. Many drugs could be smoked, but there is no good reason to do so because oral preparations produce adequate blood concentrations. This is not the case with THC. Inhaling is a better route of administration than swallowing. Inhaling is about equal in efficiency to intravenous injection, and considerably more practical.

10. "Cannabis buyers' cooperatives" are the best and safest way for patients to obtain medical cannabis. Patients who rely on the criminal street markets to obtain marijuana necessarily acquire cannabis of unknown potency and purity. For example, marijuana purchased from a street dealer may contain fungal spores, which may be deadly for AIDS patients who have suppressed immune systems. As a result of the dangers of obtaining marijuana from the criminal market, some patients who need the drug may choose to forego their medication.

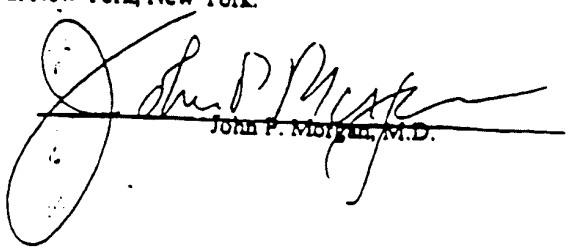
11. The Drug Enforcement Administration's own administrative law judge, Francis L. Young, concluded not only that marijuana's medical utility had been adequately demonstrated by the evidence, but that marijuana had been shown to be "one of the safest therapeutically active substances known to man." The DEA administrator ignored this opinion when he decided to maintain marijuana as a Schedule I drug.

12. For many patients medical cannabis is necessary to avert imminent and often life-threatening harm. For many patients, such as those undergoing intensive chemotherapy or experiencing AIDS-related "wasting syndrome," medical cannabis saves their lives. For patients

suffering from glaucoma, medical cannabis may save their vision. For patients suffering neurological disorders resulting from spinal cord injuries and multiple sclerosis, medical cannabis may enable them to physically cope in society, to go on with their lives and to endure pain.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct.

Executed this 13th day of August at New York, New York.



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OAKLAND CANNABIS BUYERS'
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IN THE UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

UNITED STATES OF AMERICA,

Plaintiff,

v.

CANNABIS CULTIVATOR'S CLUB, et al.,

Defendants.

AND RELATED ACTIONS.

Nos. C 98-00085 CRB
C 98-00086 CRB
C 98-00087 CRB
C 98-00088 CRB
C 98-00089 CRB
C 98-00245 CRB

DECLARATION OF DAVID SANDERS

I, DAVID SANDERS, declare as follows:

1. My name is David C. Sanders. I am over the age of 21, am of sound mind, and am competent to testify to the matters stated herein.

2. I am a member of the Oakland Cannabis Buyers' Cooperative. I have AIDS. My physician has recommended that I use medical cannabis. It works when nothing else does work at alleviating some of my symptoms.

3. I was not present at any press conference on May 21, 1998. Although I was scheduled to be at the Cooperative's offices that day to appear at a press conference, I suffer from a serious life-threatening illness, complications from which prevented me attending the event.

I declare under penalty of perjury that the foregoing is true and correct to the best of my knowledge.

Executed this 11th day of August, 1998, in Oakland, California.

David C. Sanders

David Sanders

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OAKLAND CANNABIS BUYERS'
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IN THE UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

UNITED STATES OF AMERICA,

Plaintiff,

v.

CANNABIS CULTIVATOR'S CLUB, et al.,

Defendants.

AND RELATED ACTIONS.

No. C 98-00085 CRB
C 98-00086 CRB
C 98-00087 CRB
C 98-00088 CRB
C 98 00089 CRB
C 98 00245 CRB

DECLARATION OF ANDREW A. STECKLER IN SUPPORT OF DEFENDANTS' RESPONSE TO SHOW CAUSE ORDER IN CASE NO. C 98-0088 CRB

Date: September 28, 1998
Time: 2:30 p.m.
Courtroom: 8
Hon. Charles R. Breyer

I, ANDREW A. STECKLER, declare:

1. I am a member of the bar of the State of California, and an associate at the law firm of Morrison & Foerster LLP, and represent defendants Jeffrey Jones and the Oakland Cannabis Buyers' Cooperative in this matter. I have personal knowledge of the facts stated herein, and if called as a witness, I could and would testify competently as to them.

2. Attached hereto as Exhibit A is a true and correct copy of the Report of Investigation of Peter A. Ott dated 5/21/98.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct.

Executed this 14th day of September, 1998, at San Francisco, California.

ANDREW A. STECKLER

EXHIBIT A

U.S. Department of Justice
Drug Enforcement Administration

REPORT OF INVESTIGATION

1. Program Code	2. Cross File / Related Files	3. File No.	4. G-DEP Identifier
n/a	☑ [redacted]	[redacted]	[redacted]
5. By: Peter A. Ott, S/A At: San Francisco DO		6. File Title [redacted]	
7. ☐ Closed ☐ Requested Action Completed ☐ Action Requested By:		8. Date Prepared 5/21/98	

9. Other Officers: S/A Mark Nelson

10. Report Re: Undercover and Surveillance of the OAKLAND CANNABIS BUYERS CLUB on 05/21/98

DETAILS

1. Reference is made to all previous ROI's under this investigation.

2. On May 21, 1998, at approximately 11:00 a.m., S/A's Peter Ott, Dean Arnold, Mark Nelson, and Bill Nyfeler set up surveillance in the immediate vicinity of the OAKLAND CANNABIS BUYERS CLUB located at 1755 Broadway Oakland, Ca.

3. The above agents observed individuals entering into the building that contains the OAKLAND CANNABIS BUYERS CLUB. The agents also observed numerous television news vans parked in front of the building.

4. At approximately 11:10 a.m., S/A's Ott and Nyfeler entered into the building. Both of the agents produced their identification when asked from a security guard. S/A Ott produced his undercover California Drivers' License. S/A Nyfeler produced DEA exhibit #N100, an OAKLAND CANNABIS BUYERS CLUB card #1107. Subsequently, both of the agents entered into the club on the third floor.

5. S/A Ott again produced his identification when asked by a second security guard on the third floor. The security guard allowed S/A Ott to enter the club. S/A Ott observed no less than six television crew teams taking statements and video tape of members purchasing marijuana over the counter from employees. S/A Ott also observed ten over the counter sales of marijuana to individuals. S/A Ott observed one individual purchase marijuana and begin to roll a marijuana cigarette.

11. Distribution:	12. Signature (Agent)	13. Date
Division [redacted]	Peter A. Ott	05/21/98
District	14. Approved (Name and Title)	15. Date
Other	Dale W. Sheppard	05/21/98

DEA Form -6 (Aug. 1994)
PAO

DEA SENSITIVE
Drug Enforcement Administration

1-Prosecutor

REPORT OF INVESTIGATION (Continuation)	1. File No. [redacted]	2. G-DEP Identifier [redacted]
	3. File Title [redacted]	
4. Page 2 of 2		
5. Program Code n/a	6. Date Prepared 5/21/98	

6. At approximately 11:20 a.m., while S/A Ott was waiting in the room designated for the press conference, an individual yelled into the press room that a DEA agent was in the club. Shortly thereafter, OAKLAND CBC Director Jeff JONES came into the press room and yelled to the media personnel that a DEA agent was discovered. The media personnel emptied the room and went to the elevator to where S/A Nyfeler was standing and attempting to depart the club.

7. S/A Ott walked to the elevator and stood next to S/A Nyfeler for safety purposes. The media and employees began yelling at S/A Nyfeler and refused to allow S/A Nyfeler to depart by keeping cameras jammed into the elevator door. The media personnel then began asking questions and continued to block the agents from departing. After approximately five minutes from when S/A Nyfeler's presence being known, the media and employees allowed the elevator door to close.

8. At approximately 11:25 a.m., the agents departed the club.

INDEXING

[redacted]

IN THE UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

UNITED STATES OF AMERICA,

Plaintiff,

v.

CANNABIS CULTIVATOR'S CLUB, et al.,

Defendants.

AND RELATED ACTIONS.

No. C 98-00085 CRB
C 98-00086 CRB
C 98-00087 CRB
C 98-00088 CRB
C 98 00089 CRB
C 98 00245 CRB

DECLARATION OF HAROLD SWEET

I, HAROLD SWEET, declare:

1. I am a patient-member of the Oakland Cannabis Buyers' Cooperative (the "Cooperative"). I have personal knowledge of the facts stated herein, and if called as a witness, I could and would testify competently as to them.

2. I am a retired school teacher. I taught botany and biology in a junior college. I am sixty-four years old. I suffer from glaucoma.

3. I was first diagnosed with glaucoma in 1994. At that time my field of vision was deteriorating rapidly. Also, I experienced intense pain from the build up of pressure in my eyes. I also experienced pain when I was exposed to bright lights. I often had to go lie down in a dark room just to try to escape the pain.

4. Prior to my eye disease, I was never an illicit drug user or somebody who used marijuana. Personally, I have actually always been opposed to the so-called "pot-heads" in our society.

5. Since my glaucoma diagnosis I have been taking medical cannabis for my condition. This medicine has worked wonders. First, the medical cannabis keeps my eye pressure down. When I medicate with cannabis, the pain goes away, and I no longer experience intense pain from bright lights.

6. Second, much to my doctor's amazement, not only has my field of vision not deteriorated any further since I have been medicating with cannabis, but it may have even improved. Also, my doctor has told me that my optic nerve is in good shape. I attribute this to the cannabis treatment.

7. There is a very strong possibility that I would be blind if I did not take cannabis for my glaucoma.

8. Though I have tried other drugs and treatments for my glaucoma, no other drug or treatment works for me.

9. According to my doctor's suggestion, I have been modulating my use of medical cannabis. Currently, I smoke a little bit of cannabis three times a day. This is the only way I know how to get through the day without pain. It is also the only way I know how to maintain my vision.

10. The Cooperative has provided a safe place where I can get this life-saving medicine. If cannabis were not available through the Cooperative, I would be forced to go without the only medication that has worked to alleviate my glaucoma.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct.

Executed this 10 day of September at Oakland, California.

Harold Sweet

Harold Sweet

IN THE UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

UNITED STATES OF AMERICA,

Plaintiff,

v.

CANNABIS CULTIVATOR'S CLUB, et al.,

Defendants.

AND RELATED ACTIONS.

No. C 98-00085 CRB
C 98-00086 CRB
C 98-00087 CRB
C 98-00088 CRB
C 98 00089 CRB
C 98 00245 CRB

DECLARATION OF YVONNE WESTBROOK

I, YVONNE WESTBROOK, declare:

1. My name is Yvonne Renee Westbrook. I am 45 years of age, am of sound mind, and am competent to testify to the matters stated herein.

2. I am a member of the Oakland Cannabis Buyers' Cooperative. I was present at the Cooperative during a press conference on May 21, 1998.

3. I was diagnosed with multiple sclerosis in 1979. Because of my condition, I am confined to a wheelchair. Cannabis helps me cope with many of the conditions brought on by my illness. True and correct copies from my medical record are attached as "Exhibit A."

4. Spasticity is one of my symptoms caused by multiple sclerosis—my legs will jump uncontrollably. My doctor has prescribed Valium for the spasticity, but it does not work as well as cannabis. It takes Valium approximately one hour to take effect, and during that hour my legs continue to jump around. After the Valium does take effect, I just want to fall asleep, and cannot function well. When I take Valium, I feel listless and worthless. In contrast, after I take just a few puffs of cannabis, the spasticity immediately subsides, and I can go about my normal activities. Cannabis makes it possible for me to live a fulfilling life: Currently, my primary endeavor is working as a peer counselor for other people with multiple sclerosis.

5. Chronic pain is another condition from which I suffer—my feet and legs experience throbbing aching. I also feel pain in my hands and eyes. My doctor prescribed pain relievers, which help some at night, but during the day cannabis is the one and only medicine that helps me cope with the pain. The other pain relievers, such as Vicodin, also make me feel listless and they give me constipation. Another pain medication I have tried completely knocks me out. It makes me so weak that I cannot stand at all. Cannabis does not have this side effect.

6. I suffer from terrible headaches. Cannabis helps me cope with that pain as well. My doctor prescribed Vicodin for my headaches, but I try not to use it because it can be addictive and can cause liver problems. Lord knows, I don't want liver problems along with multiple sclerosis.

7. Multiple sclerosis also makes it hard for me to sleep. Cannabis is effective at helping me sleep, and the next morning I feel rested and refreshed. Other medications my doctor prescribed for sleeping, such as Restoral, have side effects: The next morning I felt lethargic, without energy,

and not like myself. The prescription drugs rob me of energy, which is low anyway because of multiple sclerosis.

8. Being disabled can make me depressed, and I suffer from mood swings, but cannabis improves my attitude. For example, I sometimes suffer from depression because of my condition, or I can become angry at my inability to perform simple daily tasks. In those circumstances, I can medicate with cannabis and it quickly improves my mental outlook. Being depressed aggravates the headaches and fatigue I experience, which are symptoms of multiple sclerosis, whereas having a good mental attitude alleviates those symptoms and improves my condition.

9. My doctor is very supportive of my use of cannabis. He is glad I have a medicine that helps me in so many ways. In the hospital, at various times, the nurses have seen me medicating with cannabis. They, too, have been very supportive of me.

10. I only use cannabis for medical purposes, not recreationally. I am 45 years old—I have neither the time nor the inclination to use drugs recreationally. Because I smoke several cannabis cigarettes every day, it does not have a psychoactive effect on me.

11. The Oakland Cannabis Buyers' Cooperative provided a safe, clean, and comfortable place to obtain cannabis. That is important to me because, being in a wheelchair, I do not want to go to seedy places, or to parks or to the streets, in search of medicine. The elements I would have to endure in order to get medicine there are dangerous, and it would be stressful. I am afraid of the guns, neighborhoods, and unsavory people I would need to interact with in order to obtain cannabis on the black market.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct.

Executed this 11 day of September, in Oakland, California.

Y. R. Westbrook

Yvonne Westbrook

EXHIBIT A

GARY L. CHAN, M.D.
Board Certified Internal Medicine

1199 Bush Street, Suite 400
San Francisco, CA 94109
Telephone: (415) 474-7900

August 16, 1996

To Whom It May Concern,

I am writing this letter to confirm that my patient, Ms. Yvonne Westbrook does have Multiple Sclerosis. If you have any questions or concerns, please feel free to call my office. Thank you.

Sincerely,

Gary L. Chan, M.D.

Exhibit A

4416

OAKLAND CANNABIS BUYERS CLUB

PHYSICIAN STATEMENT

My patient, Yvonne Westbrook, is being treated for Multiple Sclerosis.

We have discussed the medical benefits and risks of marijuana use as a treatment for this condition. I would consider prescribing marijuana for this patient's condition if I were legally able to do so. If my patient chooses to use marijuana therapeutically, I will continue to monitor his/her condition and provide advice on his/her progress.

Gary L. Chanod '96

Physician's Signature

GARY L CHANOD MD Marked in file

Physician's Name (printed)

1199 BUSH ST #400

Address

S.F, CA 94109

City, State and Zip Code

(415) 474-7900

Phone Number

Oakland Cannabis Buyers' Club

(510) 832-5346

ER1445