DAVID Y. IGE
GOVERNOR OF HAWAII

VIRGINIA PRESSLER, M.D.
DIRECTOR OF HEALTH

STATE OF HAWAII
DEPARTMENT OF HEALTH
P. O. Box 3378
Honolulu, HI 96801-3378
doh.testimony@doh.hawaii.gov

WRITTEN ONLY

Testimony in OPPOSITION to S.B. 174 SD2
RELATING TO MEDICAL MARIJUANA

DELLA AU BELATTI, CHAIR
HOUSE COMMITTEE ON HEALTH
Hearing Date: March 21, 2017 Room Number: 329

Fiscal Implications: None

Department Testimony: The purpose of this bill is to amend the list of debilitating conditions for the medical use of marijuana by adding a number of new conditions. The Department generally opposes the passage of new laws related to marijuana until the medical marijuana dispensaries open and we can gauge the impact upon the State. We specifically oppose this bill because the Department through §11-160-7, Hawaii Administrative Rules has already laid out a comprehensive annual process to consider addition or deletion of qualifying conditions for the medical use of marijuana. Physicians or potential medical marijuana patients may petition the Department for new conditions. This process will focus on all available medical evidence and research on efficacy and safety for patients. It will include a public hearing where testimony from the public can be provided. The evidence gathered with recommendations will be provided to the Director of Health for decision making.

The Department has already queried registering physicians and several plan to petition for a variety of conditions. The first annual petition process will be implemented this year. Decisions

will be grounded in the best available science that shows that medical marijuana helps treat or relieve any proposed additional conditions.

Thank you for the opportunity to testify.

TESTIMONY OF
THE DEPARTMENT OF THE ATTORNEY GENERAL
TWENTY-NINTH LEGISLATURE, 2017

ON THE FOLLOWING MEASURE:
S.B. NO. 174, S.D. 2, RELATING TO MEDICAL MARIJUANA.

BEFORE THE:
HOUSE COMMITTEE ON HEALTH

DATE: Tuesday, March 21, 2017 **TIME:** 9:00 a.m.

LOCATION: State Capitol, Room 329

TESTIFIER(S): Douglas S. Chin, Attorney General, or
Jill T. Nagamine, Deputy Attorney General

Chair Belatti and Members of the Committee:

The Department of the Attorney General provides the following comments.

We generally oppose the passage of new laws related to marijuana until the medical marijuana dispensaries open and we have the chance to gauge the impact on the State.

This bill would expand the list of medical conditions for which a patient can be certified for the medical use of marijuana. This draft of the bill deleted anxiety, depression, insomnia, and stress from the previous draft, but it would still add lupus, epilepsy, multiple sclerosis, arthritis, and autism (page 1, lines 5-6) to the list of debilitating medical conditions already approved in section 329-121, Hawaii Revised Statutes.

While we appreciate the Legislature's limiting the proposed new conditions, we are still concerned that without a scientific or other basis to indicate that the use of marijuana helps treat or provide relief to people who have the additional proposed conditions, the proposed expansion may appear to move the State closer to deregulation of marijuana, a schedule I controlled substance under federal law. Adding these new conditions without adequate justification could increase the risk of diversion and could be viewed by the new federal administration as contrary to the goal of having a robust regulatory scheme for the medical use of marijuana in Hawaii.

If this Committee decides to pass this bill, we respectfully recommend that it add a section of findings that would provide a basis for the use of marijuana for the additional conditions.

DEPARTMENT OF THE PROSECUTING ATTORNEY

CITY AND COUNTY OF HONOLULU

ALII PLACE
1060 RICHARDS STREET • HONOLULU, HAWAII 96813
PHONE: (808) 547-7400 • FAX: (808) 547-7515

KEITH M. KANESHIRO
PROSECUTING ATTORNEY

CHRISTOPHER D.W. YOUNG
FIRST DEPUTY PROSECUTING ATTORNEY

THE HONORABLE DELLA AU BELATTI, CHAIR
HOUSE COMMITTEE ON HEALTH
Twenty-Ninth State Legislature
Regular Session of 2017
State of Hawai`i

March 21, 2017

RE: S.B. 174, S.D. 2; RELATING TO MEDICAL MARIJUANA.

Chair Belatti, Vice-Chair Kobayashi and members of the House Committee on Health, the Department of the Prosecuting Attorney of the City & County of Honolulu ("Department") submits the following testimony in opposition to S.B. 174, S.D. 2.

If passed, S.B. 174, S.D. 2 would expand the definition of a "debilitating medical condition" to include "lupus, epilepsy, multiple sclerosis, arthritis, [and] autism" among the enumerated qualifying conditions.

The Department is very concerned that the proposed amendments would open the door to individuals who would abuse the medical marijuana system, such as physicians whose sole or primary practice is issuing medical marijuana certifications, regardless of whether the patient truly has a truly debilitating medical condition that warrants use of this highly controversial drug. Indeed, under Hawaii's laws, an issuing physician need not have any specialized knowledge or expertise in the patient's qualifying condition, nor are there any requirements for face-to-face visits, physical examinations, or ongoing treatment by the issuing physician.

Rather than opening the floodgates to make medical marijuana available to anyone diagnosed with arthritis or similarly common conditions, the Department maintains that any expansion of the medical marijuana qualifiers must be done in a very careful and measured way. To this end, we note that the Department of Health ("DOH") is currently preparing to hold annual petition hearings— as permitted by statute—to consider additional conditions, not already listed as a "debilitating medical condition," on a case-by-case basis.

As always, the Department's primary concern is for public safety and welfare. Given the huge potential for the amendments proposed in S.B. 174, S.D. 2 to facilitate abuse and/or outright illicit activity, using our medical marijuana laws, the Department is strongly opposed to this proposition. For all of the foregoing reasons, the Department of the Prosecuting Attorney of the City and County of Honolulu opposes S.B. 174, S.D. 2. Thank you for the opportunity to testify on this matter.

the Drug Policy Forum of hawai'i

Dedicated to safe, responsible, humane and effective drug policies since 1993

TO: House Committee on Health
FROM: Carl Bergquist, Executive Director
HEARING DATE: 21 March 2017, 9AM
RE: SB174 SD2, Relating to Medical Marijuana, **SUPPORT**

Dear Chair Belatti, Vice Chair Kobayashi, Committee Members:

The Drug Policy Forum of Hawai'i (DPFHI) supports this measure to add various new medical conditions as qualifying for the legal use of medical cannabis in Hawai'i. All of the conditions specifically listed in this SD2 amended version (lupus, autism, multiple sclerosis, arthritis and epilepsy) are approved by at least one other state.

Of these conditions, the one that attracts the most attention is autism. There is growing evidence, however, that certain patients can benefit from medical cannabis therapy. In fact, success in some cases of autism mirror those seen in high profile cases of epilepsy (Dravet's Syndrome), a fact that is unsurprising given that epilepsy frequently accompanies autism. If a physician or advanced practice registered nurse determines that an autism patient could benefit from medical cannabis, we believe that this should be a decision left up to the parent based upon informed consent. As dispensaries get set to open, the very products that can best address the symptoms of these conditions will go on the market. **We believe it is better to allow parents to make decisions within the medical system rather than force them to seek help elsewhere**.

While we support the Department of Health's ongoing work to set up a petition process to add further conditions – indeed we are planning to help petition for "opiate use disorder" – we see it as a complement to expeditiously adding specific conditions by statute. Accordingly, we respectfully request your support for this bill that can help relieve the suffering of many patients who otherwise may find no relief or risk becoming addicted to more powerful narcotics.

Mahalo for the opportunity to testify.

P.O. Box 83, Honolulu, HI 96810-0083 Phone: 808-518-3213 Email: info@dpfhi.org
Website: www.dpfhi.org

kobayashi2 - Jessi

From: mailinglist@capitol.hawaii.gov
Sent: Sunday, March 19, 2017 6:27 PM
To: HLTtestimony
Cc: wailua@aya.yale.edu
Subject: Submitted testimony for SB174 on Mar 21, 2017 09:00AM

SB174
Submitted on: 3/19/2017
Testimony for HLT on Mar 21, 2017 09:00AM in Conference Room 329

Submitted By	Organization	Testifier Position	Present at Hearing
Wailua Brandman	Hawaii Assoc. of Professional Nurses	Support	No

Comments: HAPN strongly supports this bill. We know now that most, if not all, chronic illness is highly associated with inflammation. Cannabis has been shown to mediate inflammation and also supports the immune system (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2828614/). This excellent study is an example of the fine work that is being done to verify the medicinal use of cannabis. As noted in previous testimonies, leaving the addition of new qualifying conditions to the DOH is costly and time consuming. The Legislature has the ability to cut through the red tape and get appropriate medicine to the people suffering from these debilitating conditions. Please use your authority to get the medicine to the sick folks who desperately need it. Thank you so very much for all the fine work you do on the behalf of the people of Hawai`i. Wailua Brandman APRN FAANP, Chair HAPN Legislative Committee. 255-4442

Please note that testimony submitted less than 24 hours prior to the hearing, improperly identified, or directed to the incorrect office, may not be posted online or distributed to the committee prior to the convening of the public hearing.

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HAWAII EDUCATIONAL ASSOCIATION
FOR LICENSED THERAPEUTIC HEALTHCARE

To: Representative Della Au Belatti, Chair Health Committee
Representative Bertrand Kobayashi, Vice-Chair Health Committee
Members of the House Health Committee

Fr: Blake Oshiro, Esq. on behalf of the HEALTH Assn.

Re: Testimony in **Support** of **Senate Bill (SB) 174, Senate Draft (SD) 2**
RELATING TO MEDICAL MARIJUANA.
Amends the definition of debilitating medical condition to include lupus, epilepsy, multiple sclerosis, arthritis, and autism as conditions that qualify for the legal use of medical marijuana. Takes effect on 1/7/2059.

Dear Chair Belatti, Vice-Chair Kobayashi, Members of the Committee:

HEALTH is a recently formed trade association made up of the eight (8) licensed medical marijuana dispensaries under Haw. Rev. Stat. (HRS) Chapter 329D. HEALTH's members are all committed to ensuring the goals of patient safety, product safety and public safety. We **strongly support** SB174 SD2 which adds additional conditions to qualify for the legal use of medical marijuana. Attached, is a list of the state's that allow medical marijuana and the qualifying conditions. See https://www.leafly.com/news/health/qualifying-conditions-for-medical-marijuana-by-state

While we note that the range of conditions vary state to state with some more restrictive, some broader, than Hawaii, we think it is important to note that Hawaii was one of the first states to authorize the use of medical marijuana program in 2000. Yet, since that time, the list of conditions remained the same until 2015's Act 241 added "post-traumatic stress disorder."

However, we believe that there is an abundance of evidence to demonstrate and substantiate the medicinal benefits of medical marijuana for certain conditions, including those in this bill.

As with any other medication, a patient has the opportunity to try the product and see if it produces positive results, and weigh that against any negative side-effects. In close collaboration with their physician who provided the certification, they can then make their own decision whether to continue or discontinue the use of medical marijuana.

Therefore, we support this bill. Thank you for your consideration.

Alaska

Qualifying conditions to become a medical marijuana patient in Alaska include:

- Cancer
- Glaucoma
- HIV/AIDS
- Cachexia (wasting syndrome)
- Pain
- Nausea
- Seizures
- Muscle spasms
- Multiple sclerosis

For a complete list of qualifying conditions and guidelines, please refer to Alaska's application for medical marijuana registry, or catch up on the latest Alaska cannabis news.

Arizona

Qualifying conditions to become a medical marijuana patient in Arizona include:

- Cancer
- Glaucoma
- HIV/AIDS
- Cachexia (wasting syndrome)
- Pain
- Nausea
- Seizures
- Muscle spasms
- Multiple sclerosis
- PTSD

For a complete list of qualifying conditions and guidelines, please refer to the Arizona state legislature concerning medical marijuana, or catch up on the latest Arizona cannabis news.

Arkansas

Qualifying conditions for the Arkansas Medical Marijuana Amendment include:

- Cancer
- Glaucoma
- HIV/AIDS
- Hepatitis C
- ALS or Lou Gehrig's Disease
- Tourette's Syndrome
- Crohn's disease
- PTSD
- Severe arthritis
- Fibromyalgia
- Alzheimer's disease
- A chronic or debilitating disease that produces:
- Cachexia or wasting syndrome
- Peripheral neuropathy
- Intractable pain
- Severe nausea
- Seizures

- Severe or persistent muscle spasms

Arkansas' medical marijuana qualifying conditions are currently effective, but licenses for dispensaries will not be accepted until June 1, 2017.

California

Qualifying conditions to become a medical marijuana patient in California include:

- Cancer
- Anorexia
- AIDS
- Chronic pain
- Cachexia
- Persistent muscle spasms, including those associated with multiple sclerosis
- Seizures, including, but not limited to, those associated with epilepsy
- Severe nausea
- Glaucoma
- Arthritis
- Migraines
- Any other chronic or persistent medical symptom that substantially limits the ability of the person to conduct one or more major life activities (as defined by the Americans with Disabilities Act of 1990) or, if not alleviated, may cause serious harm to the patient's safety or physical or mental health

For a complete list of qualifying conditions and guidelines, please refer to California Proposition 215, with revised Senate Bill 420, or catch up on the latest California cannabis news.

Colorado

Although Colorado has implemented a legal recreational cannabis market, it still operates medical marijuana dispensaries for valid patients. Colorado medical marijuana patients still pay standard sales tax on cannabis but are exempt from the high excise taxes and additional state taxes collected from recreational cannabis sales.

Qualifying conditions to become a medical marijuana patient in Colorado include:

- Cancer
- Glaucoma
- HIV/AIDS
- Cachexia (wasting syndrome)
- Persistent muscle spasms
- Seizures
- Severe nausea
- Severe pain

For a complete list of qualifying conditions and guidelines, please refer to Colorado's Debilitating Conditions for Medical Marijuana Use, or catch up on the latest Colorado cannabis news.

Connecticut

Qualifying conditions to become a medical marijuana patient in Connecticut include:

- Cancer
- Glaucoma
- HIV/AIDS
- Parkinson's disease
- Multiple sclerosis

- Damage to the nervous tissue of the spinal cord with objective neurological indication of intractable spasticity
- Epilepsy
- Cachexia (wasting syndrome)
- Wasting syndrome
- Crohn's disease
- Post-traumatic stress disorder (PTSD)

For a complete list of qualifying conditions and guidelines, please refer to Connecticut's medical marijuana qualification requirements, or catch up on the latest Connecticut cannabis news.

Delaware

Qualifying conditions to become a medical marijuana patient in Delaware include:

- Cancer
- HIV/AIDS
- Hepatitis C
- Lou Gehrig's disease (amyotrophic lateral sclerosis, or ALS)
- Alzheimer's
- Post-traumatic stress disorder (PTSD)
- Cachexia (wasting syndrome)
- Intractable nausea
- Seizures
- Muscle spasms
- Multiple sclerosis

For a complete list of qualifying conditions and guidelines, please refer to Delaware's medical marijuana program guidelines, or catch up on the latest Delaware cannabis news.

District of Columbia (Washington, D.C.)

Qualifying conditions to become a medical marijuana patient in Washington, D.C. include:

- HIV/AIDS
- Cancer
- Glaucoma
- Muscle spasms
- Multiple sclerosis
- Lou Gehrig's disease (ALS)
- Cachexia (wasting syndrome)
- Decompensated cirrhosis
- Alzheimer's
- Seizure disorders
- Any condition diagnosed as "debilitating" by a licensed physician

For a complete list of qualifying conditions and guidelines, please refer to the District of Columbia's Medical Marijuana Program Patient FAQ, or catch up on the latest Washington, D.C. cannabis news.

Florida

Qualifying conditions to become a medical marijuana patient in Florida include:

- Cancer
- Epilepsy
- Glaucoma
- HIV/AIDS

- PTSD
- ALS or Lou Gehrig's disease
- Crohn's disease
- Parkinson's disease
- Multiple sclerosis

For more information on the Florida Medical Marijuana Legalization, please refer to Amendment 2.

Georgia

Georgia only allows for the use of low THC oil (less than 5% THC by weight).
Qualifying conditions to become a medical marijuana patient in Georgia include:

- Cancer
- Lou Gehrig's disease (ALS)
- Seizure disorders related to diagnosis of epilepsy or trauma-related head injuries
- Multiple sclerosis
- Crohn's disease
- Mitochondrial disease
- Parkinson's disease
- Sickle cell disease

For a complete list of qualifying conditions and guidelines, please refer to House Bill 1 (Haleigh's Hope Act), or catch up on the latest Georgia cannabis news.

Hawaii

Qualifying conditions to become a medical marijuana patient in Hawaii include:

- Cancer
- Glaucoma
- HIV/AIDS
- Cachexia (wasting syndrome)
- Pain
- Nausea
- Seizures
- Muscle spasms
- Multiple sclerosis

For a complete list of qualifying conditions and guidelines, please refer to Hawaii Senate Bill 862, or catch up on the latest Hawaii cannabis news.

Illinois

Qualifying conditions to become a medical marijuana patient in Illinois include:

- Acquired Immunodeficiency Syndrome (AIDS)
- Alzheimer's disease
- Lou Gehrig's disease (ALS)
- Arnold-Chiari malformation and syringomyelia
- Cachexia/wasting syndrome
- Cancer
- Causalgia
- Chronic inflammatory demyelinating polyneuropathy
- Crohn's disease
- CRPS (Complex Regional Pain Syndrome Type I)
- CRPS (Complex Regional Pain Syndrome Type II)

- Dystonia
- Fibromyalgia (severe)
- Fibrous dysplasia
- Glaucoma
- Hepatitis C
- Human Immunodeficiency Virus (HIV)
- Hydrocephalus
- Hydromyelia
- Interstitial cystitis
- Lupus
- Multiple sclerosis
- Muscular dystrophy
- Myasthenia gravis
- Myoclonus
- Nail-patella syndrome
- Neurofibromatosis
- Parkinson's disease
- Post-concussion syndrome
- Post-Traumatic Stress Disorder (PTSD)
- Reflex sympathetic dystrophy
- Residual limb pain
- Rheumatoid arthritis (RA)
- Seizures
- Sjogren's syndrome
- Spinal cord disease (including but not limited to arachnoiditis, Tarlov cysts, hydromyelia & syringomelia)
- Spinal cord injury
- Spinocerebellar ataxia (SCA)
- Syringomyelia
- Tarlov cysts
- Tourette syndrome
- Traumatic brain injury (TBI)

For a complete list of qualifying conditions and guidelines, please refer to the Illinois Medical Cannabis Pilot Program's FAQ, or catch up on the latest Illinois cannabis news.

Iowa

Iowa allows for the use of high-CBD cannabis extracts with less than .3% THC.

Qualifying conditions to become a medical marijuana patient in Iowa include:

- Intractable epilepsy

For a complete list of guidelines, please refer to Iowa Medical Cannabidiol Act Quick Facts, or catch up on the latest Iowa cannabis news.

Kentucky

Kentucky allows for the use of low-THC cannabis or industrial hemp-derived CBD oil. Only those who are participating in a clinical trial or expanded access program are legally allowed to possess CBD oil.

For more information on accessing CBD in Kentucky, please refer to Senate Bill 124, or catch up on the latest Kentucky cannabis news.

Louisiana
Qualifying conditions to become a medical marijuana patient in Louisiana include:
- Symptoms related to cancer
- Glaucoma
- Spastic quadriplegia

For more information on Louisiana's medical marijuana law, please refer to Senate Bill 143, or catch up on the latest Louisiana cannabis news.

Maine
Qualifying conditions to become a medical marijuana patient in Maine include:
- Chronic pain that has not responded to conventional therapy for more than six months
- Post-traumatic stress disorder (PTSD)
- Lou Gehrig's disease (ALS)
- Alzheimer's
- Cachexia (wasting syndrome)
- Cancer
- Crohn's disease
- Glaucoma
- Hepatitis C (active form)
- HIV
- Inflammatory bowel disease (IBS)
- Seizure disorders
- Severe muscle spasms (including multiple sclerosis and other diseases causing severe and persistent muscle spasms)
- Severe nausea

For a complete list of qualifying conditions and guidelines, please refer to Maine's medical use of marijuana guidelines, or catch up on the latest Maine cannabis news.

Maryland
Qualifying conditions to become a medical marijuana patient in Maryland include:
- Cachexia (wasting syndrome)
- Severe, debilitating, or chronic pain
- Severe nausea
- Seizures, including those characteristic of epilepsy
- Severe and persistent muscle spasms
- Multiple sclerosis
- Crohn's disease
- Alzheimer's
- Cancer
- Glaucoma
- HIV/AIDS
- Hepatitis C

For a complete list of qualifying conditions and guidelines, please refer to Maryland Senate Bill 757, or catch up on the latest Maryland cannabis news.

Massachusetts
Qualifying conditions to become a medical marijuana patient in Massachusetts include:
- Cancer

- Glaucoma
- AIDS
- Hepatitis C
- Lou Gehrig's disease (ALS)
- Crohn's disease
- Parkinson's disease
- Multiple sclerosis
- Other debilitating conditions as determined in writing by a qualifying patient's certifying physician.

For a complete list of qualifying conditions and guidelines, please refer to the Massachusetts medical use of marijuana overview, or catch up on the latest Massachusetts cannabis news.

Michigan

Qualifying conditions to become a medical marijuana patient in Michigan include:

- Cancer
- Glaucoma
- HIV/AIDS
- Hepatitis C
- Lou Gehrig's disease (Amyotrophic lateral sclerosis, or ALS)
- Alzheimer's
- Nail-patella syndrome
- Cachexia (wasting disease)
- Severe and chronic pain
- Severe nausea
- Seizures
- Epilepsy
- Muscle spasms
- Multiple sclerosis

For a complete list of qualifying conditions and guidelines, please refer to the Michigan Medical Marihuana Registry Program FAQ, or catch up on the latest Michigan cannabis news.

Minnesota

Minnesota does not allow for smokeable cannabis, only a 30-day supply of oils, edibles, and concentrates. Qualifying conditions to become a medical marijuana patient in Minnesota include:

- Lou Gehrig's disease (Amyotrophic lateral sclerosis, or ALS)
- Cancer
- Cachexia
- Crohn's disease
- Glaucoma
- HIV/AIDS
- Seizures
- Severe and persistent muscle spasms
- Terminal illness
- Tourette syndrome
- Intractable pain*

*Recently recommended qualifying condition soon to be available for Minnesota patients.

For more information, please visit the Minnesota Department of Health – Medical Cannabis, or catch up on the latest Minnesota cannabis news.

Mississippi

Mississippi allows access to CBD oil only. Qualifying conditions to become a medical marijuana patient in Mississippi include:

- Debilitating epileptic seizure disorders

Patients must receive medical recommendations by a physician from the University of Mississippi Medical Center to participate in the clinical trial. For more information, please refer to House Bill 1231 or Harper Grace's Law, or catch up on the latest Mississippi cannabis news.

Missouri

Missouri allows access to CBD oil only. Qualifying conditions to become a medical marijuana patient in Missouri include:

- Intractable epilepsy

For more information, please refer to House Bill 2238, or catch up on the latest Missouri cannabis news.

Montana

Qualifying conditions to become a medical marijuana patient in Montana include:

- Cancer
- Glaucoma
- HIV/AIDS
- Cachexia (wasting syndrome)
- Chronic pain
- Intractable nausea or vomiting
- Epilepsy or an intractable seizure disorder
- Multiple sclerosis
- Crohn's disease
- Painful peripheral neuropathy
- A central nervous system disorder resulting in chronic, painful spasticity or muscle spasms

For a complete list of qualifying conditions and guidelines, please refer to Montana Code Annotated 2013, or catch up on the latest Montana cannabis news.

Nevada

Qualifying conditions to become a medical marijuana patient in Nevada include:

- AIDS
- Cancer
- Glaucoma
- Condition or treatment for a medical condition that produces cachexia (general physical wasting and malnutrition)
- Persistent muscle spasms (including multiple sclerosis)
- Seizures (including epilepsy)
- Severe nausea
- Severe pain

For a complete list of qualifying conditions and guidelines, please refer to the Nevada Medical Marijuana Program, or catch up on the latest Nevada cannabis news.

New Hampshire

Qualifying conditions to become a medical marijuana patient in New Hampshire include:

- A chronic or terminal disease
- Cachexia (wasting syndrome)

- Severe pain
- Severe nausea/vomiting
- Seizures
- Severe, persistent muscle spasms

For a complete list of qualifying conditions and guidelines, please refer to New Hampshire House Bill 573, or catch up on the latest New Hampshire cannabis news.

New Jersey

Qualifying conditions to become a medical marijuana patient in New Jersey include:

- Lou Gehrig's disease (amyotrophic lateral sclerosis, or ALS)
- Multiple sclerosis
- Terminal cancer
- Muscular dystrophy
- Inflammatory bowel disease (IBS)
- Crohn's disease
- Terminal illness if the physician has determined a prognosis of less than 12 months of life
- Seizure disorder, including epilepsy
- Intractable skeletal muscular spasticity
- Glaucoma
- HIV/AIDS
- Cancer

For a complete list of qualifying conditions and guidelines, please refer to the New Jersey Medicinal Marijuana Program, or catch up on the latest New Jersey cannabis news.

New Mexico

Qualifying conditions to become a medical marijuana patient in New Mexico include:

- Severe chronic pain
- Painful peripheral neuropathy
- Intractable nausea/vomiting
- Severe anorexia
- Cachexia (wasting syndrome)
- Hepatitis C infection currently receiving antiviral treatment
- Crohn's disease
- Post-traumatic stress disorder (PTSD)
- Lou Gehrig's disease (amyotrophic lateral sclerosis, or ALS)
- Cancer
- Glaucoma
- Multiple sclerosis
- Damage to the nervous tissue of the spinal cord with intractable spasticity
- Epilepsy
- HIV/AIDS
- Inflammatory autoimmune-mediated arthritis
- Hospice patients

For a complete list of qualifying conditions and guidelines, please refer to the New Mexico Medical Cannabis Program FAQ, or catch up on the latest New Mexico cannabis news.

New York

Qualifying conditions to become a medical marijuana patient in New York include:

- Cancer
- Epilepsy
- HIV/AIDS
- Huntington's disease
- Inflammatory Bowel Disease (IBS)
- Lou Gehrig's disease (ALS)
- Parkinson's disease
- Multiple sclerosis (MS)
- Neuropathies
- Spinal cord damage

For a complete list of qualifying conditions and guidelines, please refer to the New York State Medical Marijuana Program FAQ, or catch up on the latest New York cannabis news.

North Carolina

North Carolina allows for the use of CBD oil only. Qualifying conditions to become a medical marijuana patient in North Carolina include:

- Intractable epilepsy

For more information, please refer to House Bill 1220, or catch up on the latest North Carolina cannabis news.

North Dakota

North Dakota's qualifying conditions for the North Dakota Compassionate Care Act include:

- Cancer and its treatments
- HIV/AIDS
- Hepatitis C
- ALS or Lou Gehrig's disease
- PTSD
- Alzheimer's disease, dementia, or treatment of these conditions
- Crohn's disease
- Fibromyalgia
- Spinal stenosis
- Chronic back pain, including:
- Neuropathy or damage to the nervous tissue of the spinal cord with objective neurological indication of intractable spasticity
- Glaucoma
- Epilepsy
- A chronic or debilitating disease, medical condition, or its treatment that produces one or more of the following:
- Cachexia or wasting syndrome
- Severe, debilitating pain that has not responded to previously prescribed medication or surgical measures for more than three months or for which other treatment options produced serious side effects
- Intractable nausea
- Seizures
- Severe or persistent muscle spasms, including but not limited to those characteristic of multiple sclerosis.

For more information, please refer to the North Dakota Compassionate Care Act.

Oklahoma

Oklahoma allows for the use of CBD oil only. Qualifying conditions to become a medical marijuana patient in Oklahoma include:

- Must be under the age of 18 suffering from:
- Lennox-Gastaut syndrome
- Dravet syndrome
- Severe myoclonic epilepsy of infancy
- Any form of refractory epilepsy not treatable by traditional medical therapies

For more information, please refer to Katie and Cayman's Law (House Bill 2154), or catch up on the latest Oklahoma cannabis news.

Oregon

Qualifying conditions to become a medical marijuana patient in Oregon include:

- Cancer
- Glaucoma
- Alzheimer's
- HIV/AIDS
- Cachexia (wasting syndrome)
- Severe pain
- Severe nausea
- Seizures, including but not limited to seizures caused by epilepsy
- Persistent muscle spasms
- Multiple sclerosis

For a complete list of qualifying conditions and guidelines, please refer to the Oregon Medical Marijuana Act, or catch up on the latest Oregon cannabis news.

Pennsylvania

Qualifying conditions to become a medical marijuana patient in Pennsylvania include:

- Cancer
- HIV/AIDS
- Amyotrophic Lateral Sclerosis (ALS)
- Parkinson's Disease
- Multiple sclerosis
- Damage to the nervous tissue of the spinal cord with objective neurological indication of intractable spasticity
- Epilepsy
- Inflammatory bowel disease (IBS)
- Neuropathies
- Huntington's disease
- Post-traumatic stress disorder (PTSD)
- Intractable seizures
- Glaucoma
- Sickle cell anemia
- Severe, chronic or intractable pain of neuropathic origin or severe chronic or intractable pain in which conventional therapeutic intervention and opiate therapy is contraindicated or ineffective
- Autism
- "Terminally ill" – a medical prognosis or life expectancy of approximately one year or less if the illness runs its normal course.

For more information, please refer to Senate Bill 3.

Rhode Island

Qualifying conditions to become a medical marijuana patient in Rhode Island include:

- Cancer
- Glaucoma
- HIV/AIDS
- Hepatitis C
- Cachexia (wasting syndrome)
- Chronic pain
- Severe nausea
- Seizures, including but not limited to those characteristic of epilepsy
- Severe and persistent muscle spasms
- Multiple sclerosis
- Crohn's disease
- Alzheimer's

For a complete list of qualifying conditions and guidelines, please refer to Rhode Island's medical marijuana approved qualifying debilitating medical conditions, or catch up on the latest Rhode Island cannabis news.

South Carolina

South Carolina allows for the use of CBD oil only. Qualifying conditions to become a medical marijuana patient in South Carolina include:

- Certain forms of epilepsy as part of a state-run clinical trial

For more information, please refer to the Medical Cannabis Therapeutic Treatment Research Act, or catch up on the latest South Carolina cannabis news.

Tennessee

Tennessee allows for the use of CBD oil only. Qualifying conditions to become a medical marijuana patient in Tennessee include:

- Intractable seizures (as part of a clinical research study)

For more information, please refer to Senate Bill 280, or catch up on the latest Tennessee cannabis news.

Texas

Texas allows for the use of CBD oil only. Qualifying conditions to become a medical marijuana patient in Texas include:

- Intractable epilepsy

For more information, please refer to Senate Bill 339, or catch up on the latest Texas cannabis news.

Utah

Utah allows for the use of CBD oil only. Qualifying conditions to become a medical marijuana patient in Utah include:

- Intractable epilepsy

For more information, please refer to House Bill 105, or catch up on the latest Utah cannabis news.

Vermont

Qualifying conditions to become a medical marijuana patient in Vermont include:

- Cancer
- AIDS/HIV
- Multiple sclerosis

- Cachexia (wasting syndrome)
- Severe pain
- Nausea
- Seizures

For a complete list of qualifying conditions and guidelines, please refer to the Vermont patient marijuana registry FAQ, or catch up on the latest Vermont cannabis news.

Washington

Changes to Washington state's marijuana laws via Senate Bill 5052 will result in the state's medical marijuana industry being absorbed by its recreational cannabis market. These changes will go into full efect July 1, 2016. Until then, medical marijuana dispensaries will still be operational but are ultimately expected to close or incorporate themselves into an existing licensed retail cannabis shop.

Qualifying conditions to become a medical marijuana patient in Washington include:

- Cancer
- HIV/AIDS
- Multiple sclerosis
- Epilepsy or other seizure disorder
- Spasticity disorders
- Intractable pain
- Glaucoma
- Crohn's disease
- Hepatitis C
- Diseases, including anorexia, which result in nausea, vomiting, wasting, appetite loss, cramping, seizures, muscle spasms, or spasticity

For a complete list of qualifying conditions and guidelines, please refer to the Washington state legislature regarding medical cannabis, or catch up on the latest Washington state cannabis news.

Wisconsin

Wisconsin allows for the use of non-psychoactive CBD oil only. Qualifying conditions to become a medical marijuana patient in Wisconsin include:

- Seizure disorders

For more information, please refer to Lydia's Law (Act 267), or catch up on the latest Wisconsin cannabis news.

Wyoming

Wyoming allows for the use of CBD oil only. Qualifying conditions include:

- Intractable epilepsy

For more information, please refer to House Bill 32, or catch up on the latest Wyoming cannabis news.

March 20, 2017

TO: Representative Della Au Belatti, Chair Health Committee
Representative Bertrand Kobayashi, Vice-Chair Health Committee
Members of the House Health Committee

FROM: Gregory Park, MD, Chief Compliance Officer & Cofounder, Maui Grown Therapies

RE: TESTIMONY IN SUPPORT OF SB174 RELATING TO MEDICAL MARIJUANA

SB 174: Amends the definition of debilitating medical condition to include lupus, epilepsy, multiple sclerosis, arthritis, autism, anxiety, depression, insomnia, and stress as conditions that qualify for the legal use of medical marijuana.

Dear Chair Belatti, Vice-Chair Kobayashi, and Members of the Committee:

I write to you to express my support for Senate Bill (SB) 174, which proposes to broaden the list of debilitating medical conditions for which medical marijuana can be recommended under Hawai'i law.

As a medical oncologist with 36 years of experience practicing medicine in Hawai'i, I have witnessed first-hand the range of therapeutic effects marijuana can bring to patients. Medical cannabis is useful to help relieve a variety of symptoms that cancer patients often experience including: gastrointestinal symptoms and nausea from the disease and its treatment, lack of appetite resulting in weight loss, pain and anxiety. The plant can safely be used for these conditions and often adds to and complements the conventional pharmaceutical medicines we use to help our patients.

I believe that including lupus, epilepsy, multiple sclerosis, arthritis and autism as qualifying conditions is sound, rational and compassionate. However, the list of debilitating medical conditions for which marijuana can be recommended under current Hawai'i law lags peer- reviewed clinical findings; there is data to support its use in anxiety, sleep and neurological disorders in adults.

In the case of anxiety – which is a very common symptom of numerous illnesses, but can also manifest as a standalone debilitating condition – there is data that suggests that cannabidiol (commonly referred to as CBD), a non-psychoactive compound found in certain types of marijuana, is a powerful and non-addictive anti-anxiety agent. The usual agents used to treat anxiety, including the benzodiazepines, can be addicting and can cause harmful side effects. Medical cannabis high in CBD offers an excellent alternative to these medicines which are so commonly used to treat anxiety. I believe that anxiety disorders warrant inclusion in the list of debilitating conditions.

Included with my testimony are links to recent abstracts from peer-reviewed journals relating to the medical use of CBD as an anti-anxiety agent. I respectfully ask the members of the committee to evaluate the findings of this clinical research during your deliberations on the current measure.

https://www.ncbi.nlm.nih.gov/pubmed/22729452 https://www.ncbi.nlm.nih.gov/pubmed/24923339
https://www.ncbi.nlm.nih.gov/pubmed/21307846 https://www.ncbi.nlm.nih.gov/pubmed/20829306

Respectfully, Gregory Park, M.D.

March 20, 2017

TO: Representative Della Au Belatti, Chair Health Committee
Representative Bertrand Kobayashi, Vice-Chair Health Committee
Members of the House Health Committee

FROM: Gregory Yim, MD, Chief Medical Officer, Maui Grown Therapies

RE: TESTIMONY IN SUPPORT OF SB174 RELATING TO MEDICAL MARIJUANA

Dear Chair Belatti, Vice-Chair Kobayashi, and Members of the Committee:

As a physician and a member of the Act 230 Medical Marijuana Oversight Working Group representing Hawaii's medical community, I am grateful for this opportunity to submit testimony in support of Senate Bill (SB) 174.

Until just a few years ago, I knew little about the medicinal potential of marijuana. I began to study the available clinical data on the subject only after being asked by the parents of several of my patients if marijuana-based medicines might have the potential to control their children's seizures where conventional pharmaceutical medications had failed. During my research, I learned of an emerging and increasingly robust body of clinical data supporting the efficacy of cannabinoid therapies not only for seizure control, but also for the treatment of a range of other neurological and psychiatric disorders.

In particular, cannabidiol (or CBD) – a non-psychoactive compound found only in the marijuana plant – is known to have powerful neuroprotective and anti-inflammatory properties, and there is a growing body of peer-reviewed research supporting its efficacy in the treatment of neurodegenerative diseases such as Alzheimer's, Parkinson's and Amytrophic Lateral Sclerosis (ALS). CBD is also known to be a safe and highly effective anti-anxiety agent, making it a potentially suitable alternative to conventional pharmaceutical anxiolytic drugs, many of which have adverse side effects.

Against the backdrop of these exciting clinical developments, Hawai'i has a chance to set the standard nationally in terms of evidence-based medical marijuana policy. By adding new debilitating conditions to the list allowed under Act 230, SB174 is a step in that direction, but it should go further.

In support of my testimony, I have included links to peer-reviewed medical journals relating to the effective treatment of the conditions referenced above with marijuana-based medicines.

Respectfully,
Gregory Yim, M.D.

Alzheimer's:

https://www.ncbi.nlm.nih.gov/pubmed/26757043

https://www.ncbi.nlm.nih.gov/pubmed/25024327

ALS:

https://www.ncbi.nlm.nih.gov/pubmed/20439484

Parkinson's:

https://www.ncbi.nlm.nih.gov/pubmed/25237116

Testimony in SUPPORT of THE FOLLOWING MEASURE:
SB174 SD2, RELATING TO MEDICAL MARIJUANA
BEFORE THE COMMITTEE ON HEALTH

DATE: Tuesday, March 21, 2017, TIME: 9:00 A.M.
LOCATION: State Capitol, Conference Room 329

FROM TESTIFIER: Wendy Gibson R.N./BSN. American Cannabis Nurses Association member.

Honorable Chair Au Belatti, Vice Chair Kobayashi and Members of the Committee,

My name is Wendy Gibson. I am a Cannabis Nurse Educator who STRONGLY supports HB174 SD2 as a means to increase access to patients who suffer from lupus, epilepsy, multiple sclerosis, arthritis, and autism. The medical cannabis scientific community has a large body of research, which can verify the usefulness for treating these conditions.

I believe that passing HB174 SD2 will facilitate a speedier and less costly approach for adding qualifying conditions than the process the Department of Health is currently developing.

For these reasons, I stand in STRONG SUPPORT of SB174 SD1.

Thank you very much for the opportunity to provide testimony on this measure.

Respectfully,

Wendy Gibson R.N./BSN

kobayashi2 - Jessi

From: mailinglist@capitol.hawaii.gov
Sent: Sunday, March 19, 2017 3:51 PM
To: HLTtestimony
Cc: j.bobich@tcu.edu
Subject: *Submitted testimony for SB174 on Mar 21, 2017 09:00AM*

SB174
Submitted on: 3/19/2017
Testimony for HLT on Mar 21, 2017 09:00AM in Conference Room 329

Submitted By	Organization	Testifier Position	Present at Hearing
Joseph A. Bobich	Individual	Support	No

Comments:

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kobayashi1- Oshiro

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To: HLTtestimony
Cc: mamaupin@hotmail.com
Subject: *Submitted testimony for SB174 on Mar 21, 2017 09:00AM*

SB174
Submitted on: 3/17/2017
Testimony for HLT on Mar 21, 2017 09:00AM in Conference Room 329

Submitted By	Organization	Testifier Position	Present at Hearing
Margaret Maupin	Individual	Support	No

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To: HLTtestimony
Cc: mendezj@hawaii.edu
Subject: *Submitted testimony for SB174 on Mar 21, 2017 09:00AM*

SB174
Submitted on: 3/18/2017
Testimony for HLT on Mar 21, 2017 09:00AM in Conference Room 329

Submitted By	Organization	Testifier Position	Present at Hearing
Javier Mendez-Alvarez	Individual	Support	No

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Cc: ncsugano@gmail.com
Subject: Submitted testimony for SB174 on Mar 21, 2017 09:00AM

SB174
Submitted on: 3/18/2017
Testimony for HLT on Mar 21, 2017 09:00AM in Conference Room 329

Submitted By	Organization	Testifier Position	Present at Hearing
Jari S.K. Sugano	Individual	Support	No

Comments: SB 174 Dear Chair Bellatti and members of the House Health Committee My name is Jari Sugano and I am a caregiver of a minor in the Hawaii medical marijuana program and a member of the medical marijuana dispensary working group. I strongly support changing the current list of debilitating medical conditions to include lupus, epilepsy, multiple sclerosis, arthritis, and autism, under Hawaii's medical marijuana program. We have family members affected by lupus, multiple sclerosis, arthritis, and autism. We see first hand the long term pain and suffering associated with these conditions and hope our family members will also be able to access of medical marijuana as an adjunct treatment option in the near future. For our children who both have autism, we currently use medication such as methylphenidate to control focus, hyper activeness and spontaneous rage issues for symptoms relating to autism which causes side effects such as eating and social disorders. Our daughter has severe behavior issues that includes self inflicted harm and harm of others around her. The addition of THC for her seizure control has been found to help her behavior rages as well. We look forward to evaluating new treatment options that may one day bring natural relief to our family members. Please consider expanding the current list of conditions.

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From: mailinglist@capitol.hawaii.gov
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To: HLTtestimony
Cc: eckrothkr@gmail.com
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SB174
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Submitted By	Organization	Testifier Position	Present at Hearing
Katherine Eckroth	Individual	Support	No

Comments:

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kobayashi1- Oshiro

From:	Clif Otto <cliftonotto@hotmail.com>
Sent:	Friday, March 17, 2017 5:21 PM
To:	HLTtestimony
Subject:	Fw: SB174 SD2
Attachments:	ALS and Cannabis-Carter-2010.pdf; Marijuana and Parkinson's-Lange-2015.pdf
Categories:	Purple Category

Dear House Committee on Health,

Thank you for considering SB174 SD2.

I would like to ask that you also consider adding the following two debilitating conditions:

Amyotrophic Lateral Sclerosis (ALS): a progressive fatal disease.
Parkinson's Disease: a progressive severely debilitating disease.

I believe there is sufficient evidence, both clinical and anecdotal, to warrant adding these conditions to Hawaii's Medical Use of Marijuana Program.

Peer-reviewed articles attached for your consideration.

Thank you.

Clifton Otto, MD
Honolulu, HI
C: 808-233-8267.

AM J HOSP PALLIAT CARE OnlineFirst, published on May 3, 2010 as doi:10.1177/1049909110369531

Cannabis and Amyotrophic Lateral Sclerosis: Hypothetical and Practical Applications, and a Call for Clinical Trials

American Journal of Hospice & Palliative Medicine®
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DOI: 10.1177/1049909110369531
http://ajhpm.sagepub.com

Gregory T. Carter, MD, MS[1], Mary E. Abood, PhD[2], Sunil K. Aggarwal, PhD[3], and Michael D. Weiss, MD[1,4,5]

Abstract

Significant advances have increased our understanding of the molecular mechanisms of amyotrophic lateral sclerosis (ALS), yet this has not translated into any greatly effective therapies. It appears that a number of abnormal physiological processes occur simultaneously in this devastating disease. Ideally, a multidrug regimen, including glutamate antagonists, antioxidants, a centrally acting anti-inflammatory agent, microglial cell modulators (including tumor necrosis factor alpha [TNF-α] inhibitors), an antiapoptotic agent, 1 or more neurotrophic growth factors, and a mitochondrial function-enhancing agent would be required to comprehensively address the known pathophysiology of ALS. Remarkably, cannabis appears to have activity in all of those areas. Preclinical data indicate that cannabis has powerful antioxidative, anti-inflammatory, and neuroprotective effects. In the G93A-SOD1 ALS mouse, this has translated to prolonged neuronal cell survival, delayed onset, and slower progression of the disease. Cannabis also has properties applicable to symptom management of ALS, including analgesia, muscle relaxation, bronchodilation, saliva reduction, appetite stimulation, and sleep induction. With respect to the treatment of ALS, from both a disease modifying and symptom management viewpoint, clinical trials with cannabis are the next logical step. Based on the currently available scientific data, it is reasonable to think that cannabis might significantly slow the progression of ALS, potentially extending life expectancy and substantially reducing the overall burden of the disease.

Keywords

cannabis, endocannabinoids, amyotrophic lateral sclerosis, clinical trials, motor neuron disease

Introduction

Amyotrophic lateral sclerosis (ALS), with an incident rate of 5 to 7 per 100 000 population, is the most common form of adult motor neuron disease.[1] Amyotrophic lateral sclerosis is a rapidly progressive neuromuscular disease that destroys both upper and lower motor neurons, resulting in weakness, spasticity, and ultimately death from respiratory failure. The vast majority of ALS cases are acquired and occur sporadically. Emerging evidence suggests that increased oxidative stress from free radical toxicity and/or excessive glutamate activity is what leads to motor neuron cell death in the brain and spinal cord.[2-5] Inherited forms of the disease, which occur in approximately 5% to 10% of all patients with ALS, are largely because of mutations in the superoxide dismutase gene, presumably producing a marked increase in oxidative stress. Presentations of familial ALS have more variability than in sporadic ALS and are mutation specific with the most aggressive form because of the A4V mutation.[5] Recent results have established that ALS also involves other nonneuronal cells including astroglia and microglia.[6,7] Other putative mechanisms involved in motor neuron degeneration in ALS include mitochondrial dysfunction, neuroinflammation, growth factor deficiency, and glutamate excitotoxicity.[2,3]

Significant advances have been made regarding our understanding of the molecular mechanisms of ALS.[8-12] However, this has not yet translated into an effective therapeutic treatments. To date, the only food and drug administration- (FDA) approved therapy available for ALS is the antiglutamatergic agent Riluzole, which has limited therapeutic efficacy.[10] Given

[1] Muscular Dystrophy Association/Amyotrophic Lateral Sclerosis Center, University of Washington Medical Center, Seattle, WA, USA
[2] Anatomy and Cell Biology and Center for Substance Abuse Research, Temple University, Philadelphia, PA, USA
[3] Medical Scientist Training Program, School of Medicine, University of Washington, Seattle, WA, USA
[4] Neuromuscular Disease Division, Department of Neurology, University of Washington Medical Center, Seattle, WA, USA
[5] Electrodiagnostic Laboratory, University of Washington Medical Center, Seattle, WA, USA

Corresponding Author:
Gregory T. Carter, 1800 Cooks Hill Road, Suite E, Centralia, WA 98531, USA
Email: gtcarter@uw.edu

this perspective, there remains an ongoing search for novel therapeutic approaches. There is increasing evidence that cannabinoids and manipulation of the endocannabinoid system may have beneficial disease-modifying potential in ALS.[13-21] Moreover, the clinical effects of cannabis, the principal cannabinoid-producing botanical agent, have been reported to be useful in managing the symptomatology in ALS, as well as many other neurodegenerative disorders.[22-34] Thus, significant efforts are now being directed at evaluating the role of the endocannabinoid system in the pathophysiology of ALS. In addition, there is an emerging body of science that points to a role of exogenous cannabinoids in both clinical symptom management and a positive disease-modifying effect.[13-21]

The Physiology and Pharmacology of Cannabinoids

Prior to the last decade, there was little known about the specific pharmacological and molecular effects of cannabis. However, important advances have taken place recently, which have greatly increased the understanding of the receptors and ligands composing the endogenous cannabinoid system.[35-54] Research has shown that 2 major cannabinoid receptor subtypes exist, including the cannabinoid receptor, type 1 (CB1) subtype, which is predominantly expressed in the brain, and the cannabinoid receptor, type 2 (CB2) subtype, which is primarily found on the cells of the immune system.[35,49,50] A variety of ligands for these receptors based on the cannabinoid structure have been synthesized and studied. Experiments performed with several types of neural cells that endogenously express the CB1 receptor suggest that activation of protein kinases may be responsible for some of the cellular responses elicited by these receptors.[51] The discovery of the endocannabinoids, that is, endogenous metabolites capable of activating the cannabinoid receptors, and the understanding of the molecular mechanisms leading to their biosynthesis, release, and inactivation, have created a new area in research on the pharmaceutical applications of cannabinoid-based medicines.[52] The characterization of endocannabinoids such as anandamide and the detection of widespread cannabinoid receptors in the brain and peripheral tissues suggest that the cannabinoid system represents a previously unrecognized ubiquitous network in the nervous system.

Cannabinoid receptors are G protein-coupled, 7-segment transmembrane proteins, similar to the receptors of other neurotransmitters such as dopamine, serotonin, and norepinephrine.[51,52] Dense receptor concentrations are found in the cerebellum, basal ganglia, and hippocampus, likely accounting for the effect of exogenously administered cannabinoids on motor tone and coordination as well as mood state.[53-55] Low concentrations are found in the brain stem, accounting for the low potential for lethal overdose with cannabinoid-based medicines.[56-59] A growing number of strategies for separating sought-after therapeutic effects of cannabinoid receptor agonists from the unwanted consequences of CB1 receptor activation are emerging. Recently, ligands have been developed that are potent and selective agonists for CB1 and CB2 receptors, as well as potent CB1—selective antagonists and inhibitors of endocannabinoid uptake or metabolism.[60] In addition, varieties of cannabis are known to contain a mix of partial cannabinoid agonists and antagonists, which can be rationally used. This knowledge may lead to the design of synthetic cannabinoid agonists and antagonists as well as cannabis strains with high therapeutic potential. The fact that both CB1 and CB2 receptors have been found on immune cells suggests that cannabinoids play an important role in the regulation of the immune system. Recent studies show that cannabinoids downregulate cytokine and chemokine production, both mechanisms that suppress inflammatory responses.[61-64] Manipulation of endocannabinoids (ie, via the use of exogenous cannabis) has great potential treatment viability against inflammatory disorders, including the inflammation seen in the central nervous system (CNS) of the patients with ALS. The potential use of cannabinoids as a novel class of anti-inflammatory agents may become one of the predominant indications, as that includes not only neuromodulation but pain as well.[65,66] Indeed, any number of inflammatory processes that are at least partially triggered by activated T cells or other cellular immune components could be treated with cannabis and other cannabinoid-based medicines.

Cannabinoids are chemically classified as terpenes. These are lipid-soluble hydrocarbons that function as major biosynthetic cellular messengers in many forms of life. Terpenes are widespread in plants and most species of animals as well, including humans. Any compound that resembles the basic terpenes structure, yet may be modified chemically via oxidation or other processes, is termed a terpenoid. Many hormones, including estrogens, are terpenoids, and share the same basic organic chemical structure as cannabinoids.[53,54] All terpenes are organic, readily penetrate the highly lipophilic CNS.

Interestingly, tamoxifen, which is an antagonist of the estrogen receptor in breast tissue, is terpenoid and chemically resembles cannabinoids. Tamoxifen's primary use is as a FDA-approved drug for the treatment of breast cancer.[67-69] However, phase II clinical trials of tamoxifen in ALS have now demonstrated preliminary efficacy and safety.[68] A phase 2B study demonstrated increased survival after 2 years in patients with ALS taking higher doses of tamoxifen, with no effect seen in 2 lower dose groups.[68] The 3 higher dose groups experienced a 4- to 6-month prolongation of survival over a 24-month trial, with no significant side effects observed.[68] Interestingly, glutamate uptake in cultured retinal cells is inhibited by tamoxifen, thus this mechanism may be part of a possible beneficial effect in ALS.[67] The chemical similarity between cannabinoids and tamoxifen points to a possible shared mechanism of action for neural protection.[69]

The cannabis plant is a remarkably complex plant, with several phenotypes, each containing over 400 distinct chemical moieties.[70-73] Approximately 70 of these are chemically unique and classified as cannabinoids.[70-73] Delta-9 tetrahydrocannabinol (THC) and delta-8 THC appear to produce the majority of the psychoactive effects of cannabis.[74,75] Delta-9 THC, the active ingredient in dronabinol (Marinol), is the most abundant

cannabinoid in the plant, which historically led researchers to erroneously hypothesize that it was the main source of the drug's impact. It is now known that other major plant cannabinoids, including cannabidiol and cannabinol, modify the pharmacology of THC and have distinct effects of their own. Cannabidiol is the second most prevalent of cannabis's active ingredients and may produce most of its therapeutic effects. Cannabidiol becomes THC as the plant matures and this THC over time breaks down into cannabinol. Up to 40% of the cannabis resin in some strains is cannabidiol.[72] The amount varies according to plant. Some varieties of *Cannabis sativa* have been found to have no cannabidiol.[72] Cannabidiol breaks down to cannabinol as the plant matures. Much less is known about cannabinol, although it appears to have distinct pharmacological properties that are quite different from cannabidiol. Cannabinol has significant anticonvulsant, sedative, and other pharmacological activities likely to interact with the effects of THC.[75-78] Cannabinol may induce sleep and may provide some protection against seizures for epileptics.[78]

Hypothetical Applications

Preclinical Studies of the Endocannabinoid System in ALS

The primary murine model for human ALS is the G93A-SOD1 mutant mouse, which is genetically engineered to replicate familial ALS.[4] There is strong evidence in the G93A-SOD1 mouse model of ALS that the endocannabinoid system is involved, both directly and indirectly, in the pathophysiology of the disease. Several recent studies have highlighted this. Rossi et al[17] investigated both excitatory and inhibitory synaptic transmission in the striatum of symptomatic G93A-SOD1 ALS mice, along with the sensitivity of these synapses to CB1 receptor stimulation. They reported a reduced frequency of glutamate-mediated spontaneous excitatory postsynaptic currents and increased frequency of GABA-mediated spontaneous inhibitory postsynaptic currents in recordings from striatal neurons in ALS mice. This is likely due to some presynaptic defects in transmitter release. The sensitivity of CB1 receptors in controlling both glutamate and GABA transmission was potentiated in ALS mice. This provides good evidence that adaptations of the endocannabinoid system might be involved in the pathophysiology of ALS. This is not inconsistent with current theories on pathophysiological mechanisms of ALS, which still remain largely a pathophysiologic enigma.[79-83]

Bilsland et al[18] showed that treatment of postsymptomatic, 90-day-old SOD1G93A mice with a synthetic cannabinoid, WIN55,212-2, significantly delayed disease progression. Furthermore, genetic ablation of the fatty acid amide hydrolase (FAAH) enzyme, which results in raised levels of the endocannabinoid anandamide by preventing its breakdown, prevented the appearance of disease signs in 90-day-old SOD1G93A mice. Surprisingly, elevation of cannabinoid levels with either WIN55,212-2 or FAAH ablation had no effect on life span. Ablation of the CB1 receptor, in contrast, had no effect on disease onset in SOD1G93A mice but significantly extended life span. Together, these results indicate that cannabinoids have significant neuroprotective and disease-modifying effects in this model of ALS and suggest that these beneficial effects may be mediated by non-CB1 receptor-based mechanisms.

It is now known that during active neurodegeneration from disease or trauma in the CNS, the concentration of tumor necrosis factor alpha (TNF-α) rises well above normal levels during the inflammatory response. Addition of exogenous TNF-α, both in vitro and in vivo, to neurons has been shown to significantly potentiate glutamatergic excitotoxicity. Thus, the discovery of drug targets reducing excess TNF-α expression may help protect neurons after injury. Zhao et al[84] investigated the neuroprotective role of the CB1 receptor after TNF-α exposure in the presence or absence of CB1 agonists. They demonstrated that CB1 activation blocks the TNF-α-induced increase in inflammation, thus protecting the neurons from damage. Thus, neuroprotective strategies which increase CB1 activity may help to reduce damage to motor neurons in ALS that are mediated by CNS inflammation.

Additionally, CB2 receptors are dramatically upregulated in inflamed neural tissues associated with CNS disorders, including ALS.[85] In G93A-SOD1 mutant mice, endogenous cannabinoids are elevated in spinal cords of symptomatic mice.[21] Furthermore, treatment with nonselective cannabinoid partial agonists prior to, or on, symptom appearance minimally delays disease onset and prolongs survival through undefined mechanisms. Shoemaker et al[14] demonstrated that messenger RNA (mRNA) levels, receptor binding, and function of CB2, but not CB1, receptors are dramatically and selectively upregulated in spinal cords of G93A-SOD1 mice in a temporal pattern paralleling disease progression. Daily injections of the selective CB2 agonist AM-1241, initiated at symptom onset, increased the survival interval after disease onset by 56%.[14]

Disease-Modifying Treatment of ALS

Clinical trials for ALS have been largely based on preclinical work using the G93A-SOD1 mouse. Unfortunately, translation of therapeutic success in mice to humans has proven quite difficult and a cure for ALS is not yet known. Many factors have been implicated in explaining the predominantly negative results of numerous randomized clinical trials in ALS, including methodological problems in the use of animal-drug screening, the lack of assessment of pharmacokinetic profile of the drugs, and methodological pitfalls of clinical trials in patients with ALS. Riluzole is currently the only agent approved by the FDA for the treatment of ALS.[10] This drug inhibits the presynaptic release of glutamate and reduces neuronal damage in experimental models of ALS. Four controlled trials of a total of 974 riluzole-treated and 503 placebo-treated patients showed that it prolonged survival opposed to placebo, although the benefit was fairly modest.[10] Because oxidative stress is one of the proposed pathogenic factors in ALS, antioxidants have been extensively tested, including vitamin E, vitamin C, coenzyme Q, B-carotene, *N*-acetylcysteine, and creatine, an amino acid naturally found in skeletal.[11] To date, trials of

neurotrophic factors, antioxidants, glutamate antagonists, and creatine have all failed to show any significant benefit in humans, although most had significant benefit shown in mice.[11] It is currently felt that a cocktail approach may be the ideal treatment strategy, including glutamate antagonists, antioxidants, and neurotrophic factors.[68] Recently, the kynurenine pathway (KP) has emerged as a potential target for ALS treatment.[8] The KP is a major route for the metabolism of tryptophan, generating neuroactive intermediates in the process. These catabolites include the excitotoxic *N*-methyl-D-aspartate (NMDA) receptor agonist, quinolinic acid (QUIN), and the neuroprotective NMDA receptor antagonist, kynurenic acid (KYNA). These catabolites appear to play a key role in the communication between the nervous and immune systems and also in modulating cell proliferation and tissue function. Targeting the KP, hence, could offer a new therapeutic option to improve ALS treatment, and several drugs that block the KP are already under investigation.

Although other potential neuroprotective agents have been evaluated in randomized clinical trials, none have shown unequivocal benefit for the treatment of ALS. Thus, there remains an enormous need for more trials to test other putative disease-modifying therapies. As the effectiveness of such drugs can only be definitively established by large, costly, phase III randomized controlled studies, it is imperative that researchers target compounds that have potential benefit based on demonstrated pharmacological and physiological mechanisms.

There remains the possibility that ALS could represent a state of clinical endocannabinoid deficiency (CED).[28,31] The endocannabinoid anandamide demonstrates dopamine-blocking and anti-inflammatory effects and is also tonically active in the periaqueductal gray matter.[81] Endocannabinoids also modulate glutamatergic neurotransmission indirectly via NMDA receptors, and these pathways can be modulated to produce a clinical effect, such as reduction in motor tone, seizure threshold, and perception of pain and mood state.[82-93] These clinical, biochemical, and pathophysiological patterns could reflect an underlying abnormality in the endocannabinoid system in ALS that could be potentially treated with exogenous cannabinoids, that is, via clinical use of cannabis or some derivative thereof.

Practical Applications

Symptom Management in ALS

As discussed previously, animal studies strongly suggest that the endocannabinoid system is implicated in the pathophysiology of ALS, either directly as part of the underlying disease mechanisms, or indirectly, inasmuch as this system plays a role in the homeostatic functioning of the neuromuscular system. Irrespective, it is clear that cannabinoids are able to slow down the progression of ALS in mice, likely by acting as an antioxidant, among other mechanisms.[15-18] In addition to the neuroprotective effect, patients report that cannabis helps in treating symptoms of the disease, including alleviating pain and muscle spasms, improving appetite, diminishing depression, and helping to manage sialorrhea (excessive drooling) by drying up saliva in the mouth.[24] Indeed, in a large survey it was noted that patients with ALS who were able to obtain cannabis found it preferable to prescription medication in managing their symptoms. However, this study also noted that the biggest reason patients with ALS were not using cannabis was their inability to obtain it, due to legal or financial reasons or lack of safe access.[24,26]

There are many other clinical problems faced by patients with ALS that could be helped by cannabis. The majority of patients with ALS experience significant pain.[24] The pain is largely due to immobility, which can cause adhesive capsulitis, mechanical back pain, pressure areas on the skin, and more rarely, neuropathic pain.[24,31] Pain in ALS is a frequent symptom especially in the later stages of disease and can have a pronounced influence on quality of life and suffering.[94-98] Treatment of pain, therefore, should be recognized as an important aspect of palliative care in ALS. A recent Cochrane review of the evidence for the efficacy of drug therapy in relieving pain in ALS revealed no randomized or quasi-randomized controlled trials showing significant benefit. Despite the major pain problems encountered by patients with ALS, there are no clear guidelines and few randomized clinical trials about how to manage pain in ALS. However, as noted previously, the cannabinoids have been shown to produce an anti-inflammatory effect by inhibiting the production and action of TNF and other acute phase cytokines.[35] Additionally, cannabis may reduce pain sensation, likely through a brain stem circuit that also contributes to the pain-suppressing effects of morphine.[99] Cannabinoids produce analgesia by modulating rostral ventromedial medulla neuronal activity in a manner similar to, but pharmacologically distinct from, that of morphine.[100,101] This analgesic effect is also exerted by some endogenous cannabinoids (anandamide) and synthetic cannabinoids (methanandamide) and may be prevented by the use of selective antagonists.[102-104] Thus, cannabinoids are centrally acting analgesics with a different mechanism of action than opioids, although the analgesia produced by cannabinoids and opioids may involve similar pathways at the brain stem level.[103-105]

There are now multiple, well-controlled clinical studies using cannabis to treat pain, showing ample evidence of analgesic efficacy.[106] A recent systematic review and meta-analysis of double-blind randomized controlled trials that compared any cannabis preparation to placebo among participants with chronic pain showed a total of 18 completed trials. The studies indicate that cannabis is moderately efficacious for the treatment of chronic pain.[106] In the setting of ALS, the medications should be titrated to the point of comfort. Concomitant use of narcotics may also be beneficial because, as noted above, the opioid receptor system is distinct from the cannabinoid system. In that regard, the antiemetic effect of cannabis may help with the nausea sometimes associated with narcotic medications.

In addition to pain, spasticity is also a major problem for patients with ALS. Spasticity in ALS is induced both at the

motor cortex and at the spinal cord level through the loss of motor neuron inhibition.[107-110] Cannabis has an inhibitory effect via augmentation of γ-amino-butyric acid (GABA) pathways in the CNS.[111] This produces motor neuron inhibition at spinal levels in mice. Several past studies have suggested that cannabinoid therapy provide at least a subjective reduction of spasticity, although virtually all of the studies have been done in patients with multiple sclerosis (MS).[29,112] A survey study has shown that patients with ALS do subjectively report that cannabis helps alleviate symptoms of spasticity.[24]

In addition to pain and spasticity, there are other pharmacological effects of cannabis that may be useful for patients with ALS. Patients with ALS and bulbar symptoms also usually have difficulty controlling and swallowing the saliva that is normally present in the oral cavity.[113] Cannabis is a potent antisalivatory compound that swiftly dries the oral cavity and upper airway, potentially reducing the risk of aspiration pneumonia and increasing patient comfort.[22,24]

Cannabis also increases appetite and may help prevent "ALS cachexia," a phenomenon experienced by some patients where weight loss occurs in excess of that caused by muscle atrophy and reduced caloric intake.[114-116] In addition to improving appetite, cannabis appears to also help with mood state and sleep. Patients with ALS previously have reported that cannabis is at least moderately effective at reducing symptoms of pain, spasticity, drooling, appetite loss, and depression.[24]

Cannabinoids will vaporize at temperatures in the range of 200°F and can be inhaled via a hot mist.[117-119] This delivers the cannabinoids rapidly, allowing for ease of titration and letting patients with ALS having severe dysarthria rapid access to the drug's effects. Vaporizing also helps dry up oral secretions.[24] Cannabis may also be ingested orally or through a feeding tube, although absorption is much slower. Cannabis can be titrated to desired effect, with individual, patient-specific dosing.[120-122] In terms of clinical trials for disease-modifying effects, dosing paradigm would be more complex. Fortunately, the low toxicity of cannabis would allow for trail and error. Based on the available studies, a typical dosing range for clinical effects would likely be 1 to 2 g/d of cannabis, with an average THC content of 20% by weight.[122]

A Call for Clinical Trials

In terms of symptoms management, cannabis is a substance with many pharmacological properties that are directly applicable to the clinical care of patients with ALS. These include analgesia, muscle relaxation, bronchodilation, saliva reduction, appetite stimulation, sleep induction, and mood elevation.[24] From a pharmacological perspective, cannabis is remarkably safe with realistically no possibility of overdose or frank physical addiction. There is a valid, logical, scientifically grounded rationale to support the use of cannabis in the pharmacological management of ALS. Indeed, cannabis, as a single compound, could potentially replace and provide the benefits of multiple standard medications, including analgesics, antispasmodics, anxiolytics, antidepressants, appetite stimulants, and agents used to dry the mouth (typically anticholinergic medications). There is ample clinical evidence to warrant the empiric use of cannabis to manage the symptoms of ALS.

From an experimental, disease-modifying perspective, it is not likely that a single mechanism agent would treat all of the abnormal physiological processes occurring simultaneously in this devastating disease.[123-127] Thus, some experts are now advocating for a combination drug approach to slowing the progression of ALS.[80] Based on what is known about the pathophysiology of ALS, a multidrug regimen would include glutamate antagonists, antioxidants, a CNS anti-inflammatory agent, a microglial cell modulators, including TNF-α inhibitors, an antiapoptotic agent, 1 or more neurotrophic growth factors, and a mitochondrial function-enhancing agent.[127,128] Remarkably, cannabinoids appear to have at least some activity in all of those categories.[129-131] Moreover, there is a particularly strong, growing, body of preclinical data indicating that cannabis has powerful antioxidative, anti-inflammatory, and protective neuromodulatory effects.[132-135] In the G93ASOD1 ALS mouse, this has translated to prolonged neuronal cell survival.[15,16,18,43]

There is an overwhelming amount of preclinical and clinical evidence to warrant initiating a multicenter randomized, double-blind, placebo-controlled trial of cannabis as a disease-modifying compound in ALS. Secondary outcome measures could include clinical management, with end points such as pain scores, quality-of-life measures, and so on. Developing a multicenter clinical research trial using cannabis would pose many unique barriers that would have to be overcome. Inasmuch as there is no commercial manufacturer of cannabis, the study would have to be funded either by the federal government or privately. Presumably, there would be no industry funding. Obtaining the trial drug would require the investigators to gain access to a large, reliable supply of cannabis that is legal for medical research. At present, the only source of cannabis that can be legally used in research in the United States is through the National Institute on Drug Abuse (NIDA). National Institute on Drug Abuse provides low-potency material and makes the cannabis available only to projects it approves. National Institute on Drug Abuse supplies cannabis with a THC content, by weight, of 2% to 4% typically, although it has supplied cannabis with an 8% by weight THC content on occasion.[136,137] The average THC content of cannabis at randomly surveyed medical cooperatives in California is approximately 15% to 20%.[26,117,121] Thus, an independent source of cannabis would be needed to ensure a consistently high cannabinoid content that may be strong enough to possibly alter the disease progression. An independent cannabis source would also allow investigators to avoid NIDA's arbitrary and lengthy review process that it mandates before providing any cannabis for research. Historically, NIDA has derailed clinical trial plans by refusing to supply cannabis, even after the research protocols were approved by the FDA.[117] Nonetheless, it is possible, with coordinated effort, to effectively do double-blind, randomized, placebo-controlled clinical trials with cannabis.[138-141] To properly evaluate both subjective and objective

effects, cannabinoid blood levels should be followed as well, to further ensure adequate data for a dose–response curve.

Clinical trials with cannabis would also address the issue of single versus multiple drug clinical trials. Arguable, multiple drug trials would increase the chances of success but also exponentially increase the difficulty of completing the trial and analyzing the data. Cannabis, as a single agent, in essence provides the advantages of a multiple drug trial due to its multiple mechanisms of action. Cannabis is a unique compound that possesses significant internal therapeutic synergy. The search for the underlying cause of ALS continues.[142,143] With respect to treatment, from both a symptom management and disease modifying viewpoint, the logical next step, based on the available science, would be clinical trials with cannabis. Although not expected to be necessarily curative, it is not unreasonable to think that cannabis might significantly slow the progression of ALS, potentially extending life expectancy and substantially reducing the overall burden of the disease.

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Editorial

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Herbal Marijuana and Its Application in the Treatment of Parkinson's Disease

JH Lange[1], Albert V. Condello III[2]

1 Envirosafe Training and Consultants, 2366 Golden Mile Highway, Pittsburgh, USA
2 Cocciardi and Associates, Inc. 4 Kacey Court, Mechanicsburg, USA

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Corresponding Author: JH Lange

jhlange1@hotmail.com

Envirosafe Training and Consultants, 2366 Golden Mile Highway, Pittsburgh, PA 15239, USA

Tel: 717-766-4500

Editorial

Medical (herbal) marijuana (*Cannabis sativa*) is becoming a popular therapy for treatment of degenerative neurological diseases, including Parkinson's disease (PD) and other medical conditions [1,2]. Extracts from this plant have been used by ancient herbal practitioners over millennia in the treatment for a wide variety of diseases, which forms the basis of many claims today [3]. There are other forms of marijuana (Dronabinol, Nabilone and Nabiximole) available some having approval by federal agencies (Drug Enforcement Agency) [1]. However, clinical efficiency has been shown to be highly variable regarding the various forms of cannabinoids[4]. Use of herbal marijuana has been shown with a good degree of scientific certainly to be effective in treatment of some diseases [4,5]. Most notability, this agent has been shown to be beneficial regarding multiple sclerosis (MS) [6]. Recently, there has also been suggestion of its benefit for motor and non-motor symptoms of PD [7].

Alternative therapies are commonly included in treatment of PD patients along with conventional practices [8]. Presently, much of the initiative in using marijuana for treating PD and other types of neurological problems has been based on anecdotal information. Many of the claims regarding benefits of marijuana have not been adequately evaluated; although, current studies do suggest some applicability for treatment of pain, nausea, muscle spasticity, anorexia, sleep disturbances, in support of cancer (including chemotherapy), glaucoma, and Tourette syndrome, as examples [5]. Marijuana contains over 100 pharmacological active compounds and metabolites that can be generated each having a wide variety of physiological effects. In animal studies, marijuana and derivatives have been reported to provide protection, in some form, of the substantia nigra and as such reduce those neurons from damage or deterioration [9]. What should also be noted, similar findings have also been observed for Huntington's disease, MS, and Alzheimer's disease [1]. One of the major issues with using the herbal form of this drug for treatment relates to inconsistent concentrations of the active ingredients from available sources [10].

Few actual scientific studies have been conducted on herbal marijuana and PD. A subjective study reported benefits to PD patients [11]. This investigation noted that benefits may not be observed for months after application of this agent, indicating long-term use is necessary in achieving positive results. Insufficiency of treatment time may be one reason for inconsistent results reported in the literature [12]. In a small investigation [11], it was suggested cannabis consumption (smoking) improved motor function, and reduced tremor, rigidity and bradykinesia [7] which is similar to the subjective study. However, extracts of marijuana was shown to be ineffective in treatment of long-term levodopa induced dyskinesia [13]. Due to a small number of patients these studies must be considered pilot investigation [5] making conclusions difficult. Based on the study by Venderova et al. (2004) [11], not all patients report improvement from use of herbal marijuana, which may be considered a confounder due to the variability and differences in PD. It appears that about 15% of PD patients respond; although, when applied through long-term application, this increased to about 50% [11]. Herbal marijuana may only have a benefit for a sub-population of PD patients. When all the studies are evaluated together along with a self-reporting investigation [14], benefits of herbal marijuana for PD patients appear to exist. Many of the positive benefits reported include difficult to quantify outcomes (i.e. mood improvement) creating inconsistencies among studies.

Use of herbal marijuana has been shown to have benefits increasing the quality of life for those inflected in PD. Studies evaluating this agent have employed small populations limiting conclusions, but overall can be considered positive. It is likely a select group of PD patients will benefit from use of this herb. Large randomized clinical trials are needed to better elucidate efficacy of this herb and methods of delivery for PD patients.

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