"Aegis" means to defend or protect and is the name of the mythical shield used by the Greek god Zeus. This name was chosen to represent our services that are designed to defend the integrity and welfare of our clients.
March 9, 2015

Re: The Marijuana Project

Dear Elected Representative,

Serving in elected office carries great responsibilities and often requires addressing even greater challenges. You are expected to be “all knowledgeable” and render the best decisions for your constituents and communities. Often, the issues most controversial are those with the greatest need for accurate basic knowledge.

“Medical” and legalized marijuana are two current societal challenges. Information has been provided from several advocacy groups and much of it is contradictory. Are the concerns for health and safety well founded in science and medicine, or is the control of *cannabis sativa* merely a political and emotional issue? Is the law too harsh or is the restraint on adult personal choice too severe? Where is the balance between individual rights and responsibilities?

*Cannabis sativa* is an intoxicating plant known to science and medicine since 6,000 years before the time of Christ. During this time, neither accepted medical application nor formal social acceptance has been achieved for this plant. To the contrary, medical benefits have been elusive and limited while society has dealt with negative impacts on both health and safety. In spite of claims to the contrary the factual record is clear. Only in the past several years, with generous private funding, has the science been distorted to convey that marijuana is safe and harmless. Cleverly stated mistruths and biased presentation of facts have resulted in many states enacting legalization for either “medical” or recreational use of marijuana.

In the following pages, you will find a booklet entitled “The Marijuana Project” citing scientific and medical peer-reviewed literature regarding the risks to health and safety resulting from the use of *cannabis sativa*. We have endeavored to be focused and succinct in the literature references provided. We know your time is valuable and the demand on your decision making is great. However, we believe several minutes of your time reviewing this material will allow you to make a better educated decision on this very important issue. Your decision related to this matter is a great responsibility since it will literally decide the quality of life for your constituents…and perhaps even save their lives.

Should you require extra copies of “The Marijuana Project”, additional information, or would like to discuss the issue, please do not hesitate to contact Aegis at (615) 255-2400. Our team of pharmacologists, toxicologists, physicians and other healthcare professionals will be happy to answer any questions or provide additional data.

Sincerely,

[Signatures]

David L. Black, PhD, D-ABFT, F-AIC  
Founder, CEO and Chairman

Timothy A. Robert, PhD, D-ABCC  
Chief Science Officer

Anne Z. DePriest, PharmD, BCPS  
Senior Scientist, Healthcare
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CURRENT LEGAL STATUS OF MARIJUANA

• Marijuana is a Schedule I controlled substance as established by the Controlled Substance Act (21 U.S.C.) which was passed in 1970. By definition, Schedule I substances have “no currently accepted medical use in treatment in the United States,” “a lack of accepted safety for use of the drug under medical supervision,” and a “high potential for abuse.” At least twenty-three states and the District of Columbia have passed laws allowing for public medical marijuana programs. At least eleven additional states permit limited use of “low THC, high cannabidiol” products for medical purposes. Four states and the District of Columbia currently permit recreational use. Marijuana use is still considered to be a federal offense, because it is classified as a Schedule I substance regardless of state law.

MEDICINAL USE

• Medical marijuana bypasses the safeguards established in the pharmaceutical industry to ensure the quality, safety, and effectiveness of medications consumed by the public.
• The DEA supports research on the medicinal use of active marijuana ingredients and public access to these medications once they are sent through the appropriate FDA approval process.
• Synthetic delta-9-tetrahydrocannabinol (THC), dronabinol (Marinol®), and a synthetic cannabinoid, nabilone (Cesamet®), are currently approved by the FDA to treat nausea and vomiting induced by chemotherapy in patients who have failed to respond to other antiemetic therapy. Dronabinol is also approved for use as an appetite stimulant in patients with AIDS.
• In order to argue in favor of crude marijuana being available for medicinal purposes, it must prove to offer advantages over FDA-approved medications. THC (ingredient in dronabinol and chemical analogue of nabilone) is one of > 60 active compounds, called cannabinoids, found in Cannabis sativa (crude marijuana) which includes up to 500 substances. Oral synthetic cannabinoids (dronabinol and nabilone) possess standardized concentrations and do not contain other potentially dangerous compounds.
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* Laws not yet in effect as of 19 February 2015.
PRESCRIPTION DRUG PRODUCTS

- Standardized active drug content
- Safety and efficacy established in clinical trials
- Patient information/dosing guidance available
- Quality controlled for purity
- Regulated
- Covered by insurance policies
- No medications in the U.S. are FDA-approved for administration through smoking

MEDICAL MARIJUANA

- Inconsistent drug content
- Safety not established; efficacy largely based on anecdotal evidence
- Reliable patient information/guidance not available
- Subject to contamination and inconsistency
- Unregulated/no manufacture accountability
- Lack of insurance coverage
- Smoking is considered to be a harmful mode of administration

“Charlotte’s Web” has been highly publicized as a strain of marijuana which contains relatively high amounts of cannabidiol and low amounts of THC. It is administered by mouth in an oil formulation for treatment of rare seizure disorders. Cannabidiol is one of the cannabinoids in marijuana and is thought to lack the psychotropic effects associated with THC and may also alter the effects of THC. Historically, marijuana strains have been bred to contain high THC and low cannabidiol content. “Charlotte’s Web” products lack regulatory oversight and their content, therapeutic activity, and purity are therefore not predictable or consistent.

Controlled studies concerning the use of cannabidiol for seizures are limited, and stronger clinical evidence is needed. GW Pharmaceuticals, a United Kingdom-based drug company involved in development of cannabinoid pharmaceuticals, has received an orphan drug designation for Epidiolex® (cannabidiol), which is a purified liquid formulation. This product is used for the treatment of Dravet syndrome, a severe epilepsy disorder with infantile onset that generally exhibits resistance to drug treatment. Epidiolex® is still an investigational drug and has not been approved for use by the FDA.
• The conditions below have been implicated as potential areas for intervention with medical marijuana; however, most studies showing clinical improvements with use of smoked cannabis had very small sample sizes and, if compared to FDA-approved synthetic cannabinoids or other available medications, did not demonstrate additional benefits.

♦ Nausea/vomiting with chemotherapy
♦ Appetite stimulation (HIV, Cancer)
♦ Analgesia
♦ Multiple sclerosis
♦ Spinal cord injury
♦ Tourette's syndrome
♦ Epilepsy
♦ Glaucoma
♦ Parkinson disease
♦ Dystonia
SOURCES:


SAFETY CONCERNS

- Crude marijuana is not regulated by a governing body which raises concerns regarding its content, quality, and potency. The literature describes reports of marijuana contaminated with harmful substances, including lead and pesticides. Recent data from the National Institute on Drug Abuse (NIDA) reports the current average THC content in seized marijuana samples is 12.55% compared to an average close to 4% in the early 1980s. This raises concern for an increase in harm and risks associated with use.
- A study comparing marijuana smoke to tobacco smoke showed that marijuana smoke had up to 20 times more ammonia in mainstream smoke versus tobacco. Hydrogen cyanide, nitric oxide, and several aromatic amines were 3-5 times higher in marijuana smoke versus that of tobacco smoke.
- Exposure to second hand marijuana smoke may lead to adverse effects in those exposed to it due to the presence of carcinogens and other chemicals.
- Approval of medical marijuana may lead to increases in inadvertent exposure (e.g., drug ingestion), particularly by children. One study demonstrated half of the reported exposures involved marijuana “edibles” (e.g., cookies, cake, and candy). Increased access to marijuana may correlate to increases in unintentional exposure to the drug. Edible forms of the drug may be deceptive and conceal the true content of the product.
- In Colorado, exposures in children up to 5 years old increased 268% from 2006-2009 to 2010-2013.
- Calls to U.S. poison centers regarding unintentional marijuana exposure in children have tripled in states allowing recreational and medicinal use of marijuana compared to no change in states not allowing use.
SOURCES:


14. Center for Substance Abuse Research. Rate of poison center calls for unintentional pediatric marijuana exposures more than tripled in states that decriminalized marijuana before 2005. CESAR FAX 2014; 23(8)(Rev).

ADVERSE EFFECTS

- Despite its societal reputation of being a benign drug, marijuana has been associated with a multitude of adverse effects, including severe cardiovascular and cerebrovascular events leading to death. Recent Drug Abuse Warning Network (DAWN) data implicate marijuana as second only to cocaine in the involvement of emergency department (ED) visits associated with illicit drugs.
- In 2011, 455,668 ED visits involved marijuana, affecting 36.4% of ED visits attributed to illicit drug use.
- ED visits involving marijuana increased by 62% between 2004 and 2011.

• Suicide attempts strongly correlate with substance abuse. According to 2011 DAWN data, marijuana was involved in nearly 7% of ED visits associated with drug-related suicide attempts and was the most common illicit drug associated with this type of visit.

• Neuropsychological decline and mental illness are a particular concern in individuals initiating use in early adolescence and continuing chronic use.

• Below are adverse effects associated with marijuana use. Those who already have predisposed risk factors for the adverse effects below are especially at risk.

  ◆ Acute mental effects
    o Short-term memory deficit
    o Impaired motor coordination
    o Heightened sensory perceptions
    o Alteration of time perception
    o Altered judgment
    o Anxiety/panic
    o Derealization
    o Disordered thinking
    o Emotional liability
    o Hallucinations
    o Paranoia
    o Psychosis
    o Confusion

  ◆ Neuropsychological decline
    o Altered brain development
    o Decreased IQ score
    o Decreased memory
    o Decreased visual processing speed

  ◆ Increased risk for psychotic disorders (e.g. schizophrenia) or worsening of psychotic disorders

  ◆ Hyperemesis syndrome (excessive vomiting and abdominal pain accompanied by compulsive showering)

  ◆ Pancreatitis
• Cardiovascular and cerebrovascular effects
  o Hypertension/hypotension
  o Tachycardia
  o Cardiomyopathy
  o Myocardial infarction
  o Transient ischemic attack/stroke
  o Sudden cardiac death
  o Death from cerebrovascular stroke

• Pulmonary effects
  o Wheezing
  o Cough
  o Chest tightness
  o Sputum production
  o Large airways obstruction
  o Hyperinflation

• Fertility concerns
  o Decreased luteinizing hormone levels in women during the luteal phase
  o Disruption of menstrual cycle
  o Reduced sperm count

• Drug-drug interaction concerns
  o Additive central nervous system (CNS) depression
    ■ Benzodiazepines, opiates, alcohol, barbiturates, antihistamines, muscle relaxants
  o Additive cardiovascular concerns
    ■ Amphetamines, cocaine, antihistamines, anticholinergic agents, tricyclic antidepressants
  o Case reports of drug-drug interactions
    ■ Tricyclic antidepressants (tachycardia and delirium)
    ■ Fluoxetine (manic symptoms)
    ■ Protease inhibitors (decreased drug concentrations)
    ■ Sildenafil (myocardial infarction)
    ■ Warfarin (upper gastrointestinal bleed)
    ■ Theophylline (rapid clearance of drug)
    ■ Cisplatin (stroke)
◆ Withdrawal syndrome
  o Dysphoria
  o Craving
  o Anger/aggression
  o Irritability
  o Anxiety
  o Restlessness
  o Insomnia
  o Weight loss
  o Chills
  o Fever
  o Tremor
  o Sweating
  o Headache
  o Depression
  o Stomach pain

◆ Minor effects
  o Blurred vision
  o Dizziness
  o Somnolence
  o Dry mouth and eyes
  o Conjunctivitis
  o Urinary retention
  o Increased appetite
SOURCES:


30. Lindsey WT, Stewart D, Childress D. Drug interactions between common illicit drugs and prescription thera-
PREGNANCY IMPLICATIONS

- Marijuana is the most prevalently used illicit drug during pregnancy. Because of its chemical nature, one-third of THC ingested during pregnancy will cross the placenta, which may result in harmful side effects for the fetus. The following adverse effects have been associated with gestational exposure to marijuana:

  - Neural tube defects
    - Anencephaly (a terminal condition in which the baby is born missing pieces of brain and skull)

  - Gastroschisis (a birth defect where the intestines protrude outside the abdominal wall)

  - Childhood psychiatric disorders
    - Depression
    - Attention deficit disorders
    - Hyperactivity

  - Neurodevelopmental delays
    - Decreased IQ scores
    - Decreased educational achievement and academic performance


IMAGE SOURCE: http://www.cdc.gov/ncbddd/birthdefects/gastroschisis.html
o Decreased motor development
o Memory impairment

- Other adverse effects:
  o Risk for substance use during early adulthood
  o Pre-term delivery
  o Low birth weight
  o Miscarriage
  o Meconium staining
  o Disturbed sleeping patterns of the child
  o Ventricular septal defects (a congenital heart defect)
  o Neuroblastoma (a type of malignant tumor)
  o Immune dysfunction
SOURCES:


CANNABIS DEPENDENCE AND ADDICTION

- Users may develop cannabis use disorders, including drug dependence and addiction, and may also suffer withdrawal symptoms with cessation.
- It has been estimated up to 10% of individuals who use cannabis may become dependent. According to the 2012 National Survey on Drug Use and Health, marijuana was associated with the most reported cases of past year dependence or abuse of any illicit drug, representing nearly 2% of the total population of those age 12 and older and 60% of those with illicit drug dependence or abuse.
- Substance abuse treatment admission rates for marijuana generally exceed those associated with any other illicit drug. Individuals who initiate marijuana use in adolescence are 2 to 4 times more likely to develop dependence within the first two years of initiation.
- Residents of states with medical marijuana laws have been shown to have greater odds for marijuana abuse/dependence, although future research is warranted.
- DAWN estimates that of the 250,596 drug-related ED visits for patients seeking detox or substance abuse treatment services during 2011, approximately 14.5% involved marijuana.

SPECIFIC ILLICIT DRUG DEPENDENCE OR ABUSE IN THE PAST YEAR AMONG PERSONS AGED 12 OR OLDER: 2012

SOURCES:


DRIVING UNDER THE INFLUENCE OF DRUGS (DUID)

• Driving under the influence of marijuana has been shown to negatively impact driving performance, including impaired reaction time, lane position variability, and compromised cognitive function. This may lead to increased risk for accidents, hospitalizations, and fatalities. Evidence suggests the risk of a motor vehicle accident doubles when an individual is intoxicated by cannabis, and marijuana is often used in conjunction with other drugs, such as alcohol, which further increases associated risks.

• One study found illicit drugs in 86% of blood specimens obtained from drivers stopped for driving under the influence. Marijuana was the most prevalent drug detected within this category.

• Washington State Toxicology laboratory data from 2013 demonstrated 41.4% of total DUID cases were positive for marijuana metabolite (considered positive if blood concentration was ≥2 ng/mL).

• Marijuana has been associated with fatal motor vehicle accidents. In a study across 6 U.S. states (CA, HI, IL, NH, RI, WV) of toxicology results in drivers who died within an hour of a motor vehicle accident from 1999-2010, the prevalence of marijuana results in 2010 was triple that of 1999. Marijuana had the highest prevalence of non-alcohol drugs detected by the end of the study period.

• A study by the California Department of Motor Vehicles found a 315%, 196%, and 432% increase in cannabinoid prevalence among fatally-injured drivers following the enactment of medical marijuana laws in California, Hawaii, and Washington, respectively.

• The number of fatal motor vehicle accidents increased 100% in the first five years after legalization of medical marijuana in California compared to the five-year period prior. Drivers involved in traffic fatalities and testing positive for marijuana have increased 100% in Colorado from 2007 to 2012.

• Data from the first six months of 2014 reported by the Colorado State Patrol DUID program showed that 77% of DUIDs involved marijuana; 42% involved marijuana alone.
SOURCES:


INDIVIDUAL AND SOCIETAL EFFECTS

- Use of marijuana is associated with decreased academic performance and achievement and an increased risk of school drop-out. Cannabis use may be associated with lower income, higher unemployment rates, decreased work commitment, and greater utilization of social assistance programs.

- A prospective study spanning 20 years, and including more than 1,000 subjects, demonstrated the most chronic users of cannabis from adolescence experienced an average 8-point IQ decline by adulthood.

- Heavy marijuana use in adolescence may increase likelihood for future involvement in drug and property crime and interaction with the criminal justice system. Prevention of adolescent marijuana use is imperative as marijuana use may lead to further illicit drug use, particularly when use is initiated at a younger age.
SOURCES:


QUOTES FROM PROFESSIONAL ORGANIZATIONS

“Marijuana is currently categorized as a Schedule I drug under the Controlled Substances Act (CSA), Title 21 U.S.C.§801, et seq. This classification does not interfere with allowing research, and for those drugs formulated with the plant or its crude extracts from being reviewed and approved by the FDA.”

–U.S. Department of Justice Drug Enforcement Administration

“(1) cannabis is a dangerous drug and as such is a public health concern; (2) sale of cannabis should not be legalized; (3) public health based strategies, rather than incarceration, should be utilized in the handling of individuals possessing cannabis for personal use; and (4) additional research should be encouraged.”

–American Medical Association

“The ACS is supportive of more research into the benefits of cannabinoids. Better and more effective treatments are needed to overcome the side effects of cancer and its treatment. The ACS does not advocate the use of inhaled marijuana or the legalization of marijuana.”

–American Cancer Society

“There is no current scientific evidence that marijuana is in any way beneficial for the treatment of any psychiatric disorder. In contrast, current evidence supports, at minimum, a strong association of cannabis use with the onset of psychiatric disorders...Medical treatment should be evidence-based and determined by professional standards of care; it should not be authorized by ballot initiatives.”

–American Psychiatric Association

“Data are inadequate to determine the safety or efficacy of smoked cannabis used for spasticity/pain, balance/posture, and cognition [regarding multiple sclerosis].”

“For patients with epilepsy, data are insufficient to support or refute the efficacy of cannabinoids for reducing seizure frequency...”
“For patients with Tourette syndrome, data are insufficient to support or refute efficacy of THC for reducing tic severity...”
–American Academy of Neurology

“Although marijuana can lower the intraocular pressure (IOP), its side effects and short duration of action, coupled with a lack of evidence that its use alters the course of glaucoma, preclude recommending this drug in any form for the treatment of glaucoma at the present time.”
–American Glaucoma Society

“Ultimately, the behavioral and health risks associated with marijuana use by youth should be the most salient criteria in determining whether policies that are enacted are effective in minimizing harm...The AAP opposes legalization of marijuana because of the potential harms to children and adolescents.”
–American Academy of Pediatrics

“Marijuana smoke contains a greater amount of carcinogens than tobacco smoke. In addition, marijuana users usually inhale more deeply and hold their breath longer than tobacco smokers do, further increasing the lungs exposure to carcinogenic smoke....People who smoke marijuana frequently, but do not smoke tobacco, have more health problems and miss more days of work than nonsmokers. Many of these extra sick days are due to respiratory illnesses.”
–American Lung Association

“Legalization of marijuana for medicinal or recreational purposes, even if restricted to adults, is likely to be associated with (a) decreased adolescent perceptions of marijuana’s harmful effects, (b) increased marijuana use among parents and caretakers, and (c) increased adolescent access to marijuana, all of which reliably predict increased rates of adolescent marijuana use and associated problems. Marijuana use during pregnancy raises additional concerns regarding child and adolescent development...As child and adolescent mental health advocates, AACAP (a) opposes efforts to legalize marijuana...”
–American Academy of Child & Adolescent Psychiatry
“We want to make it perfectly clear that the state initiatives will have no bearing on the Department of Transportation’s regulated drug testing program. The Department of Transportation’s Drug and Alcohol Testing Regulation-49 CFR Part 40—does not authorize the use of Schedule I drugs, including marijuana, for any reason.”

—Department of Transportation

“ASAM asserts that the anticipated public health costs of marijuana legalization are significant and are not sufficiently appreciated by the general public or by public policymakers...In summary, ASAM recommends against the approval of state initiatives to legalize marijuana.”

—American Society of Addiction Medicine
SOURCES:


