"Experience without memory is useless." —Martha Gellhorn

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Benefit too obvious to deny:

U.S. weighs rescheduling a molecule as CBD-rich cannabis proves helpful to children with epilepsy and others

By Fred Gardner

In August 2013, the widely respected neurosurgeon Sanjay Gupta, MD, documented on television the dramatic seizure relief that CBD-dominant cannabis oil was affording a little girl with Dravet Syndrome, a very severe form of epilepsy. Her name was Charlotte Figi.

In the two years that followed, reports from physicians treating pediatric epilepsy patients in various contexts —including "expanded access" programs authorized by the U.S. Food and Drug Administration— have confirmed that CBD is an effective anti-convulsant.

Bonni Goldstein, MD, in California and Margaret Gedde, MD, in Colorado have each monitored the progress of hundreds of pediatric epilepsy patients. *(See stories on pages 7 and 33.)* More than 600 patients have been treated in FDA-sanctioned programs using GW Pharmaceuticals' Epidiolex, a plant extract that is 99% CBD.

Slightly more than half the children using CBD-rich oil are having significantly fewer and less-severe seizures. Personalities and abilities emerge as children wean off debilitating synthetic anti-convulsants. The side effects of CBD are generally mild; drowsiness is foremost.

Why CBD-rich oil works for some patients but not for others is being pursued by researchers.

For a fortunate five to 10 percent of patients, CBD-rich oil eliminates seizures entirely. For an approximately equal number, it doesn't help at all, or exacerbates symptoms.

Why CBD-rich oil works for some patients but not for others is being pursued by researchers. In most pediatric epilepsy cases the conditions are caused by genetic mutations. Some but not all gene-based epilepsies are amenable to treatment with CBD, and some are proving amenable to treatment with CBD plus THC and other cannabinoids.

Doctors and patients are tracking which cannabinoid-terpenoid blends are most effective in treating various conditions.

Paige Figi's daughter Charlotte experienced dramatic seizure reduction after being given CBD-rich cannabis. Fifteen states have adopted bills legalizing CBD for medical use. Figi is lobbying Congress in support of a bill that would remove CBD from Schedule I, the category for dangerous drugs with no known medical use.

Diverse Sources of Cannabidiol

Sanjay Gupta, MD, interviewed Geoffrey Guy, MD, at a facility in England where Guy's GW Pharmaceuticals grows CBD-rich *Cannabis* plants and makes extracts for medical use. Epidiolex, a GW extract that is 99% CBD, is being given to children with severe epilepsy at research centers in the U.S. Graphic: CNN

"Mom-and-pop growers" in Nevada County, California, organized a plant giveaway featuring CBD strains ACDC, Harlequin, Medi-Haze and Cannatonic. Oil made from CBD-rich plants is distributed by dispensaries that are legal under state law. Physicians are monitoring the progress of pediatric epilepsy patients using CBD-rich oil.

Cannabis oil is made by treating harvested plants with a solvent that extracts beneficial compounds and leaves behind the cellulose. Like Charlotte Figi, many people who use CBD need large, sustained doses to deal with serious illness. The most efficient delivery vehicle is a cannabis extract —for example, 50 milligrams of CBD in a milliliter of olive or coconut oil— in droppers or tubes. Cannabis oil can be diluted to facilitate measured dosing.

Lower doses of CBD can be delivered in sprays for under-the-tongue application. Few patients who use cannabis in treating epilepsy smoke or inhale vapor from CBD-rich flowers, although some report that inhalation after a seizure can reduce the duration of a headache.

Inhaled cannabis goes through the lungs to the brain and exerts its effects almost immediately, but the effects tend to wear off within an hour. Ingested orally, the compounds in cannabis pass through the stomach and the liver on the way to the brain. They get metabolized into slightly different compounds whose effects may take close to an hour to come on, but can last eight or nine hours.

CBD counters the mood-altering effects of THC, but as a component of the *Cannabis* plant, it is defined by the U.S. government as harmful and without medical use, and it remains on Schedule I of the federal Controlled Substances Act. There is an obvious gap between federal law and reality. It can be fully closed by rescheduling or descheduling the plant, and partially closed by singling out cannabidiol for descheduling.

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For a slimmer waistline?

THCV plants being grown for medical use in California; Cannabinoid may counter metabolic-syndrome symptoms

By O'S News Service

Cannabis varieties containing unusually high amounts of THCV —tetrahydrocannabivarin—will become available to medical users in 2016, thanks to kind fate and propagators who chose not to hoard their unusual bounty.

The difference between THCV and THC is slight at the molecular level *(two fewer carbon atoms in the "tail" —see illustration on page 21)*, but susbtantial in terms of how they work and their impact on the body.

GW Pharmaceuticals began investigating THCV more than a decade ago in hopes that it could be useful in treating metabolic syndrome. The disorder is actually a set of symptoms —high blood pressure, increased abdominal fat, elevated blood sugar, and unhealthy cholesterol levels— that are associated with obesity, type II diabetes and heart disease.

Roger Pertwee and colleagues at the University of Aberdeen reported in 2005 that THCV blocked anandamide (the molecule made by our bodies that activates the CB1 receptor) while allowing THC to act almost unimpeded at CB1. John McPartland commented on Pertwee's finding: "It's as if cannabis was designed as a combination remedy that simultaneously gave our endogenous mechanism a rest (shutting down anandamide), and supplemented with an exogenous remedy (THC)."

Also in 2005 the pharmaceutical giant Sanofi-Aventis had begun marketing a drug called Rimonabant —which works by fully blocking the CB1 receptor— as a treatment for metabolic syndrome. The first-ever mention of the endocannabinoid system in the *Journal of the American Medical Association* was a paper entitled "Effect of Rimonabant, a Cannabinoid-1 Receptor Blocker, on Weight and Cardiometabolic Risk Factors in Overweight or Obese Patients: RIO-North America: A Randomized Controlled Trial," published in February 2006 —about 14 years after the components of the system had been identified.

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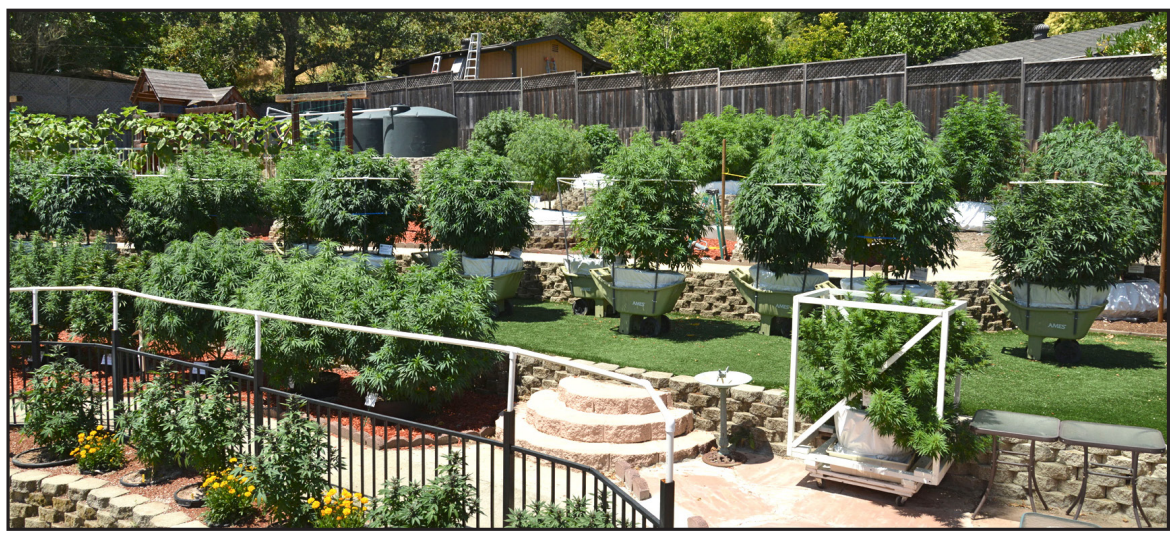


'Black Beauty' plants high in THCV were grown in western Marin County, California, in the summer of 2015. Elevated pots enable "wicking" of water (with fertilizer).

CBDevelopments *from page 1*

The Road to FDA Approval

In 1998 GW Pharmaceuticals received approval from the British Home Office to develop medicines from *Cannabis* plant extracts featuring cannabinoids other than THC and delivered by means other than smoking. In numerous lab studies CBD has been shown to exert various beneficial effects, and GW has been developing medicines designed to treat a wide range of illnesses.

GW's flagship product Sativex —which contains an equal mix of CBD and THC— was the first plant-derived cannabinoid medicine to win approval from regulatory authorities. An extract formulated for spraying under the tongue, it has been approved in 27 countries (starting with Canada in 2005) for treating pain and spasticity in Multiple Sclerosis.

In recent years GW has been testing various formulations and providing CBD to scientists conducting preclinical studies in animals. GW supplied Ben Whalley and colleagues at the Center for Integrative Neuroscience and Neurodynamics, University of Reading, who used mouse models of epilepsy to establish safety and show that CBD and another cannabinoid, CBDV, exert anti-seizure and anti-inflammatory effects. This research came to the attention of families in the U.S. who had loved ones with epilepsy.

In late 2012 some American parents contacted GW in hopes of obtaining CBD.

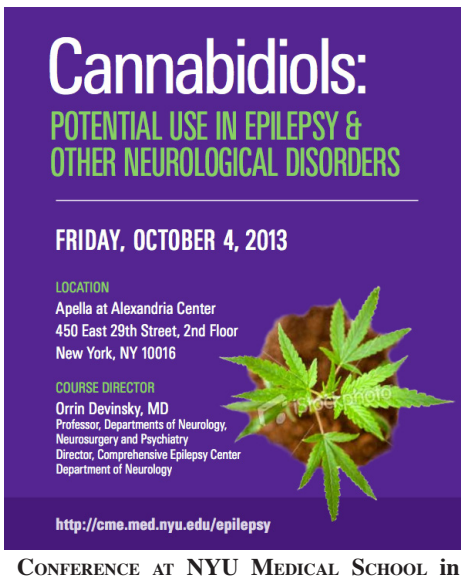
"Expanded Access"

Physicians, patients, and parents know that currently used anti-epilepsy drugs (AEDs) are detrimental to cognition and longterm development. CBD is way, way milder than conventional anti-convulsants in terms of side effects.

In late 2012 some American parents contacted GW in hopes of obtaining CBD. They asked if the company could provide CBD to the physicians treating their children under the Food and Drug Administration's "Expanded Access" IND program.

GW, which had been working closely with the FDA in connection with Sativex, looked into the IND option and decided the expanded access regulations might indeed allow the company to provide Epidiolex to the parents, even though it was an investigational medicine.

Back in 1978 —the Jimmy Carter era— the FDA had established a so-called "compassionate IND program" through which a few patients received marijuana grown at the University of Mississippi for the National Institute on Drug Abuse. The program was closed to new patients in 1990 —the George H.W. Bush era— as AIDS patients began applying en masse, thanks to the organizing efforts of Robert and Alice O'Leary Randall. The IND program existed in bureaucratic limbo until 1997, when Congress passed the Food and Drug Administration Modernization Act.



Conference at NYU Medical School in October 2013 featured a report by Orrin Devinsky, MD, on a Dravet Syndrome patient achieving dramatic seizure reduction by medicating with a 99%-CBD plant extract from GW Pharmaceuticals. Other epilepsy specialists at US research centers are now using GW's "Epidiolex" in Investigational New Drug studies. Some 400 children were being treated at 17 sites as of October 2014.

The FDA then developed regulations covering IND studies for unapproved drugs. These were revised over the years, and in August 2009 FDA issued its "final rule" on "Expanded Access to Investigational Drugs for Treatment Use." The summary states:

"Expanded access to investigational drugs for treatment use is available to individual patients, including emergencies; intermediate-size patient populations; and larger populations under a treatment protocol or treatment investigational new drug application (IND). The final rule is intended to improve access to investigational drugs for patients with serious or immediately life-threatening diseases or conditions who lack other therapeutic options and who may benefit from such therapies."

The FDA regulations spell out criteria for INDs. The would-be investigator must submit, among other things: "Chemistry, manufacturing, and controls information adequate to ensure proper identification, quality, purity, and strength of the investigational drug."

In other words, FDA wants to see a highly standardized, tested, "Good-Manufacturing-Practices" medication —which Epidiolex is. NIDA is still providing Mississippi-grown cannabis cigarettes to four surviving beneficiaries of the old, informal IND program. Those cigarettes would not be approved as a treatment under the current FDA regulations.

The FDA requires "Pharmacology and toxicology information adequate to conclude that the drug is reasonably safe at the dose and duration proposed for the treatment use."

When GW was approached by the parents of epilepsy patients in late 2012, the company already possessed extensive preclinical data —five-and-a-half years' worth— establishing the safety of its CBD product, as well as information the FDA would require concerning its chemistry, manufacturing, controls, pharmacology, and toxicology.

In December 2012 GW agreed to provide purified CBD and the requisite data for single-patient INDs conducted by epileptologists Roberta Cilio, MD at UC San Francisco, and Orrin Devinsky, MD at NYU School of Medicine

In October 2013 GW supported and NYU sponsored a meeting in New York of epilepsy specialists interested in conducting clinical research with purified CBD in the United States. Devinsky described dramatic benefit provided to his initial patient by CBD treatment, and his plans to conduct an IND treatment program at NYU. Many of the doctors at the conference asked to sponsor INDs at their institutions. GW agreed to provide them with Epidiolex.

By January, 2014, INDs conducted by Devinsky at NYU (60 patients) and Roberta Cilio at UCSF (25 patients) were underway. The patients were children and young adults with various forms of Treatment Resistant Epilepsy. Each patient's frequency of seizures had been determined by parents keeping detailed diaries for a month to establish baselines prior to treatment with Epidiolex. Patients continued taking the anti-epilepsy drugs they'd been on. They were started on Epidiolex doses of five milligrams per kilogram of body weight per day, divided into morning and evening portions. The dose was increased weekly by five mg/kg/day up to 25 mg/kg/day.

In June 2014 GW announced efficacy and safety data on the first 27 patients to have been treated for 12 weeks (the minimum amount of time determined to offer accurate effectiveness measure). Epidiolex had enabled 48% to achieve at least a 50% reduction in seizure frequency compared to baseline.

Epidiolex enabled 48% to achieve at least a 50% reduction in seizure frequency compared to baseline.

Over the course of 2014, physicians would conduct Treatment-Resistant Epilepsy INDs at The Children's Hospital of Philadelphia, Lurie Children's Hospital in Miami, Pediatric and Adolescent Neurodevelopmental Associates in Atlanta, Texas Children's Hospital, MassGeneral Hospital for Children, the University of Utah Medical Center, Wake Forest School of Medicine, and Nationwide Children's Hospital in Columbus, Ohio.

Thanks to organizing efforts led by Paige Figi, a dozen states enacted laws in 2014 that legalized the medical use of CBD; some even provided money for research. By 2015 health departments in four states —Georgia, New York, Alabama, and Florida— were funding INDs, picking up the tab for physician visits, lab tests, data collection, and Epidiolex (which GW donated to hospital-funded INDs). More than 200 patients would soon be enrolled in state-sponsored INDs.

Efficacy documented

In April, 2015, at a meeting of the American Academy of Neurology, Devinsky was lead author on a poster presenting efficacy data on 137 patients who had completed 12 weeks of treatment with Epidiolex. There were 25 Dravet Syndrome and 22 Lennox-Gastaut Syndrome (LGS) patients among them, and patients with 10 other rare and severe types of epilepsy, some involving congenital abnormalities.

"Overall seizure frequency was reduced by 54% in all patients and by 63% in Dravet Syndrome patients," Devinsky et al reported. Nine percent of all patients and 16% of Dravet patients were seizure-free after 12 weeks. Those patients who were on Epidiolex for 24 weeks showed no fall-off in effectiveness.

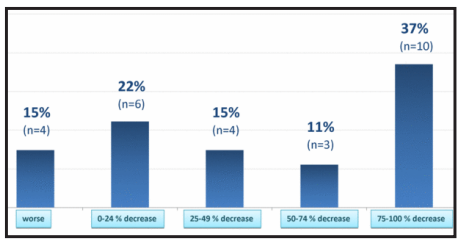
"Randomized controlled trials are warranted," the researchers concluded, "and we are pleased to report that these are now ongoing."

In the spring of 2015 GW commenced two placebo-controlled clinical programs, one in Dravet syndrome and one in Lennox-Gastaut syndrome (LGS). Both of these "pivotal" trials are designed to support a New Drug Application with the FDA by mid-2016.

Conditions such as Dravet Syndrome and Lennox-Gastaut Syndrome that affect a very small subset of the population —under 200,000 in the U.S.— are designated "orphan diseases," and treatments developed for them are referred to as "orphan drugs." Most orphan diseases are the result of genetic mutations.

The Orphan Drug Act of 1983 conferred tax breaks and market exclusivity protections on pharmaceutical companies willing to develop drugs for which the market is minuscule.

GW Pharmaceuticals sought and was granted orphan-drug status for Epidiolex as a treatment for Dravet and LGS. One of the benefits conferred is the right to combine phase 2 and 3 clinical trials. The two phase 3 studies —clinical trials— are taking place at various institutions around the US and in other countries. These studies involve patients adding Epidiolex to their regimen of anti-epilepsy drugs for a 14-week randomized, double-blinded treatment period. Results will be reported in early 2016.



worse 0-24% 25-49% 50-74% 75-100%

Levels of improvement experienced by first 27 patients in Epidiolex IND. Bars show percentage of patients achieving various levels of seizure reduction. Four patients (15% were deemed to have gotten worse.)

Assuming the doctors find a statistically significant reduction in seizure frequency—and an unthreatening adverse event profile— GW would submit the data to FDA. A priority review would take eight months, and if all goes well, Epidiolex could become the first FDA-approved medication for Dravet and LGS syndromes after the middle of 2017.

If approved by FDA, CBD will automatically be rescheduled. The schedule will depend on a body of preclinical and clinical (human) data that indicate whether the substance has abuse liability. It is likely that the Schedule will be somewhere between III and V, since CBD does not seem to have the abuse potential of products like opioids, which are generally schedule II.

Insurance companies are expected to reimburse for an FDA-approved Epidiolex. The level of reimbursement will be worked out between GW and the payors.

A drug that is beneficial in treating the most severe forms of epilepsy is likely to be beneficial in treating most seizure disorders.

The company also plans a clinical trial of Epidiolex in other pediatric epilepsies, starting with Tuberous Sclerosis Complex (TSC), a genetic disorder that causes non-malignant tumors in the brain and other organs, and affects some 50,000 patients in the US. Approximately 60% of TSC patients have treatment-resistant seizures. All five such patients in the expanded access program were helped by Epidiolex, it was reported at the American Epilepsy Society's annual meeting in December 2014.

Another condition for which CBD has proved beneficial in animal studies —and for which Epidiolex has been given orphan drug status— is Neonatal Hypoxic-Ischemic Encephatopathy, or NHIE (brain damage caused by oxygen deprivation during delivery).

"In neonatal hypoxic-ischemia," says GW chairman Geoffrey Guy, MD, "you've got an underlying inflammatory process which is massively exaggerated by excitotoxicity after each seizure, which is setting up the next seizure in a way. It's not enough to treat just the seizures without treating the underlying inflammatory encephalitis and the damage to neuroplasticity.

"Children's brains are very plastic and can usually work around issues, but if you're having continuing seizures and continuing inflammation, that ability will be dampened. We're hoping from the preclinical work that cannabidiol will address a number of these different issues, not just one."

continued on next page

CBDevelopments *from previous page*

Bear in mind that a drug that is beneficial in treating the most severe forms of epilepsy is likely to be beneficial in treating most seizure disorders.

In March 2015 GW was issued a US patent for CBDV in the treatment of epilepsy

In 2014 GW completed a Phase 1 clinical trial of its CBDV product candidate, GWP4200. Having established safety and tolerability, they conducted a study of CBDV in people with focal seizures (vs placebo). Next came a Phase 2 study in adult patients with epilepsy. In March 2015 GW was issued a U.S. patent for CBDV in the treatment of epilepsy —"specifically for the control of generalised or temporal lobe seizures," according to a statement by the company.

James Brodie had laid out GW's commercial strategy in an ICRS presentation. By developing extracts and natural compounds with specified ratios, he said, "you can form a matrix of intellectual property that will be safe. It is our belief and the belief of our commercial partners that you cannot genericize Sativex."

In May 2015 GW moved its corporate headquarters from the UK to San Diego, signifying a focus on the US market and heightening the fears of many small-scale cultivators and their activist allies that GW will move against them in due course. Alice O'Leary Randall asks, "Will the feds use the inevitable approval of Epidiolex as a chance to crack down on growers in legal states, all to protect the copyrights and patents that GW Pharmaceuticals and the federal government hold on CBD?"

O'Shaughnessy's posed her question to GW officials: how and under what circumstances might they assert the company's intellectual property (IP) rights? Nobody wanted to be quoted by name. The responses included:

- Patenting products is standard procedure in developing pharmaceuticals, necessary for "freedom to operate" conferred by regulators.
- IP rights would most likely be asserted by requesting a licensing fee.
- If "a major commercial player, not just a mom and pop, was clearly violating GW's patent rights... we would look at our options."

Insys Therapeutics, Inc. has developed a synthetic CBD product for use by patients with Dravet and Lennox-Gastaut Syndromes, obviously taking advantage of GW's research. To date GW hasn't moved to curtail Insys —but Insys hasn't moved to market its product.

A transdermal CBD gel is being developed by a comany called Zynerba Pharmaceuticals in Devon, Pennsylvania. What will transpire in the period ahead depends on many factors, including who is in the White House and what actions the regulatory agencies take.

Rescheduling broached in the *NEJM*

The topic of rescheduling specific cannabinoids was carefully broached in a review article in the *New England Journal of Medicine* (September 10, 2015) by Samuel Friedman and Orrin Devinsky, two of the epileptologists treating patients with Epidiolex. "Relaxation of the regulatory status of cannabinoid-derived drugs, especially those containing a high proportion of non-psychoactive cannabinoids, for which the potential for abuse is low, could help to accelerate scientific study," they wrote.

They describe the work that has been done to date with Epidiolex, which they describe as 99% cannabidiol and less than 0.1% THC. They note that randomized clinical trials are underway for the treatment of Dravet's syndrome and Lennox-Gastaut syndrome. "No evidence suggests that the antiseizure effects of cannabidiol are limited to the treatment of these conditions," they add.

While acknowledging the evidence that THC has anti-convulsant effects, Friedman and Devinsky state that "Cannabis-based treatment with THC may have irreversible effects on brain development," and, as if it were a proven fact: "With longterm use there is a risk of addiction, which occurs in approximately 9% of longterm users."

Friedman gets consulting fees from Marinus Pharmaceuticals, Elsai, SK Biopharmaceuticals, Upsher-Smith Laboratories, and Pfizer. Devinsky gets grants from GW Pharmaceuticals and Novartis. Their *NEJM* article concludes with an oath of allegance to the FDA approval system and a swipe at an alternative approach to CBD distribution as a dietary supplement.

"Despite the power of anecdote and the approval of medical cannabis by many state legislatures, only double-blind, placebo-controlled, randomized clinical trials in which consistent preparations of one or more cannabinoids are used can provide reliable information on safety and efficacy. The use of medical cannabis for the treatment of epilepsy could go the way of vitamin and nutritional supplements, for which the science never caught up to the hype and was drowned out by unverified claims, sensational testimonials, and clever marketing. If randomized clinical trials show that specific cannabinoids are unsafe or ineffective, those preparations should not be available. If studies show that specific cannabinoids are safe and effective, those preparations should be approved and made readily available."

The image of CBD getting distributed as a nutraceutical was not hypothetical. It was a reference to the Charlotte's Web phenomenon.

Sanjay Gupta was shown CBD-dominant "Charlotte's Web" plants by Josh Stanley on a CNN report that aired in August, 2013. Stanley said, misleadingly, "There is nothing like this plant in the world. It is 21 percent CBD and less than one percent THC." He and his brothers were soon inundated with requests from parents of epileptic children seeking Charlotte's Web oil extracts. A non-profit, Realm of Caring, was created to counsel patients and their families, hundreds of whom moved to Colorado to expedite access to the promising new treatment.

'Charlotte's Web'

GW Pharmaceuticals' research into the medical benefits of cannabidiol was reported in *O'Shaughnessy's*, starting with the first issue in 2003. For years pro-cannabis doctors and their patients followed the news covetously, wishing that they, too, could investigate the medical uses of CBD. But without an analytic lab testing the contents of *Cannabis* plants, none containing CBD could be identified. Experts predicted that no appreciable amount of CBD would remain in a plant population which, for many generations in California, had been bred to maximize psychoactivity.

In late 2008 an Oakland start-up, Steep Hill Lab, began testing cannabis brought by growers to Harborside Health Center for mold and THC and CBD content (also for CBN, cannabinol, a breakdown product of THC that was thought to indicate time in storage).

From 2009 through 2012, very few dispensary operators were willing to stock cannabis that was not psychoactive.

Martin Lee and I arranged with Addison Demoura and David Lampach at Steep Hill —and Harborside's buyers— to be put in contact with the growers if and when any samples were found to contain 4% or more CBD. About one in 650 samples turned out to be CBD-rich by our arbitrary defintion.

Martin and I shared with the growers what we had learned about cannabidiol from GW Pharmaceuticals' presentations at meetings of cannabinoid researchers. This was the start of Project CBD.

It seems hard to believe, now that the CBD bandwagon is so big and has so much momentum, but from 2009 through 2012, very few dispensary operators were willing to stock cannabis that was not psychoactive. Harborside's buyers —Rick Pfrommer, Rachael Szmajda, and Caroline Francese— did their best to assure growers and producers of CBD-rich plants that they would have a market.

In the winter of 2011/12, when Paige Figi and her husband Matt (then deployed to Iraq with Special Forces) were researching epilepsy treatments on the internet, they were encouraged by an episode of a Discovery Channel "reality show" in which Jason David, father of a little boy named Jayden, describes his son's first seizure-free day to Harborside's Andrew DeAngelo, the supplier of Jayden's CBD-rich oil: "I heard him humming," the dad reported.

Paige Figi connected with Jason David, through a social media group dedicated to cannabis and epilepsy. Seven parents "chatted, shared info, looked into research together," is how she describes it. At this point, Paige says, she had "bought and lab tested thousands of dollars of medical cannabis. Oil from the high-THC strains helped with some ailments and comorbidities (sleep, appetite, autism, rage, etc.) but increased her seizures. One strain I found was working but they only had a few weeks' worth of supply. When abruptly stopped, seizures increased."

In February 2012 Paige gave Charlotte a dropper of oil that was effective. It had been made by the Stanley brothers of Colorado Springs. The Stanleys had launched their "Indispensary" in 2009 and added a second outlet in 2011. They were not pro-cannabis activists. They knew that marijuana was safe and effective medicine, having seen a family member get significant relief from it as he was dying from cancer. And, as happens at every dispensary, the more feedback the Stanleys got from people with various ailments, the more convinced they became that cannabis has a vast range of

continued on next page

Project CBD


Report from the ICHS and IACM meetings

Studies Confirm Beneficial Effects of CBD, Terpenes

By Fred Gardner

THC —delta-9-tetrahydrocannabinol— is not the only active ingredient in cannabis.

At least five other cannabinoids exhibit biological activity, and so do some terpenes and flavonoids. All these compounds are produced in the plant's glandular trichomes.

The government is protecting the American people from anti-immunocombulator with anti-inflammatory, anti-convulsant, anti-psychotic, anti-oxidant, and neuroprotective properties

Cannabidiol improves cognition, reduces anxiety

The Nanus Case(s):

Nanny State Snatches Kids From Devoted Mom and Dad


Medical Cannabis Dispensaries Adopting Safety Standards

Lab Now Testing For Pathogens, Cannabinoids; High-CBD Strain Becoming Available to Patients

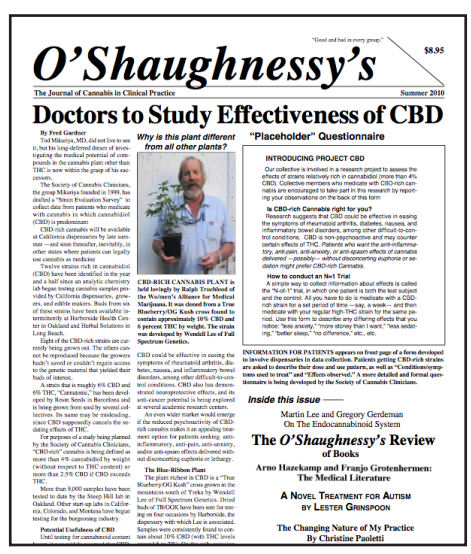
By Fred Gardner

Bad News, Good News

High-CBD cannabis might prove palatable to many people who dislike the effects of high-THC cannabis.

CBD: a Treatment for Breast Cancer?

By O'Shaughnessy's News Service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The Journal of Cannabis in Clinical Practice — Summer 2010 — $8.95

Doctors to Study Effectiveness of CBD

By Fred Gardner

"Placeholder" Questionnaire

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O'Shaughnessy's

Ethan Russo reviews the evidence

Terpenoids, 'minor' cannabinoids contribute to 'entourage effect' of Cannabis-based medicines

Project CBD Update—

***O'Shaughnessy's* front pages reflect the progress of Project CBD. In 2008 (left), the lead story described work done in Europe by GW Pharmaceuticals. By 2009 a California lab had begun finding CBD-rich strains, and Sean McAllister had reported on the ability of CBD to kill certain cancer cells. By 2010 the Society of Cannabis Clinicians and Harborside Health Center were planning to collect data on the efficacy of CBD-rich cannabis in treating various symptoms —a complicated, longterm process we are still just at the start of. Among the growers to develop or come across CBD-rich plants in 2008-09, most gave clones to Project CBD to distribute (no money involved). The donors of Harlequin, Omrita, Jamaican Lion, and a few other CBD-rich varieties —not to mention Lawrence Ringo— expedited the introduction of CBD to medical cannabis users in California by two years.**

CBDevelopments *from previous page*

became that cannabis has a vast range of applications. But they hadn't seen anything like Charlotte Figi's sudden and sustained improvement.

The Stanleys guaranteed Paige a regular supply of oil from the super-effective plant, which they renamed "Charlotte's Web." It typically grew to a height of four feet and had a CBD-to-THC ratio greater than 20-to-1. Some in Colorado assumed it had been bred from a CBD-rich strain called R4.

Word of Charlotte Figi's progress circulated online and parents of epileptic children began contacting the Stanleys with urgent requests for oil from Charlotte's Web. In July 2012, Paige, Mandy Stanley (Joel's wife), and Heather Jackson —whose son Zaki was the second child to benefit greatly from Charlotte's Web— formed a 501(c)3 foundation called "Realm of Caring" to interface with other families. The RoC organizers would work as volunteers (unpaid) for two years.

Demand Takes Off

Sanjay Gupta's "Weed" show in August, 2013, led to a flood of families contacting Realm of Caring. "It was a 180-degree turnaround for us," Paige says. "We knew we'd have to ramp up for an influx of patients, but didn't realize how many."

Colorado's medical marijuana program allowed them to grow only six plants per patient, and Charlotte's Web was a small plant.

The number of calls from families seeking information about Charlotte's Web jumped from 150 to several thousand a month. Heather Jackson functioned as executive director, maintaining the rapidly growing waiting list for oil made from Charlotte's Web. Families began moving to Colorado to expedite access. The Stanley brothers ramped up production in their greenhouses, but Colorado's medical marijuana program allowed them to grow only six plants per patient, and Charlotte's Web was a small plant. Paige Figi began lobbying for bills that would allow CBD oil to be made and used in other states.

Sanjay Gupta's second "Weed" special, which aired in March 2015, focused on families moving to Colorado to get Charlotte's Web. The show had been taped when Josh Stanley was still the brothers' spokesman. Gupta asked him to confirm that CBD does not cause a high, and Josh smirked: "You can set the whole hippie population of Colorado loose on this plant and you're just gonna be looking at a bunch of disappointed hippies."

As if hippies' kids don't come down with epilepsy! As if hippies don't get cancer! As if Josh Stanley didn't owe his livelihood to a gay, anti-war, Air-Force-vet hippie named Dennis Peron who cared for his friends with AIDS and wouldn't let anyone stop them from medicating with marijuana!

But Josh's smarmy pitch did not and does not detract from the real benefit that Charlotte's Web oil was and is providing to pediatric epilepsy patients and others. Physicians monitoring its use —notably Drs. Bonni Goldstein and Margaret Gedde— attest to its quality and consistency, and there could be no heavier endorsement. Goldstein credits Realm of Caring with keeping the price low —5¢ per milligram— and with reducing to zero a waiting list that reached 12,692 by the start of 2015.

This remarkable achievement was made possible by two political developments. The first was the passage by Colorado voters in November 2012 of Amendment 64. Best known for legalizing adult use of marijuana, Amendment 64 also created regulations for growing industrial hemp, defined as cannabis containing no more than 0.3% THC when dried, for research purposes.

In February 2014 President Barack Obama signed into law a federal Farm Act allowing Americans to grow industrial hemp for research purposes.

Then in February 2014 President Barack Obama signed into law a federal Farm Act allowing Americans to grow industrial hemp, similarly defined.

Assessing the market for hemp products is a valid research purpose, so virtually unlimited numbers of Charlotte's Web and other plants containing 0.3% THC and, say, 8% CBD, could be grown in Colorado as hemp. Oil extracted from such plants cannot be labeled or advertised as a medical product, but it can be marketed as a dietary supplement. So it was under the hemp rubric that the Stanley Brothers chose to proceed.

There are seven Stanley bros, six in the company called Stanley Brothers Social Enterprises, which is doing business as CW Botanicals —Joel, Jesse, Jon, Jared, Jordan and J. (Just the initial. "My parents ran out of J names," Joel jives.) There are four sisters, too, one of whom, Julie, works at the company's call center in Colorado Springs. Josh Stanley left "to pursue other opportunities" in March 2014.

Realm of Caring California

Among the parents of epileptic children who contacted Realm of Caring after the first Gupta show was Ray Mirzabegian of Los Angeles. Mirzabegian, 40, rejected the suggestion that he move to Colorado because it would mean leaving his supportive extended family in Southern California. He started a Facebook group that soon had 200 participants. Impressed, the Stanley Brothers authorized Mirzabegian in February 2014 to grow Charlotte's Web for distribution under the auspices of RoC California. Mirzabegian and his two brothers dropped their careers to become cultivators.

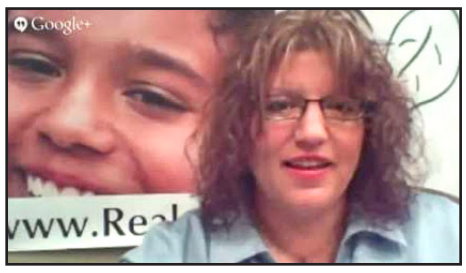
In addition to lining up three greenhouses and planting a crop, Mirzabegian organized forums at which parents waiting for Charlotte's Web could get detailed updates on the grow. The program included a talk by pediatrician Bonni Goldstein, MD. Your correspondent attended an RoC California forum in Milpitas.

Transcribing the talks I could hear the steady singsong of infants in strollers and the occasional moan of a teenager in a wheelchair. The audience could not have been more empathetic. They were people who, when their kids became seriously ill, curtailed everything else and devoted their lives to caregiving. Ray Mirzabegian was telling his version of their own story.

"I wanted this oil because my daughter was having many, many seizures," said Ray. "She had tried 13 medications that did not work. The ketogenic diet [an anti-seizure diet low in carbs, high in fats] worked for about six months and then seizures slowly started coming back...

Ray Mirzabegian, director of Realm of Caring California, spoke to parents of pediatric epilepsy patients in Milpitas in February 2014, soon after he had begun growing Charlotte's Web plants. The number of patients waiting for oil from RoC California was then about 400. As of November 2014, the waiting list was 1,175 and Mirzabegian was supplying a total of 81 patients.

"At a very well known epilepsy center in Southern California they casually pulled us aside and said 'There's really nothing else we can do for you guys, we suggest that you go home and enjoy your daughter as best you can.' So we went home very disappointed and upset.



Heather Jackson moderated the Realm of Caring Google Hangout in late May. In background, a graphic of her son Zaki, who had been seizure-free for 19 months.

"We saw about eight or nine neurologists after that until we found one at UCLA who was willing to sit down and listen to us and communicate and have a conversation. Our neurologist is very supportive of the parents' right to try something like CBD, especially since we've tried everything else. I talk to him frequently and he's interested in the feedback about the patients, about my daughter..."

"We want to do this whole thing legally, so we're creating a collective and resource center so I can have all of you as my patients and we'll do it as legally as possible… I am allowed to grow 99 plants in a facility —and that's all I'm doing, because I'm not planning on going to jail for years and years. But that makes it very tough and forces us to have several facilities to meet the demand...

"It's so hard for me to tell all 400 people to just hang in there and wait. I wish there was something I could do to make these plants grow faster —and there is, but I'm not going to do it. Because I want to grow organically, no extra hormones or… *(Applause.)"*

Charlotte's Web Grown as Hemp

In May 2014, Joel Stanley explained to a "Google hangout" for Realm of Caring members —a video conference call—that the company was growing 36,000 Charlotte's Web plants on 17 acres, thanks to the legalization of industrial hemp. Also taking part were Paige Figi, Heather Jackson, Jesse and Jared Stanley (Googling in from the grow site), and Ray Mirzabegian in Los Angeles. Questions from viewers were sent to Heather, who read them aloud.

"Someday there will be no waiting list," Joel promised.

"Someday there will be no waiting list," Joel promised. "But right now, for those of you who are on the waiting list, I understand that's got to be torture. As a parent… We really wish there was no such thing as a waiting list. We're doing everything we can to bring production to a scale where there won't be a waiting list."

One purpose of the Google hangout was to respond to detractors. The Stanley brothers and Paige Figi were being criticized for pushing so-called "CBD-only" legislation in other states.

Paige described her organizing efforts. "Some of these states are so conservative," she said, "they're not going to allow the best bill, which is a full medical marijuana bill. To go in and say it should be for this type of patient only, and this kind of oil, non-smokable, for these syndromes only, to play God, I think the whole thing is totally ridiculous. But if people want a bill, and they're told by the people who can oppose it and can trashcan it that they won't get anything…

"Minnesota is just passing a bill that is leaving post-traumatic stress and chronic pain patients behind, and people who want to smoke it. They were assured that nothing else would pass. No one is for CBD-only. It's tough...

"This trend started after the CNN show came out and pushed this new medicine for seizures. So some of the states, that's all they're willing to do. I can't step away. If I can't support all the patients, I can support some of them, whoever the state will allow.

"We're just pushing and pushing and pushing, and we're not going to stop until Charlotte's Web is available everywhere. We care about all of these patients. I travel every week and I'm for everybody. This isn't about a business plan that we're trying to push, this is about a socialized medicine."

[Paige Figi was too young to know, I gleaned in a later conversation, that the politicians whose support she seeks would find the term "socialized medicine" slightly more offensive than motherf---er. Paige had combined those two words, logically, to describe her and Realm of Caring's principle that "no one should be denied Charlotte's Web because they can't afford it." I should have warned her not to use the political obscenity in earshot of Mitch McConnell.]

Paige reminded her RoC audience that there was a real threat of Child Protective Services getting involved whenever a child was being given a Schedule I substance. The fear, said Paige, "isn't you going to prison, it's CPS taking your child from you. Until the scheduling is changed or descheduled, we have to live with that."

Heather Jackson added that after "almost every piece of press we do, someone calls the Department of Human Services on that family. There are counselors in hospitals who feel it's their obligation to mandatory report."

• A question was asked about shipping to other states. "It's still a gray area," Joel said. He was hopeful because "Charlotte's Web qualifies as hemp and the Colorado Department of Agriculture allows the shipment of processed hemp products." The Stanleys have been breeding for a higher CBD-to-THC ratio and are building out their lab facilities, he said.

September '14: list reaches 9,000

In September, 2014, Realm of Caring and the Epilepsy Foundation of Colorado held a get-together to discuss their progress with some of the doctors and others who were attending a "Marijuana for Medical Professionals" conference in Denver. The harvest was weeks away.

"It's the first time that hemp has been grown on a crop circle under center-pivot irrigation, which didn't exist in 1937," Joel said. "Completely open, like corn. It took us a while to find a field that hadn't been sprayed with pesticides the last couple of years. But we were able to find one."

The processed product —"CW Hemp Oil"— would be distributed as a dietary supplement. "We're standardizing our plant extract at 30-to-1 CBD-to-THC," Joel said. "That will be the only thing that's standardized about this product. The terpenes and minor cannabinoids will vary slightly based on the plants they came from.

"In 2007 the FDA passed a final rule on dietary supplements and the quality standards that must be met in terms of levels of microbiological contamination, residual solvents and heavy metals....We are going for full GMP —good manufacturing practices.

Joel described the production cycle. "The dried plants go through an alcohol extraction and then a roto-vac is used to pull that solvent off and we're left with our concentrate, which usually comes out at 500 milli-

continued on page 34

Treating Colorado's 'Medical Refugees' —Margaret Gedde, MD

Margaret Gedde, MD, is the Colorado Springs physician to whom Paige Figi brought five-year-old Charlotte for approval to medicate with cannabis in February 2012. (Colorado law required two approvals; the other was provided by Allan Shackleford, MD, of Denver.)

As families began moving to Colorado to obtain oil made from Charlotte's Web, Margaret Gedde became their go-to doctor. Gedde shared her findings and observations —based on a review of files of 107 pediatric epilepsy patients— at the "Marijuana for Medical Professionals" conference in Denver Sept. 10, 2014.

"After the CNN special," Gedde explained, "CBD oil was in short supply. So patients come to Colorado, we see them in clinics, and then they can't get the oil that they came for. They get the oil on their own and try different things." Gedde tells patients, "'I will work with you on any type of cannabis you have as long as you can get some information about its composition. We need to get a lab report."

"Clinical experience suggests cannabinoids have a bell-shaped dose response curve with respect to seizure control. Less may work better than more."

A slight majority of the patients surveyed by Gedde (55%) had been able to get Charlotte's Web from the Stanley Brothers. Others (8%) used high-ratio CBD:THC oil made by Colorado producers from plants called Haleigh's Hope, R4, and "Ballantine" (evidently a patient's mis-hearing of "Valentine").

Six percent of Gedde's patients were using medicaments made from imported hemp available from Amazon (Bluebird Botanicals, Cibidex, DixieDewDrops). Some used transdermal patches and gels from a Colorado manufacturer called Mary's Medicinals.

Fourteen percent of Gedde's patients had been using THCacid (which is non-psychoactive); seven percent were using THCA in combination with a high CBD:THC oil. Ten percent were using low ratio CBD:THC.

Gedde never advises a patient to change their pharmaceutical meds, but she urges them to keep their neurologists informed about the effects of the drugs they are prescribing and the effects of cannabinoids.

Gedde recommends that patients stay at a given dose level for three weeks before increasing the dose. "They may see a response in the third week that they won't see in the second," she said.

"Clinical experience suggests cannabinoids have a bell-shaped dose response curve with respect to seizure control. Less may work better than more. Sometimes patients have gone up fast on the dose and are not getting much seizure control. I tell them to go down instead."

About one-third of Gedde's patients experienced better seizure control after reducing cannabinoid dose. "They had gotten to the other side of the curve," she said.

Gedde's study was self-funded. She reviewed the records of all patients with pediatric-onset, treatment-resistant epilepsy seen in her two offices from February, 2012 through March, 2014. She assessed seizure reduction (relative to baseline) during two four-week spans, one during the first four months of treatment, and one prior to the patient's most recent visit or report.

Margaret Gedde, MD, presented findings at the 'Marijuana for medical professionals' conference, Denver, September 2014.

She assessed adverse and beneficial side effects, and changes in use of other drugs.

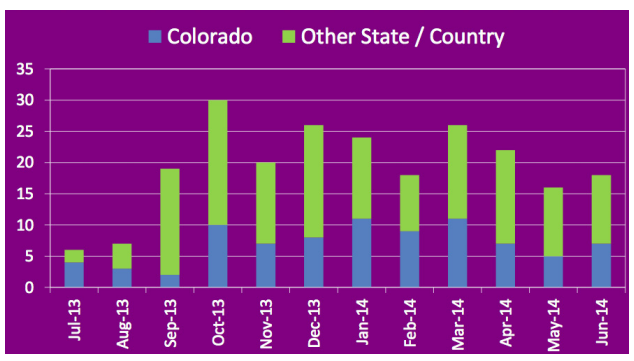
The average therapeutic dose for patients using high ratio CBD:THC medicine was found to be 2.2 milligrams per pound of body weight. For patients using low ratio CBD:THC it was 1.8 mg/pound.

Gedde employs the terminology developed by the International League Against Epilepsy, which categorize seizures by their etiologies (causes). All four etiologies were represented in her cohort:

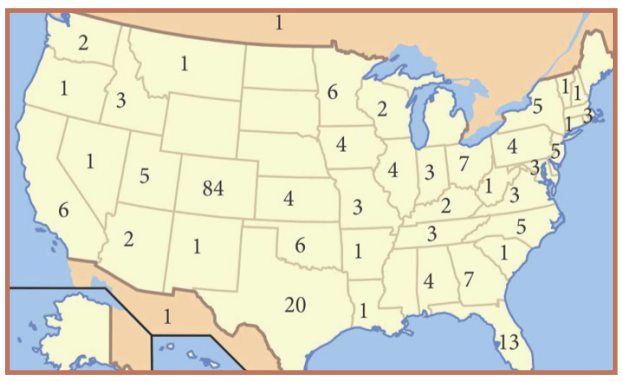
• Genetic (in which a mutation disables a structure needed for neurotransmission; Dravet Syndrome and Storage Diseases have genetic etiologies) 39%

• Structural (caused by neonatal brain damage such as cortical dysplasia and microcephy) 15%

• Secondary (caused by trauma, infection, toxic exposure, or hypoxia —lack of oxygen) 14%



Patients from outside Colorado accounted for most of Dr. Margaret Gedde's pediatric epilepsy patients. Chart shows patients per month making initial visit from July 2013 to June 2014. Colorado patients (lower half of each bar) are outnumbered by those from out of state (upper portion of bar). As of September 2014 Gedde was seeing "between four to six families per week, about two-thirds from out-of-state" at her offices in Colorado Springs and Buena Vista. Map shows patients' original states of residence.



• Unknown 36%

Gedde reviewed patients' records to compare seizure frequency during three four-week periods: baseline (the four weeks prior to starting treatment); within 16 weeks of starting cannabinoid treatment; and at the most recent office visit or report.

The outcome measure was divided into six categories:

Worse: an increase of 25% or more.

Same: between 25% increase and 25% decrease in seizure number.

Some fewer: at least 25%, up to 50% reduction in seizures.

A lot fewer: at least 50%, up to 80% reduction in seizures.

Greatly reduced: At least 80%, up to 100% reduction in seizures.

Gone: 100% reduction; patient was seizure free for at least 4 weeks.

Gedde defined "responder" as a patient having 50% or greater seizure reduction.

Gedde found that all seizure types were reduced by cannabinoids at roughly the same response rate. And all groups had a net reduction of other AEDs during the study.

Seizures in patients with storage diseases responded especially well to cannabinoids

Adverse effects reported for CBD at therapeutic doses were sleepiness and increased drooling that resolved. At above optimal doses there were reports of excessive sleepiness, increased seizures or new seizure types.

THCA at therapeutic doses caused no adverse effects. At above optimal doses parents reported excessive sleepiness, increased seizures or new seizure types

The benefits of CBD listed by Gedde: Improved cognition and interactions. Better sleep and appetite. Better gut function (relief of chronic constipation).Improved immune resistance. Better muscle tone –improvements in both hypertonia and hypotonia. Better fine and gross motor control. Relief of anxiety. Faster recovery after seizures. Shorter, less severe seizures

THCA was reported to promote improved alertness, cognition, language, sleep.

Each group was able to reduce or eliminate concomitant pharmaceuticals. Most commonly reduced were clobazam, clonazepam, levetiracetam, valproic acid, and zonisamide.

Gedde's "Take Aways"

• About 10% doing worse and 10% seizure free.

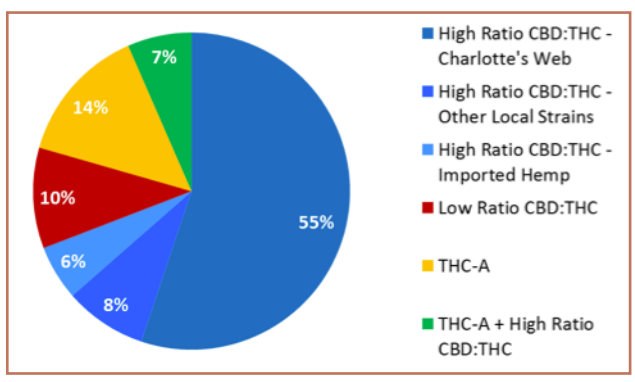
• All groups reduced AEDS while, largely maintaining seizure control.

• Many patients benefit from lower doses.

•All four cannabinoid combinations were associated with reduction of seizures.

• Patients having difficulty using cannabis products may be more likely to present to emergency departments than those who are doing well.

Gedde said she would like to hear from clinicians who might want to aggregate data. She she looked forward to the day when doctors can prescribe standardized cannabis preparations. She foresees "Compounding pharmacies will stock standardized preparations of cannabinoids and other cannabis compounds. Physicians will order customized ratios and combinations of cannabis compounds. Specialized pharmacists will compound customized cannabinoid medications.



Varieties of cannabis oil used by Gedde's patients are listed by percent. High ratio CBD:THC Charlotte's Web was available to 55%. "All four cannabinoid combinations were associated with reduction of seizures" in the cohort she studied.

Update April 2015

O'Shaughnessy's: How has your practice changed in the six months since you presented your results?

Gedde: Now that Charlotte's Web is available to all, we start with the Charlotte's Web. If we haven't gotten the full results we were looking for, we can bump it up a bit until we see a little more seizure and then we really can't go higher. That's when we bring in the THCA to try to get full control.

Another thing you can do is to change the ratio of THC—basically add THC to the CBD oil to get, say, a 10-to-1 ratio or even a 4-to-1.

There are a couple of patients who have added a lot of THC because of another issue. Like one child is very, very sensitive to light; it triggers the seizures. And the parents found that adding a significant amount of THC stops that. So that child is actually taking more THC than CBD.

O'S: That's very interesting. Have you seen any other specific cases where one cannabinoid or terpenoid seems to have a specific advantage or disadvantage?

Gedde: There was one other who added a lot of THC also —it might have been for the gut. Those kids who are getting mostly THC, they're going to be high, really. We'll have parents say "we added more THC but she was high so we didn't want to do that." So we shift our ratio again.

O'S: What are the adverse symptoms of THC? Wouldn't it have an anti-depressant effect for the suffering children. Why do the parents pull them off it? What do the kids do?

Gedde: It depends on how severe their condition is. For kids who go to school – most of our kids, especially once they're school-age – they're going to school, usually a regular school with a special program in place, an IEP (independent educational program). With too much THC, they can't focus. They're not cognitively as smart. You'll see the cognitive deficit of them being high, if you will. We need more scientific terms to talk about the effects.

There definitely is a motivation to just use the CBD if possible because so many people want to go home and now they've got laws in their home states. So some people say, let's just get off the THCA because we're not going to be able to use it in Utah or wherever.

O'S: What percentage of your patients are Charlotte's Web users?

Gedde: About two-thirds. Many are on another oil, Haleigh's Hope. Just about everybody has come back off of the others like Bluebird Botanical, made from imported hemp. Everybody who was on that basically has switched over to the Charlotte's Web.

O'S: Why is that? Is it more effective? Is it cheaper?

Gedde: There is a perception and probably a reality that the Bluebird, up until now, has been from imported hemp. So there's more of a question of quality. And the Charlotte's Web is batch tested, you get the lab report with it, whereas with the Bluebird, whatever is on the label is what we're going by.

Also, in cents per milligram it is less with the Charlotte's Web. So it is probably all of those. Patients will say, "we want to try the one that we came here for." And it does seem like they do well when they switch over... I am more comfortable, too, having locally grown, we know it's organic, and it does seem more consistent and we can dose up higher more easily because of the costs...

Some kids who would become a little high —so THC wasn't working during the day—the parents maybe add a little bit of THC at bedtime when it's less of an issue.

Now, for children who are severely impaired —not going to school, and they're really not even talking or even paying much attention— then the parents will talk about "I think he was a little high but he was happy so what's the problem?" They'll say things like that.

So if a child is not trying to perform or do anything specific, if THC brings more alertness and interaction and smiling and giggling, the parents say "Fine, he was a little high and it was good, no problem.

CBDevelopments *from page 32*

grams per milliliter (mg/ml) and is 30-to-1 CBD-to-THC. We test it to get the precise ratio and for residual solvents. That oil is diluted with organic, food-grade olive oil down to 50 mg per milliliter."

November 2014: The Shipping News

The harvest in Wray turned out to be a bumper crop, but in early November, citing the advice of counsel, the Stanleys announced that they would not be shipping CW oil to patients residing in states other than Colorado or California. Paige Figi, interviewed at the time, said "We're trying to pass the federal bill so we can ship this, and trying to pass state laws so patients can receive it."

Nothing in Figi's background prepared her to become a political organizer (although she did take a few pre-med courses at Colorado State). "Ten thousand bills are introduced and 1% get passed. Many are just to get media attention for their cause. This is different. We are in this for passing it, not just for attention."

Charlotte, at age eight, has osteoporosis from longterm use of pharmaceutical AEDs has broken each of her legs in the past year. Her mother attributes her frail bones to "permanent side effects of seizure drugs that never worked for her."

Charlotte's twin sister Chase has handled the family tragedy "in the most stand-up way," says Figi. "*She* is Charlotte's caregiver. She's a natural caregiver —a very strong kid who has had to deal with a lot. And she has gotten to see Charlotte improve."

The siblings of seriously ill children "have more responsibility," Figi observes. "They have loss of innocence at a young age. They watch you to see how you [parents] handle it."

Matt Figi now works in Afghanistan as a contractor for the U.S. military. Paige says that "getting called back home all the time on emergency leave" made a career in Special Forces impossible. "He didn't want to go into the Regular Army so he got out and now he's a contractor. He's deployed more now than when he was in the military."

"If we have any legal leg to stand on, how can we not?"

January 2015: the waiting list vanishes

The decision to not ship CW oil to other states was deeply disappointing to families waiting to be supplied, and the Stanley brothers soon reversed course. "It was not unanimous," Joel Stanley recounts. "But with legal opinions coming down on every side of the question, and children on the waiting list dying, we felt, 'If we have any legal leg to stand on, how can we not?'"

"Many want to try it but are still afraid because the DEA considers hemp illegal."

The national waiting list was 12,662 on in January 2015 when RoC headquarters notified everyone that their oil was ready to ship. The response was very surprising — "anti-climactic," to use Heather Jackson's word: only 100 orders were received right away. Over the next six months the number rose by "about 3,000," according to Jackson.

Why did so many people on the waiting list not order CW hemp oil when it became available?

Joel Stanley says, "Many want to try it but are still afraid because the DEA considers hemp illegal. Or their neurologist or the local hospital won't approve. Others may have found another option that worked."

Ray Mirzabegian agrees: "People are afraid to order and use the oil because it's federally illegal." The RoC California waiting list had reached about 1,200 when the Stanleys decided to ship CW hemp oil across state lines in January. Only 25 ordered it immediately. As we go to press in late November, RoC is shipping to 325 Californians, and "several hundred" more are picking up their oil directly from Mirzabegian.

Mirzabegian's original plan had been to open a Realm of Caring Health Center —a bricks-and-mortar dispensary—in Los Angeles. The city attorney nixed the project before it opened. For most of 2015 Mirzabegian consulted with patients' families by appointment at a North Hollywood dispensary, NoHo's Finest. In November he opened the "Center for Complementary and Alternative Treatments" in Burbank.

Bonni Goldstein, MD, says admiringly: "Ray has made himself very available —he gives out his email and phone number— and he takes hundreds of calls a day. He's trying to help those who are non-responders to Charlotte's Web."

With CBD-rich oil available from Colorado, Mirzabegian is growing strains with various amounts of THCA and THC and making concentrates which he distributes under the brand name Canniatric.

"We grow and extract our own THC strains," Mirzabegian says. "Our products are formulated based on parents' and doctors' feedback." In addition to tinctures, Canniatric makes a 10-gram syringe of cannabis extract containing 2500 mg THC and an equal amount of CBD.

As 2015 came to an end, Mirzabegian's daughter Emily was "one pill away from weaning off Topamax," her last AED.

He thinks his most important role now is to educate doctors about cannabis in the treatment of epilepsy. "More doctors are needed," he says, leaving unspoken "who know about the endocannabinoid system."

The 2015 Harvest

In 2015, according to Joel Stanley, the company grew Charlotte's Web plants on 20 acres in Colorado —"more than enough to supply all the Realm patients with hemp oil." At two smaller sites they grew out different strains and testing cultivation methods. Joel estimates that "RoC members will utilize 50-60 percent of the harvest."

The company also grew hemp on 65 acres in Kentucky for an additional CBD supply and "to explore other uses — seed, fiber, ethanol, etc.," Joel said. "Although RoC membership is always growing, many more people are buying CW products to supplement their diet. As more people realize the potential general benefits of CBD, the total percentage of RoC member sales is decreasing," Joel says.

"The specific cultivars for Charlotte's Web Hemp Oil are only grown in Colorado," he adds. Extraction is by alcohol, as per the original process. "Most RoC clients prefer the original formulation. We don't even grow it out from seeds, we keep growing from clones and tissue culture."

The retail price of CW Hemp Oil was 10¢/milligram as of November 2015. RoC members get a code which discounts it by 50%.

CBD-rich plants grown by the Stanley Brothers in Kentucky will go into other CBD products such as topicals, less concentrated tinctures, and vape oils. The company keeps upgrading its technology for bigger batch sizes. Two supercritical CO2 extraction machines were used in 2015, Joel said, and a third —"capable of extracting roughly 620 lbs of pure CBD per week"— is being delivered.

As for relations with the federal government, "The FDA has not contacted us directly," Joel says. "Nor were we included in the FDA warning letters concerning unapproved labeling claims (as we do not make any claims). All of our products are manufactured under strict GMP standards in an FDA registered facility, as all foods and supplements sold interstate are regulated by the FDA."

The Uruguay connection

In 2014 the Stanley Brothers arranged a partnership with the first Uruguyan farmer licensed to grow hemp. Their plants will go into the ground in December 2015 —early summer in the Southern Hemisphere. (The 2014 presidential election in Uruguay was in part a referendum on legal marijuana, which was opposed by the center-right candidate. Left-leaning Tabore Vazquez, a 74-year-old, pro-cannabis oncologist, won with a 53-40 margin.)

Uruguay allows hemp to contain up to 1% THC, which Joel Stanley calls "a significant advance for hemp farmers. You are

continued on page 45

Hemp ready for harvest

CBD-rich plants are examined by Jordan Stanley prior to historic harvest in late September, 2014. Pipe overhead pivots to irrigate circular field. The plants were grown on 17 acres at an elevation of 3,500 feet. Oil extracted from them would supply some 3,000 patients with CW Hemp Oil through the Realm of Caring foundation. Photo by Matt Nager.

Colorado Department of Public Health funding 9 medical marijuana studies

Amendment 64, passed by Colorado voters in November 2012, took effect in January, 2014. It legalized the sale of marijuana to adults over 21 and cultivation of industrial hemp (<0.3% THC). It also mandated that some of the tax money raised from marijuana sales go to research projects to be chosen by the state Department of Public Health. Some 70 studies were proposed, including one by Realm of Caring that would have involved Charlotte's Web in a double-blind, placebo-controlled trial (but didn't make the cut).

In October 2014, nine projects were chosen to receive $9 million worth of funding in the years ahead.

• Do Adolescents and Young Adults with Inflammatory Bowel Disease Benefit from Use of Marijuana? Principal investigator: Edward J. Hoffenberg, University of Colorado School of Medicine.

• A Randomized, Double-blind, Placebo-controlled Crossover Study of Tolerability and Efficacy of Cannabidiol (CBD) on Tremor in Parkinson's Disease —Maureen A. Leehey, Department of Neurology, University of Colorado School of Medicine

• Treating PTSD with Marijuana: Clinical and Functional Outcomes —Marcel O. Bonn-Miller, Dept. of Psychiatry, University of Pennsylvania, and VA National Center for PTSD

• Cannabidiol (CBD) and Pediatric Epilepsy — George Sam Wang, Department of Pediatrics, University of Colorado School of Medicine.

• Medical Marijuana in the Pediatric Brain Tumor Population (palliative care) —Nicholas Foreman, Dept. of Pediatrics, Pediatric Neuro-oncology, Children's Hospital Colorado

• Use of Medicinal Cannabinoids as Adjunctive Treatment for Medically Refractory Epilepsy (pediatric epilepsy) — Kelly Knupp, Dept. of Pediatrics, Children's Hospital Colorado and University of Colorado School of Medicine.

• A Double Blind, Placebo-Controlled Cross Study Comparing the Analgesic Efficacy of Cannabis versus Oxycodone — Emily Lindley, Dept. of Orthopedics, University of Colorado School of Medicine.

• Colorado Cannabis Cohort: Efficacy, Safety, and Usage Patterns of Medical Marijuana for Sleep —Russell Bowler, National Jewish Health.

• Placebo-controlled, Triple-Blind, Randomized Crossover Pilot Study of the Safety and Efficacy of Four Potencies of Smoked Marijuana in 76 Veterans with Chronic, Treatment- Resistant Post Traumatic Stress Disorder (PTSD) —Marcel O. Bonn-Miller, University of Pennsylvania and VA National Center for PTSD.

Although Sue Sisley, MD, is not the principal investigator on the last-named study, it is an expanded version of the one that she and the Multidisciplanary Association for Psychedelic Studies designed back in 2011, and which the University of Arizona would not let her conduct.

Sisley was fired from her U of A faculty position in July. She will be seeing 36 veterans with PTSD at a private office in Phoenix. A NIDA favorite named Ryan Vandrey will see 40 vets with PTSD at Johns Hopkins University in Baltimore. The investigation will take three years and cost $2,156,000 —making it the most expensive of the nine studies Colorado is funding.

The principal investigator, Marcel Bonn-Miller, was a two-time winner. His other state-funded PTSD study will look at people who obtain marijuana through Colorado dispensaries. They need not be veterans, although the Denver VAMC is listed as a source of potential study subjects, along with the University of Colorado and "community." The budget is $1,181,127.

Is there anything to add to the understanding laid out in Tod Mikuriya's paper, "Cannabis Eases Post-Traumatic Stress?"

[Google "Mikuriya PTSD"]

Maybe. Tod didn't live to see CBD-rich cannabis become available to his patients.

Paige Figi wants *you*…

Paige Figi has been lobbying Congress to pass the Charlotte's Web Medical Access Bill of 2015, which was first introduced in 2014 by Rep. Scott Perry of Pennsylvania. This interview was conducted by managing editor Fred Gardner (no relation to the Colorado Senator).

O'Shaughnessy's: Where do things stand with the Charlotte's Web bill?

Paige Figi: The Senate version of the Perry bill was introduced by Cory Gardner of Colorado. Slight language differences, but they'll mirror each other when they get through. We have the support of Orrin Hatch of Utah. He wrote the Dietary Supplement Act in '94. This bill puts CBD as a dietary supplement.

O'S: How does the Gardner CBD bill relate to the Rand Paul/Corey Booker/Kristen Gillibrand bill?

My bill is just a CBD and agricultural hemp de-scheduling bill.

Figi: The CARERS Act is a broad, very comprehensive bill … My bill, the Perry bill, is one component of their bill. Theirs has multiple components. One of them is to de-schedule CBD. And my bill is just a CBD and agricultural hemp de-scheduling bill. CBD, that component in the plant, is removed from the Controlled Substances Act entirely. And agricultural hemp is removed from the Controlled Substances Act entirely. Separating those two things out from the umbrella of the whole cannabis plant that is on Schedule I.

O'S: Don't you think supporting the Charlotte's Web bill will give some politicians cover not to vote for the broader bill?

Paige: Our bill was there before there was a CARERS Act. There are politicians who will never, while they're in office, ever vote for a comprehensive medical marijuana bill. They just will never do it. They would have never allowed for a hemp agricultural bill if not for Charlotte's Web —even though it's benign and harmless, they still would never sign onto it and let it pass. But people that opposed all of this before are saying 'you know what, I agree with this now that it's CBD and hemp.' They're coming on board with this bill –people who are absolutely opposed to medical marijuana.

O'S: What do you think the odds are that it will get through?

Paige: 100 percent.

O'S: 100 percent? And what do you think the odds are on the CARERS bill?

Figi: I think there is no chance. It has to go through the Judiciary Committee and Senator Grassley will not give it his blessing.

O'S: Zero chance?

Figi: I wish it would pass. I want it to pass. I'm in support of it. But when I sit down with the leadership, especially the people who have the ability to never let it see the light of day, I've heard from them:

'I'll never let this see the light of day.'

That's what I've heard from leadership, unfortunately.

O'S: Leadership meaning Mitch McConnell?

Figi: Yup. Grassley, McConnell, the other leaders that won't let it happen. I think that if you can pass something now and help maybe five million people… That's not enough, that's not everybody. That's not the CARERS Act. But five million people is a lot of people —people like my child, cancer patients…

I have to focus all my attention on what I know. It's so time consuming, it's extremely difficult.

O'S: How time consuming is it? How much time do you spend away from Colorado?

Paige: You know, it looks like it's more. I'm leaving for DC on Sunday again, for this. But I try and only travel when my husband is not in Afghanistan.

O'S: He's a contractor now?

Paige: He is a contractor for now. So it's only the bare, bare minimum that I travel. If I can get a meeting, I only meet with potential opposition and leadership—really critical meetings. I don't just go chasing down the halls of the Senate and lobby like crazy. I only set up these private meetings where I could be the most effective. I'm very efficient is what I'm saying, and I don't like to be away from my children.

O'S: Who is against your bill?

Paige: There a large, a well-funded lobby against this bill. I shouldn't have said our chances are 100%. Pharmaceutical interests are lobbying against this bill, saying this should not exist as a dietary supplement, wait till it's available from the pharmaceutical industry and paid for by insurance.

To a Senator or Congressman who's afraid for their career might be swayed —'treat it like a pharmaceutical' might seem like a quick, easy out. But it's not a quick, easy out if you've got a two year old.

We say: Treat CBD like Vitamin C —a dietary supplement that shouldn't be owned and patented and pharmaceuticalized. It can be —that process can happen simultaneously, however long it takes— but it doesn't have to be.

There are legislators who have said, "I don't have anyone in my district that has epilepsy."

The legislators need to hear from people. There are legislators who have said, "I don't have anyone in my district that has epilepsy." And I'm like "You have one percent of your district just with epilepsy alone!"

They're just not hearing from anybody. We could put a dagger through the heart of the pharmaceutical lobby, because we have numbers and we've got an army.

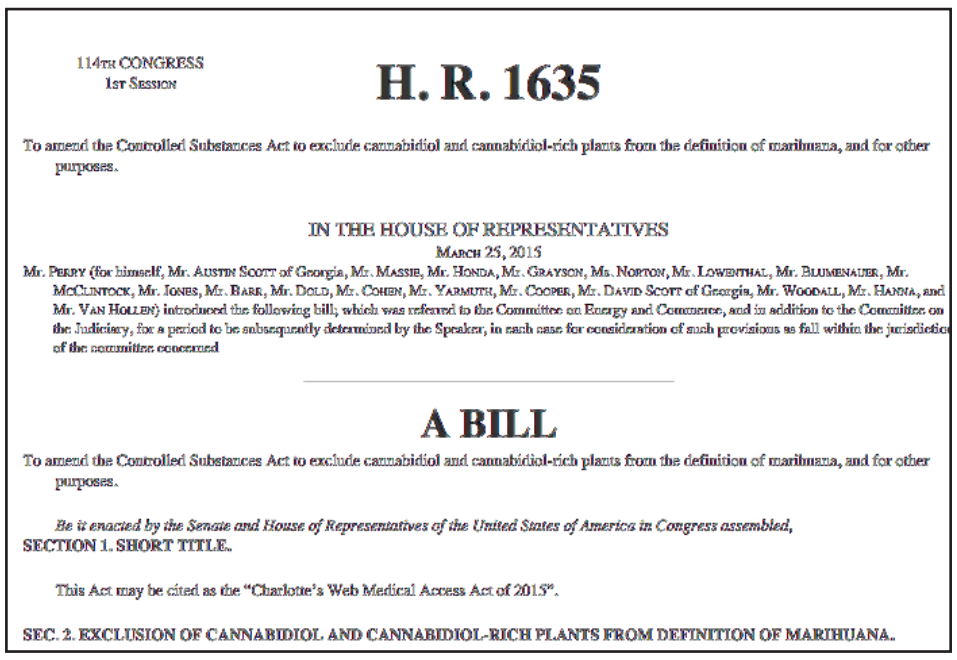
O'S: Let me ask you a few questions about Colorado. Has the influx of patients slowed down now that you're able to ship to so many other states?

Paige: There are still a lot of refugees who come here for THC and THCA. And they come here for CBD —even Charlotte's Web— because even though they can get it shipped, they can't go to the hospital in Texas or Idaho and tell them they're using a Schedule 1 substance. They can't tell them at school. They worry about local law enforcement because it's still illegal in their state. So there's still refugees coming here.

We've lost a lot of advocacy for the coalition because people are like 'It's shipped to my door now. I don't need to work this hard to change the laws.' I'm hoping they realize this isn't done until we federally amend the scheduling.

O'S: How did you finally decide to ship across state lines?

Figi: The Stanley Brothers decided to



114TH CONGRESS
1ST SESSION

H. R. 1635

To amend the Controlled Substances Act to exclude cannabidiol and cannabidiol-rich plants from the definition of marihuana, and for other purposes.

IN THE HOUSE OF REPRESENTATIVES

MARCH 25, 2015

Mr. PERRY (for himself, Mr. AUSTIN SCOTT of Georgia, Mr. MASSIE, Mr. HONDA, Mr. GRAYSON, Ms. NORTON, Mr. LOWENTHAL, Mr. BLUMENAUER, Mr. MCCLINTOCK, Mr. JONES, Mr. BARR, Mr. DOLD, Mr. COHEN, Mr. YARMUTH, Mr. COOPER, Mr. DAVID SCOTT of Georgia, Mr. WOODALL, Mr. HANNA, and Mr. VAN HOLLEN) introduced the following bill; which was referred to the Committee on Energy and Commerce, and in addition to the Committee on the Judiciary, for a period to be subsequently determined by the Speaker, in each case for consideration of such provisions as fall within the jurisdictio of the committee concerned

A BILL

To amend the Controlled Substances Act to exclude cannabidiol and cannabidiol-rich plants from the definition of marihuana, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

This Act may be cited as the "Charlotte's Web Medical Access Act of 2015".

SEC. 2. EXCLUSION OF CANNABIDIOL AND CANNABIDIOL-RICH PLANTS FROM DEFINITION OF MARIHUANA.

THE CHARLOTTE'S WEB MEDICAL ACCESS ACT OF 2015 would "amend the Controlled Substances Act to exclude cannabidiol-rich plants from the definition of marijuana, and for other purposes." It states that "The Federal Food, Drug and Cosmetic Act shall not apply to cannabidiol or cannabidiol-rich plants as those terms are defined in section 102 of the Controlled Substances Act as amended by this Act." Also, "Nothing in this Act shall prohibit or otherwise restrict any activities related to the use, production, or distribution of marijuana in a State in which such activities are legal under State law."

that. Because the state of Colorado Department of Agriculture governs the crop and tests it, inspects it and it meets the definition of hemp under the federal farm bill, they believe they're in their legal rights to ship it. People are dying, this is ridiculous! The brothers decided to ship it to support parents. It's the parents who have to face local law enforcement and make that decision for themselves.

I want to push that we have this really powerful army of voices. And everyone is kind of scattered on so many different bills happening. And if we could all align and push them all, we could be a very, very scary force. I know there's a lot of dissension, but there's a majority now. If you poll the country, there's over 50 percent in support of medical cannabis. We don't have funds, money on our side, but we have the numbers.

O'S: Do you have any dealings with the reform groups like Americans for Safe Access or NORML?

Figi: I am in touch with them. I've heard two different statements —they're not in support of CBD and then they are in support of some of the CBD states. I've heard different back-and-forth on that.

The hemp industry is fully in support of these bills. They've never been able to get Orrin Hatch or Lamar Alexander on board for anything [without us] and they've been trying for 15 years.

O'S: What were the changes that Perry made in his bill between 2014 and 2015?

Figi: They added a sunset provision into the bill. They made it a little more conservative so that if the sky falls because you legalized CBD and agricultural hemp, it will sunset after three years. And then they changed the name, in the Senate bill to "The Therapeutic Hemp Medical Access Act—S.1333."

O'S: It's odd to see "cannabidiol-rich" defined in terms of THC content. "Therapeutic hemp" seems more accurate —although the Hemp Industry Association thinks it creates confusion.

Figi: This bill has a big chance of passing. They just need to hear from people.

O'S: Some observers say that having a CBD-only law in Florida hurt the chances of the broader bill, Amendment 2.

Figi: The CBD bill in Florida —the Charlotte's Web bill, they nicknamed it—existed before Amendment 2. And I don't feel that it did hurt, because people were made aware [of the medical benefits of marijuana] through the media around the Charlotte's Web bill. I think they actually help each other.

O'S: What happens next to the federal Charlotte's Web bill?

Figi: The bills have to pass out of the Senate and House Judiciary Commitees. If you're in a district of anyone on those two committees, we should be reaching out to them. Just educating them and asking 'Please co-sponsor this bill. … When they're in Washington, I can explain 'This is what you're signing onto exactly' and put them in touch with doctors and law enforcement to answer questions. But first they need to hear from their constituents.

Also, we need the Democrats who are for the CARERS bill. If they would see the importance of this one piece of their bill, they can help five million people right now. Once they're on board, all the Democrats will see this as something they can support. Now they see it as a Republican bill, even though the co-sponsors are bipartisan.

Hemp should be an industry in this country. Why import it?

O'S: Do you have any allies?

Figi: The Coalition for Accesss, a 501(c)4, is a platform for all the voices backing this bill. Everyone told me it takes money to pass a bill and I didn't believe it because everybody knows that CBD helps these kids —it's not controversial. I'm sad to say that it does take money. There are very few people who don't want this to pass, but they're heavily funded. We have public opinion but no funding.

I have a leader in each state that collects advocates. If it's a large state like Texas and California, two or three. And they help all the advocates that contact us either to do media, go to DC, or when their legislator is on recess, ask them to co-sponsor it.

So these parents go push our narrow message —they show pictures of their children wearing helmets— and reach out and help drive up that advocacy number, drive up the co-sponsorship number.

O'S: Many small reforms get sold to progressives as "a first step" towards bigger reforms. And then they turn out to be all we get —the last step, not the first. So there's reason to fear that a CBD-only bill could take the wind out of the sails of the medical marijuana movement, like some people say Obamacare took took the wind out of the sails of Single Payer Healthcare.

But this situation could be different because so many people are educated about cannabis and know that THC is beneficial and in many cases necessary. And especially if you, Paige Figi, are committed to keep pushing for the CARERS Act.

Figi: Absolutely. And why make the farmers wait? The farmers don't care about THC. They want this crop. Hemp should be an industry in this country. Why import it? And the kids need CBD. Why is it ethical to make them wait?

Introduced by Senators Paul, Gillibrand and Booker

ASA pushing the CARERS Act

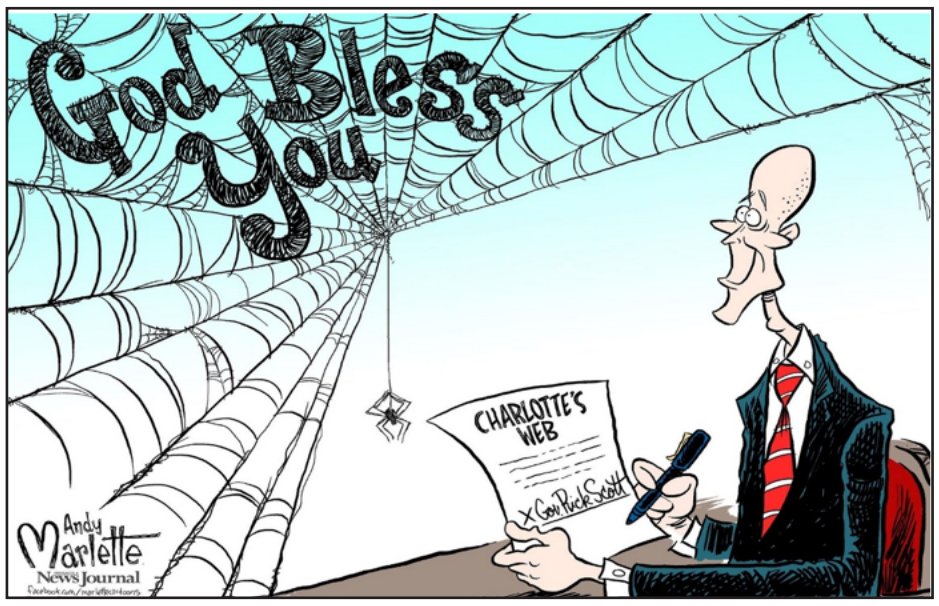
Steph Sherer, Executive Director of Americans for Safe Access, helped educate Kirsten Gillibrand of New York and Cory Booker of New Jersey on the need for changes in federal law to make marijuana available as a medicine to all who need it. It's understandable why Sherer strongly supports the CARERS Act —she had a hand in writing it.

Some backers of the CARERS Act fear that bills legalizing CBD will enable politicians to mollify constituents who want access to medical marijuana. These skeptics point to the 2014 vote in Florida, in which a ballot initiative to legalize medical marijuana (the whole plant, starring delta-9-tetrahydrocannabinol) fell less than 2% shy of the 60% needed for passage.

Governor Rick Scott had stated that he would never allow any kind of medical marijuana bill to be enacted in the Sunshine State. But during the campaign, strategists convinced him that signing SB-1030 (dubbed "Charlotte's Web" by the media), would make his opposition to medical marijuana seem less inhumane. With a stroke of the pen, Scott transformed his image from arch foe of medical marijuana to pro-CBD centrist. (*See cartoon below by Andy Marlette of the* Penascola News-Journal.)

In signing. Scott said, "As a father and grandfather, you never want to see kids suffer" —as if aunts and uncles just might. "Charlotte's Web will ensure that children in Florida who suffer from seizures and other debilitating illnesses will have the medication needed to improve their quality of life."

A very skeptical, previously reliable source in Washington source says, "Feinstein and Grassley don't want Charlotte's Web, they don't want farmers here growing crops to produce CBD, they want this thing locked up for the pharmaceutical industry."



Steph Sherer, Executive Director of Americans for Safe Access, speaking at ASA's "Unity Conference" in Washington, DC, March 28. Sherer launched the group in 2002, with support from dispensary operators. Only four dispensaries had representatives at the 2015 conference. "Now we have trade associations," one of them explained.

What it would do

By Mike Liszewski

On March 15, 2015, U.S. Senators Cory Booker (D-NJ), Rand Paul (R-KY), and Kirsten Gillibrand (D-NY) introduced the Compassionate Access, Research Expansion, and Respect States (CARERS) Act —the first comprehensive piece of medical marijuana legislation to be introduced in the U.S. Senate. Americans for Safe Access was honored to have played a role in shaping direction of the bill, and many of the patient-focused issues we brought up were addressed in the final legislation.

The bill's introduction comes just a few months after passage of the Rohrabacher-Farr Amendment, which was guided through the conference committee by the leadership of Senator Mikulski (D-MD). The Rohrabacher-Farr Amendment arguably should have defunded the prosecution of the Kettle Falls Five by the US Attorney for Eastern Washington, but the denial of their motion to dismiss shows that there is some legal dispute as to whether Rohrabacher-Farr Amendment will end federal prosecutions. There is no question that such prosecutions would end under the CARERS Act, which states:

"Notwithstanding any other provision of law, the provisions of this title relating to marihuana shall not apply to any person acting in compliance with State law relating to the production, possession, distribution, dispensation, administration, laboratory testing, or delivery of medical marihuana."

Prior to introduction of the CARERS Act, many Senators have avoided taking an official position on medical marijuana because there was no legislation in the Senate on the issue. Now Senators must confront it.

Patient advocates and other stakeholders have an opportunity to discuss each of the bill's issues in a substantive way. Rather than decry any perceived shortcomings, patient advocates can make strategic use of their time lending support to help get the bill heard before the Senate Health, Education, Labor, and Pensions Committee and offering suggested amendments to improve the bill.

To help better understand the bill, below is some section-by-section analysis (skipping Section 1, which is simply the title of the bill):

2. Federalism in Drug Policy

This is the section quoted above. It allows all state-legal medical marijuana conduct to continue to exist without any federal interference. Unlike the Department of Justice's August 2013 Cole Memo or even the Rohrabacher-Farr Amendment to the DOJ budget, this protection is both binding and permanent. ASA was successful in making certain that testing labs were included along with producers and dispensers. The exemption from the Controlled Substances Act does two additional things:

1) It will provide 280e tax relief to medical marijuana businesses (which should result in lower prices for patients) and

2) It will allow state programs to go on unimpeded, regardless of where marijuana is placed in the CSA, because the CSA will no longer apply in those states where medical marijuana is legal under state law.

Section exempts state programs from the Controlled Substances Act, so they could continue to operate regardless of any potential implications of Schedule II status.

This section creates binding and unequivocal legal protections from federal interference for anyone abiding by their state's medical marijuana law.

It is unclear whether or not dual-licensed medical/adult-use businesses would be covered, but it appears they would for the medical portion of their business.

114TH CONGRESS
1ST SESSION

S. 683

IN THE SENATE OF THE UNITED STATES

March 10, 2015

Mr. Booker (for himself, Mrs. Gillibrand, and Mr. Paul) introduced the following bill; which was read twice and referred to the Committee on the Judiciary

A BILL

To extend the principle of federalism to State drug policy, provide access to medical marijuana, and enable research into the medicinal properties of marijuana.

Section 1. Short title

This Act may be cited as the "Compassionate Access, Research Expansion, and Respect States Act of 2015" or the "CARERS Act of 2015".

3. Rescheduling of Marijuana

The rescheduling portion of the bill is probably the section that will get the most criticism from patient advocates and others. While placement in Schedule II does not appear to be appropriate based on its widespread medical acceptance and lower abuse potential than other Schedule II substances like cocaine and methamphetamine, it would show that the U.S. government has finally accepted that there *is* medical use for marijuana.

Placement on Schedule II could also potentially open up health insurance coverage to medical marijuana therapy, but that would not happen automatically. There are some who have expressed concerns that if marijuana were placed in Schedule II that it would mean pharmacies would have to take over distribution and that pharmaceutical companies would take over production.

However, Section 2 of the bill, completely exempts state programs from the CSA, so they could continue to operate regardless of any potential implications of Schedule II status.

4. Exclusion of Cannabidiol from Definition of Marijuana

The concept of this section of the bill similar to Rep. Scott Perry's HR 5226 from the 113th Congress, but has been slightly modified. This language would completely remove derivatives of marijuana with less than 0.3% THC content from the CSA, which would help enable transportation of high-CBD extracts across state lines.

States that have not already passed full medical marijuana laws or CBD-only laws would still need to pass such laws for protections to be complete in those states. It is a fairly safe assumption that most, if not all remaining states without CBD protections would adopt such laws in the wake of federal passage.

5. CBD Determination by States

This section was inspired by a similar provision in the S. 134, Industrial Hemp Farming Act of 2015, which had a safety valve provision for states that allow more than 0.3% THC in their CBD laws. ASA provided the Senate offices with language that will protect the patients in states that allow 0.5% to 5% THC in their CBD laws, such as Alabama, Florida, Iowa, Missouri, South Carolina, Tennessee, and Virginia.

6. Banking

The banking section of the bill used Rep. Perlmutter's HR 2652, the Marijuana Access to Banking Act of 2013, as its basis. The provision would allow anyone acting in conformity with their state marijuana laws to be able to access banking services. This section would exempt banks from filing suspicious activity reports on marijuana businesses. It would explicitly forbid the federal government from penalizing marijuana businesses or incentivizing banks to discriminate against legal marijuana businesses.

7. Research

ASA urged the Senate sponsors to make sure that the two biggest barriers to medical marijuana research in the US were addressed, the Public Health Service Review Process and the NIDA monopoly on the supply of available research marijuana. The Obama Administration has already removed the Public Health Service review. The CARERS Act would end the single source monopoly for federal marijuana made available for FDA-approved research. This will help ensure that a greater variety of marijuana is available to help foster meaningful research in the U.S.

8. Veterans

ASA also urged the bill sponsors to include a section that would allow VA doctors to fill out state medical marijuana recommendation forms.

Mike Lisziewski is government affairs director for Americans for Safe Access.

Senate Drug Caucus investigates the political potential of cannabidiol

By O'S News Service

The Senate Caucus on International Narcotics Control was created in 1985 (the height of the Ronald Reagan era) and given special powers to issue subpoenas and call hearings. Chairman Chuck Grassley (Republican, Iowa), arranged for a hearing June 24, 2015 on "Barriers to Cannabidiol Research and Potential Medical Benefits."

After opening statements by Grassley and his Democratic counterpart, Dianne Feinstein of California, three Senators who have introduced CBD-related bills —Orrin Hatch, Kirsten Gillibrand, and Cory Booker laid out their views. Then came testimony by Joe Rannazzasi of the DEA, Dr. Douglas Throckmorton a deputy director at FDA, and Dr. Nora Volkow, the director of NIDA. Booker and Gillibrand joined Grassley and Feinstein in questioning the agency officials.

Grassley recounted the basic story —kids with epilepsy getting seizure relief from "a substance called cannabidiol, or CBD... a compound derived from the marijuana plant that can be administered in the form of an oil. It's not smoked, and it can't be used to get high."

Desperate parents are "buying CBD products that haven't undergone the usual testing for safety and efficacy associated with new medicines, and in many cases haven't been evaluated for concentration or purity. Sometimes these products may be helping children, but sometimes they have no effect, or may even cause harm."

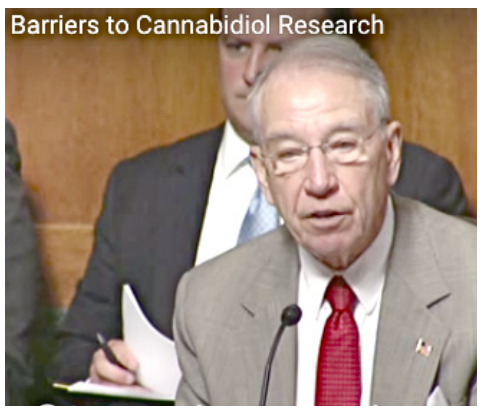
Grassley described GW Pharmaceuticals' Epidiolex, which is "undergoing FDA-approved clinical trials to treat two rare forms of pediatric epilepsy. I'm glad that one of the sites at which it's being tested is the University of Iowa."

Earlier in the year Grassley and Feinstein had urged the Department of Justice and the Department of Health and Human Services Department to get rid of impediments to CBD research. Grassley took credit for HHS dropping its requirement that the Public Health Service approve all studies involving cannabinoids. PHS approval had not been required "for any other Schedule I substance," Grassley noted. (Indeed, the requirement had been imposed by HHS under Donna Shalala in the Bill Clinton era.)

Dianne Feinstein

Even the staunchest Drug Warriors in Congress have constituents whose epileptic children have been helped by CBD. Dianne Feinstein said she did, too. But "I've heard from other constituents, like Catherine Jacobson, who, after researching cannabidiol as a treatment, went to a medical marijuana dispensary to obtain it for her six-year-old son who has epilepsy. Instead she was given plant material, not cannabidiol in any form that her son could ingest.

"Ms. Jacobson is still trying to find a safe and reliable form of cannabidiol to treat her son, but is worried about a lack of data, the high variability in oils, dosing, and cannabidiol's potential interaction with other medications. All of this points toward the need for research and regulation."



Senators Chuck Grassley (Republican, Iowa) and Dianne Feinstein (Democrat, California) at the Senate Caucus on International Narcotic Control's June 24 hearing on "Barriers to Cannabidiol Research and Potential Medical Benefits."

Orrin Hatch

The Senator from Utah began his testimony with the story of Charlotte Figi, and his words echoed her mom: "I understand the desire for caution. We're Congress. We act slowly. But we must remember that these are people whose lives we're dealing with... for whom a five- or 10-year delay is not an inconvenience but a potential death sentence.

My home state of Utah —certainly no redoubt of hippie liberalism— was the very first state to legalize CBD.

"Given that CBD produces no psychoactive effect, I frankly see no reason why it should remain illegal under federal law... Parents who wish to obtain CBD to treat their suffering children risk federal prosecution for the sole reason that CBD is derived from the cannabis plant. Never mind that it produces no high, never mind that it actually counteracts the effects of THC. Under current law, because it is derived from the cannabis plant it is unlawful.

"To remedy this situation I've recently co-sponsored bipartisan legislation with Senators Gardner, Wyden, Alexander, and others, to exempt CBD from the definition of marijuana under federal law. Our bill, 13-33, will allow parents to obtain this life-changing therapy without threat of federal prosecution. It will enable parents, if they choose, to use a therapy that has shown great success in reducing seizures in children for whom all other treatments have failed.

"Now I want to reiterate that CBD cannot be used to get high. That point is critical. It's what differentiates CBD from all these other attempts to legalize marijuana, whether for medical purposes or otherwise. CBD is not a camel's nose under the tent for advocates of full marijuana legalization. Fifteen states have now legalized CBD. These include some of the most rock-ribbed conservative states in the country such as Alabama, Oklahoma, and Texas. In fact, my home state of Utah —certainly no redoubt of hippie liberalism— was the very first state to legalize CBD.

"And I continue to oppose marijuana and efforts to legalize its use. I remain unconvinced by claims that it is safe and that the side effects it causes are no big deal..."

Sen. Orrin Hatch (Rep.-Utah), introduced the "Therapeutic Hemp" Act, which would remove CBD from the Controlled Substances Act. In 1994 Hatch wrote the Act in which Congress defined "dietary supplement" and advised the Food and Drug Administration that dietary supplements were to be regulated as the former. The dietary supplement industry has been booming ever since. In Utah it's a $7 billion bnsiness.

Hatch told the Senate Drug Caucus that he wants to see the medicine that reduced Charlotte Figi's seizures —cannabidiol— available as a dietary supplement.

23 and DC

Sen. Kirsten Gillibrand of New York, had also met with parents of children suffering seizure disorders, and said she had come to understand that cannabis (not just CBD) could be beneficial in treating a wide range of disorders (not just epilepsy). Gillibrand said that 23 states and Washington, DC, had passed medical marijuana laws that could not be fully implemented "until we change our outdated federal laws."

Without referring to the CARERS Act, Gillibrand said, "Let's pass a new, modern law on medical marijuana that respects state laws and respects modern scientific research."

Nor did Cory Booker of New Jersey use the occasion to pitch the more comprehensive bill. He described constituents whose children had been helped by CBD and found themselves forced to choose between breaking the law or seeing their children go without the best anti-seizure medicine. "There is a moral urgency here," he said.

"Although this hearing is limited to CBD," Booker added, "I do not want to lose sight of the government's overall policy on medical marijuana. Other Americans are dealing with other conditions. We need to consider the issue as a whole."

Throckmorton of the FDA

Douglas Throckmorton, MD, is deputy director for regulatory programs in the Center for Drug Evaluation and Research at the FDA. He testified:

"FDA is the agency that is responsible for the assessment and regulation of new drugs in the United States, including drugs derived from plants like marijuana. The Food, Drug and Cosmetics Act requires that those drugs be shown to be safe and effective for their intended use before being marketed.

"In addition, drugs must be shown to be manufactured consistently, lot-to-lot, with high quality. Because many factors influence the make-up of plant materials, such as temperature, time of year, location grown, this essential part of drug development presents special challenges when the drug is derived from a botanical source like marijuana.

"To address these challenges, FDA has published guidance to investigators to give recommendations about the types of studies to be conducted when developing drugs from plants... In addition to working directly with investigators to support their studies, FDA has several [expediting] mechanisms... such as 'fast track designation,' 'accelerated approval,' 'priority review,' and 'breakthrough' designation.

"Wherever possible we are applying these tools to the development of the products derived from marijuana and cannabidiol. For example, fast-track designation was granted to an investigation of cannabidiol, Epidiolex, being developed for a rare form of childhood epilepsy."

Throckmorton said that, according to the manufacturers, "20 Epidiolex intermediate-sized expanded access programs have been authorized to treat approximately 420 children."

He saw it as a win-win: "Importantly, these children are getting access to an investigational product under close medical supervision, and the data obtained from their use of the investigational agent is being collected to help support drug development."

Exposing Scammers

Throckmorton said, "We are also mindful of protecting consumers. In February of 2015, FDA took action against marketed, unapproved drug products that were making egregious health claims, including products that allegedly contained cannabidiol and other compounds from marijuana. For example, products containing cannabidiol were advertised nationally making unsubstantiated claims as being effective in the treatment of conditions such as breast cancer, rheumatoid arthritis, and ebola infection.

"We analyzed the products and found that many did not even contain the ingredients listed on their labels. For example, when we tested products that allegedly contained cannabidiol, around one-third of those products, in fact, contained no cannabidiol...

"These products and their marketing can create false hope in those seeking relief from serious medical conditions for themselves or their loved one. Moreover, it can divert patients from products with demonstrated safety and effectiveness.

Cannabinoids 101

Dr. Nora Volkow, the head of NIDA, gave the Senators a fast introduction to the endocannabinoid system. "Cannabidiol has a very low affinity for these receptors," she said reassuringly, "and is devoid of rewiring or pleasurable effects...

"Pre-clinical research has indeed suggested that CBD may have a range of therapeutic effects, most notable of which are anti-seizure, neuroprotective, anti-inflammatory, analgesic, anti-tumor, anti-psychotic, and anti-anxiety relieving properties. Most of the recent public interest has focused on the potential value of CBD in the treatment of seizure disorders. And indeed, multiple studies using animal models have shown that CBD reduces the severity of seizures. And ongoing studies are in-

text continues on next page

Douglas Throckmorton, MD, Deputy Director for the Center for Drug Evaluation and Research, Food and Drug Administration

Senate Drug Caucus *continued from previous page*

vestigating its mechanism of action. In the meantime, clinical case studies and reports from patients have provided suggestive evidence that CBD may be effective in treating children with drug resistant epilepsy...

"The evidence is insufficient to arrive at a firm conclusion. This is likely to change in the near future," Volkow said, citing the "ongoing clinical trials being conducted by GW Pharmaceuticals to test the efficacy of Epidiolex in pediatric epilepsy."

"NIH identifies CBD as an interesting target for therapeutic studies that go beyond its value as an anti-seizure medication."

Volkow seemed relieved to be talking, for a change about possible benefits. "NIH [National Institutes of Health] identifies CBD as an interesting target for therapeutic studies that go beyond its value as an anti-seizure medication... NIH institutes are funding work on the therapeutic value of cannabinoids, including CBD, in the treatment of neurologic, psychiatric, immunological, metabolic, and oncological disorders."

Volkow concluded: "It appears that CBD is a safe drug with no addictive effects. The preliminary data suggests that CBD may have therapeutic value for a number of medical conditions. Addressing barriers that slow clinical research with CBD would accelerate progress."

Questions and Answers

Grassley said that each Senator could ask seven minutes' worth of questions. He started with one for Volkow. "NIDA," he said, "is the agency responsible for providing researchers with marijuana to support CBD research. NIDA does so by contracting with the University of Mississippi to grow multiple strains of marijuana and recently NIDA, in consultation with the Drug Enforcement Administration. dramatically increased the supply of research marijuana grown at the university.

"However, there is still a question about whether the arrangement as it currently exists will continue to meet the needs for research-grade marijuana. Do you believe that it would be beneficial to allow NIDA ,in coordination with the DEA, to grant more than one contract to approved entities to grow marijuana for research?"

Volkow was unequivocal: "The answer is yes. I think it would be beneficial."

In the 1980s, Grassley recalled, there was a program under which the drug Marinol [synthetic THC] was used experimentally by some 20,000 cancer patients prior to approval by FDA. Could large numbers of patients use Epidiolex, too?

"Absolutely," said Throckmorton. "That program was a precursor to the current expanded access program through which 400 children are getting access to Epidiolex now. It's a program set up by the manufacturer to work with an individual physician or medical center to allow access to an investigational product."

Joseph Rannazzisi, Deputy Assistant Administrator of Drug Diversion with the Drug Enforcement Agency.

Dr. Nora Volkow, Director, National Institute on Drug Abuse.

Grassley asked, "Is there any reason that more children couldn't be enrolled in that program?

Throckmorton explained: "The manufacturer has to make the decision to set up an expanded access program. In this case, GW Phamaceuticals has made that decision and so they're making the product available.

"The product is available under medical supervision, so it requires that the patient be under care of a physician to watch for side effects, to monitor for adverse effects and efficacy... and report back to us.

"It also requires that institutional review boards be aware of and approve the administration of this investigational drug to the patient.

"The fourth thing for a controlled substance like this is that the manufacturer would need to work with the DEA and make certain that there was authorization to manufacture enough of that controlled substance. I know that the DEA has made that step possible in this case, so that's not an issue here today. But, so as long as those four conditions are met, and so long as other reporting requirement are met by the manufacturer, FDA has approved 99 percent of these expanded access programs since 2010. We don't get in the way. And they are being used broadly.

Grassley made reference to the CARERS Act without naming it. "There are legislative proposals before Congress to change marijuana from Schedule I to Schedule II," he said. " Some believe that these proposals will make CBD products being sold on the black market immediately available under federal law." He directed his question to Throckmorton: "Would moving marijuana to Schedule II change the legal requirements that CBD-based medicines, like all medicines, have to be approved by the DEA and the FDA before being prescribed by doctors? And if not, could you describe the federal regulations that would govern the approval process for a medicine developed from a Schedule II substance.

Throckmorton said that a scheduling change "would not affect the drug development and approval process... The major impact would be on the controls that would be in place over research."

DiFi Heart GWP

Feinstein asked again if a scheduling change would have an impact on research. Throckmorton tried to kick it to the DEA man: "Well, there are additional controls. I think as Mr. Rannazzisi said, there –

Feinstein: "Answer that, yes or no."

Throckmorton: "There are additional steps, so to the extent that those additional steps exist they are additional things that need to happen."

Feinstein: "Okay, now this company GW that the 400 children are utilizing the cannabidiol, are the doses standardized? Are they by prescription? How does it work?

Throckmorton: "Absolutely, and I should have made that clearer. Thank you for that question. Absolutely, and it's one of the really important things about the expanded access program is it takes place in the context of a drug development program. GW Pharmaceuticals has developed a formula-

Senator Kirsten Gillibrand, (Democrat, New York).

tion of cannabidiol with dosing and manufacturing information – all of the things that we'd expect for a drug that you take every day or are given in a hospital or something like that. And then, they're using that exact same product, the same product that they would hopefully be able to market once they've provided the clinical trials to us, that's the product being given to the children under the expanded access program."

Feinstein *(impressed)*: "Can that program be expanded now?"

Throckmorton: "The limitations on it are the ones that I mentioned before, which is the manufacturers control this. So the FDA can't force a manufacturer to do this or not do this. This is something that they have chosen to do. There needs to be a physician that's able to supervise the patient to make certain that the adverse events are identified."

Feinstein: "Well, that's very good news, I think. And my sense is the Senate would certainly support that."

Throckmorton: "We've had a very good relationship working very closely with this manufacturer. I have an expanded access crew that is trying to do anything we can to help them.

Feinstein: "Right. Well, I think that's very good to hear... I understand that our country has a patent on cannabinoids, including CBD, which states that 'non-psychoactive cannabinoids such as CBD are particularly advantageous to use because they avoid toxicity that is encountered with psychoactive cannabinoids.' How, if in any way, will that patent factor into the scientific and medical evaluation?

Volkow explained that the federal patent on CBD is specifically for its use as an anti-oxidant for neuroprotection, and has nothing to do with its potential as an anti-seizure medication. [O'Shaughnessy's broke the story of the federal patent. Hey, dude, where's our Pulitzer?[

Feinstein repeated her admiration for GW Pharmaceuticals' approach. Throckmorton reiterated that the company "has enrolled fully two trials of children for severe seizure disorders... Those clinical trials are important because they're going to form the data that the FDA is going to to use to [assess] the efficacy and safety of the product while we make it available under the expanded access program."

He ran it by her one more time: The investigational new drug is being given to patients under the expanded access program by doctors conducting placebo-controlled trials.

Feinstein: "Well, for whatever it's worth, I'm really pleased that FDA is taking that position and allowing expansion."

Gillibrand Skeptical

Senator Gillibrand didn't open with any niceties. "How many patients nationwide need access to CBD?" she asked Throckmorton. He said "I don't have that information."

"Estimate," she demanded. "Is it tens of thousands? Is it hundreds of thousands? Is it hundreds? I just need to know because 400 patients [a reference to the Epidiolex patients, down from 420 when first mentioned] is not even meeting the need for New York state. So how many patients need access to medicine?

Throckmorton: "The challenge is that we have many medicines approved for the treatment of seizure disorders. We recognize they have side effects. We recognize that not all of them work in all patients. So to identify the subgroup of individuals that have tried all of those – and they're not working for them – I wouldn't have an estimate. It's many patients. Rather than trying to decide what that number is, I really – my job is –"

"So what I hear from you is that having this one drug company who's got 400 patients –we're solving the problem? That's outrageous!

Gillibrand *(with increasing anger):* I don't want to limit the access to CBD to one drug company. It is absurd that we're saying that that's going to solve the problem. So what I hear from you is that having this one drug company who's got 400 patients – we're solving the problem?! That's outrageous. That's an outrageous impression to leave on this committee, because you have thousands of patients in my state alone who need access to this medicine and they don't all get accepted by the drug trials.

"And when you talk to a parent they tell you, 'The other medicines that are approved for my kid are barbituates that knock him out and put him in a coma-like state, that's not a quality of life I want for any child.'

"So, let's be clear. We need to change the laws to remove impediments so we have research being conducted across the country as is being done in other countries like Canada and Israel. We cannot have only one place where this plant can be grown. It needs to be distributed more widely so that people can get access to the materials they need to do the research.

"We have to change the Schedule, you said Schedule 1 to Schedule 2 releases impediments. What are those impediments? Explain to us what is the difference between Schedule 1, Schedule 2 in terms of a researcher's ability to research this drug and a drug company's ability to produce a medicine that has the protections that Sen. Feinstein needs for her constituents?"

Throckmorton: "Be happy to talk about the one particular role that Schedule 1 has in terms of the FDA, and then I'd ask Mr. Rannazzisi to talk about the DEA's role.

When a Schedule 1 product is being studied they have to report to us any changes in their protocol. So if they've got a clinical trial and they are enrolling a number of patients and they're following it for six weeks, and they decide that they need to change the conditions of that study so that instead of three weeks it's going to be followed for four weeks –something like that. Typically those changes come into us but the trial is allowed to continue to go forward. For controlled substances, for Schedule 1 substances, there's a review that's required. The DEA sends that protocol change to us. We are on a 30-day clock to look at that and get an answer back to the DEA. And then the DEA goes back to that investigator and says yes the trial can go forward.

Gillibrand: Is it fair to say the process is very cumbersome?

Throckmorton: It is not a straight – there is that additional step. This additional exchange that has to happen that doesn't occur for products that are in different schedules, less controlled schedules.

Throckmorton explained that Schedule II products have a high risk of abuse but

continued on next page

Senate Drug Caucus *from previous page*

an accepted medical use. For example opioids, approved by the FDA for treatment of pain in cancer, etc.

Rannazzisi: "The Schedule 1 researcher has to apply for separate research registration. He submits protocols. The protocols basically outline who he is, what his background is, then what his research is going to be and under what authority he's doing that research. For instance, is he doing it with an institution? Is he doing it pursuant to an IND? We get that protocol. We submit it to FDA for approval. And once it's approved it comes back to us. We ensure that he's got a secure container to keep his drugs in, and we explain the paperwork to him for procurement, and he gets his registration."

Gillibrand confronted Volkow: "Given that NIDA's mission is to lead the nation in bringing the power of science to bear on drug abuse and addiction, what specific steps is NIDA taking to advance research into the medical *benefits* of marijuana? To put it another way, how can NIDA control the research supply in medical marijuana studies that seek to find benefits when the mission is solely focused on the negative consequences of marijuana use? And is there an agency better suited to handle the research supply of marijuana?

Volkow: "I want to answer that question... One of the things that NIDA does is study the effects of drugs in the human brain. But the research is not just focused per se on the negative effects of marijuana, and in fact as I very explicitly stated, we're very interested on doing research that relates to the potential benefits that cannabidiol may have on the treatment of drug addiction.

"Being the only source of research material for marijuana, that's not something that NIDA chose to do."

"We're also interested in understanding how cannabidiol or other cannabinoids may be utilized for the better management of pain, as well as for the potential management of patients suffering from HIV.

"Being the only source of research material for marijuana, that's not something that NIDA chose to do. There is a law that requires that we be that agency, and we comply with the law.

Gillibrand asked, "Given that marijuana is a multi-compound botanical substance? Is it reasonable to expect that marijuana could ever make it through the FDA approval process? If not, would it make sense to develop a new approval protocol for multi-compound botanical substances such as marijuana in the FDA?

Throckmorton: "It's absolutely reasonable to expect that marijuana would be able to be developed as a drug. We've done it before. We've approved other plant-derived drugs. We have guidance that we put out. I have in place a team whose job it is to help developers who want to develop drugs from plants– to give them any advice and help that they can. So, yes, there is a pathway laid out. Yes, it's been done."

Gillibrand: "What's the timing for that pathway currently?"

Throckmorton: "What we need is an interested investigator working with us and doing the studies that we need to have to be certain that we have a product that's well characterized, that's studied appropriately in a patient population, that we can identify, so I can give a prescription, I can tell a prescriber that they can prescribe that medicine to those patients."

Gillibrand: "So the current 400-person study, is that sufficient for you to begin the process?"

Throckmorton: "This process begins with conversations about the drug itself. So in the case of a plant-derived product like

Senator Cory Booker (Democrat, New Jersey) asked why the DEA was ignoring an Act of Congress ordering an end to raids on medical marijuana providers operating legally under state law.

a marijuana product, it would start with a discussion how they want to develop it, what patients they want to study it in, what kinds of treatments they want to measure, what outcomes they –"

Gillibrand: "Is that happening with this company that you talked about?"

Throckmorton: "That's already happened with this company. It happened. And any additional conversations they need, we're having. Any investigator that's interested in coming in and talking to us about developing a drug for marijuana we have a process to put them into involving a discussion with the right review division, specifically to lay out what kinds of trial designs they'd need to use."

Booker of New Jersey

Booker decried "NIDA's monopoly" on marijuana for research and cited an instance of egregious delaying.

Volow said she had already expressed her view: "If there were alternative sources of cannabidiol, would I support that? The answer is yes. It should make the research much more efficient. So some of these delays –

Booker: I only have five minutes, so I just want to get my answers –

Feinstein *(sourly correcting him)*: You have seven minutes.

Booker *(to Feinstein):* I have five left. *(Gillibrand taps him under the table as if to say "Stay cool." Booker returns his attention to Volkow.)* In other words efficiency, effectiveness, availability for research would be better if it was not a monopoly.

Volkow: Correct.

Booker: And so, does that monopoly exist for other Schedule 1 drugs?

Volkow: Not to my knowledge.

Booker observed that researchers could obtain heroin from more than one supplier. "Why would you treat heroin differently than you're treating pot?" he asked. "Why would that be? Is there any scientific reason whatsoever?

Volkow: There is no scientific reason. No.

Booker asked Throckmorton if he acknowledged the "chokehold on the ability for us to conduct research... as a problem?"

Throckmorton said, "I think there are advantages to broad availability of a variety of different kinds of marijuana.... Expanding the numbers of growers is one potential solution."

Booker asked if moving marijuana to Schedule II would expedite research.

Throckmorton said yes, not just logistically but politically. Rescheduling might kindle "the perception that it is now easier, it is now something that an investigator could be interested in doing, could make a career of, a sort of sense of the possible. It sends a message that it's important to do this and it's possible to do it.

Booker said, "I'm going to take that as a 'yes,' and turned to Rannazzissi (whose name he mangled. "One year ago Senator-Paul and I offered an amendment to a federal spending bill that would prohibit the Department of Justice and the DEA from using taxpayer money to undermine state medical marijuana laws. The amendment was ultimately inserted into the House and Senate omnibus Appropriations Act, which subsequently passed and was signed into law. I'm concerned now, though, that the DEA is failing to implement this amendment and continuing to erect barriers to prevent states from making CBD and other medicines available without federal interference.

"What steps is the DEA taking to implement this policy? What assurances can you give that state medical marijuana programs are not being undermined by federal laws? Because I see people moving out of my state to go to states so that they can get access to this medicine, I'm concerned that they still have the threat of the DEA enforcement.

Rannazzasi said, "I'm not aware of any effort to undermine that particular provision within the law. And I'll go back to the department and bring this up."

Booker pressed on: "In April, a spokesperson for the Justice Department told the *Los Angeles Times* that the bipartisan Medical Marijuana Amendment does not prevent it from prosecuting people for medical marijuana and seizing their property, including CBD...If you can find out for me why does the department ignore the clear intent of Congress for the amendment to protect marijuana including CBD patients and providers from prosecution and forfeiture."

Rannazzasi said he would look into it.

Booker's concern would be addressed in October when US District Judge Charles Breyer ruled that the DEA was prevented by wording in the 2015 Appropriations Act from interfering with medical marijuana production and distribution when it is allowed under state law.

Fairfax dispensary can reopen

Breyer to DOJ: Acts of Congress Matter

"This court has a lengthy history with this defendant on these issues," wrote US District Judge Charles Breyer in an order filed October 19 allowing the Marin Alliance for Medical Marijuana to reopen because Congress has changed its spending priorities.

MAMM proprietor Lynette Shaw first appeared before Breyer in 1998, when the US Attorney for the Northern District of California sought an injunction to close hers and five other dispensaries (including the San Francisco and Oakland Cannabis Buyers' Clubs).

Back then Breyer granted a preliminary injunction on the grounds that the federal Controlled Substances Act took precedence over the medical marijuana law enacted by California voters.

Some of the dispensaries remained open, however, arguing that they were serving patients whose cannabis use was a matter of necessity. This argument was rejected by Breyer, then accepted by the Ninth District Court of Appeal, then rejected by the US Supreme Court. Breyer issued a permanent injunction in 2002, but Shaw stayed open for business in the small Marin County city of Fairfax. MAMM had thousands of members and a business license from the city.

It wasn't until 2011 that US Attorney Melina Haag closed the dispensary by threatening to seize the property from the landlord. Slammed with a $3 million claim from the IRS, Shaw retreated to Los Angeles. In 2014, when she returned to the Bay Area to auction off MAMM memorabilia, she was at loose ends. Now she plans to reopen the dispensary at another location in Fairfax if she can get financial backing.

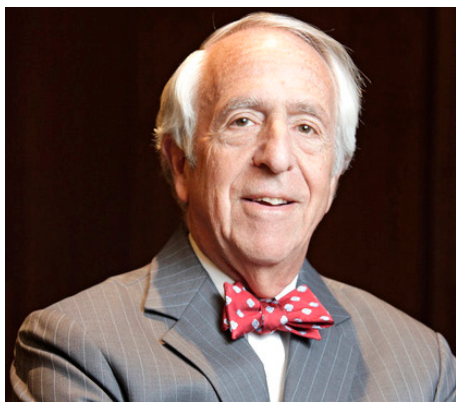
Greg Anton of Sebastopol is the lawyer who sought to get the injunction against MAMM "dissolved" on the grounds that it violates Section 538 of the Appropriations Act of 2015, also known as the Rohrabacher-Farr Amendment after the Santa Ana Republican and Santa Cruz Democrat who introduced it. The Amendment forbids the Department of Justice (DOJ) to spend funds to prevent California and 32 other states "from implementing their own State laws that authorize the use, distribution, possession or cultivation of medical marijuana."

Although Breyer left the injunction against MAMM in place, "The plain reading of the text of Section 538," he wrote, "forbids the Department of Justice from enforcing this injunction against MAMM to the extent that MAMM operates in compliance with California law."

Breyer's order was sharply critical of the US Attorney. "Where to start?" he asked after summarizing the DOJ arguments. He was appalled by the notion that closing down an occasional dispensary "may be presumed to have such a minimal effect on California's medical marijuana regime that it does not 'prevent' California from 'implementing' its State law.

"This 'drop-in-the-bucket' argument is at odds with fundamental notions of the rule of law. It has never been a legal principle that an otherwise impermissible goventment intrusion can be countnanced because any one defendant is a small piece of the legal landscape.

"To the extent the Government cites a few cases addressing Section 538, none are analogous or even particularly favorable to the Government's position," Breyer observed scornfully. The cases cited by DOJ all involved individuals or organizations that violated state law. But DOJ never alleged that MAMM had violated state law. Lynette Shaw treasured her license from the city and ran a legal operation, according to former Fairfax mayor Larry Bragman, whose letters of support Breyer cited in his order.



US District Judge Charles Breyer ruled that Congressional action superceded the injunction closing the Marin Alliance for Medical Marijuana. Breyer originally issued the injunction 2002. The DEA, acting on orders from US Attorney Melinda Haag, finally enforced in 2011.

photo by Hillary Jones-Maxon, The Recorder

Lynette Shaw may get the last laugh in her long struggle to operate a medical cannabis dispensary in Fairfax, California.

photo from the Marin I-J.