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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.

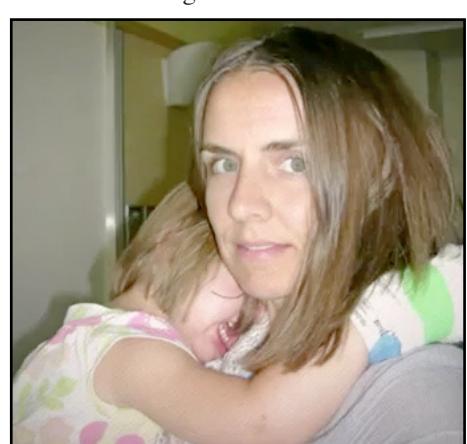
Slightly more than half the children using CBD-rich oil are having significantly fewer and less-severe seizures. Personalities and abilities emerge as children wean off debilitating synthetic anti-convulsants. The side effects of CBD are generally mild; drowsiness is foremost.

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 substantial 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.

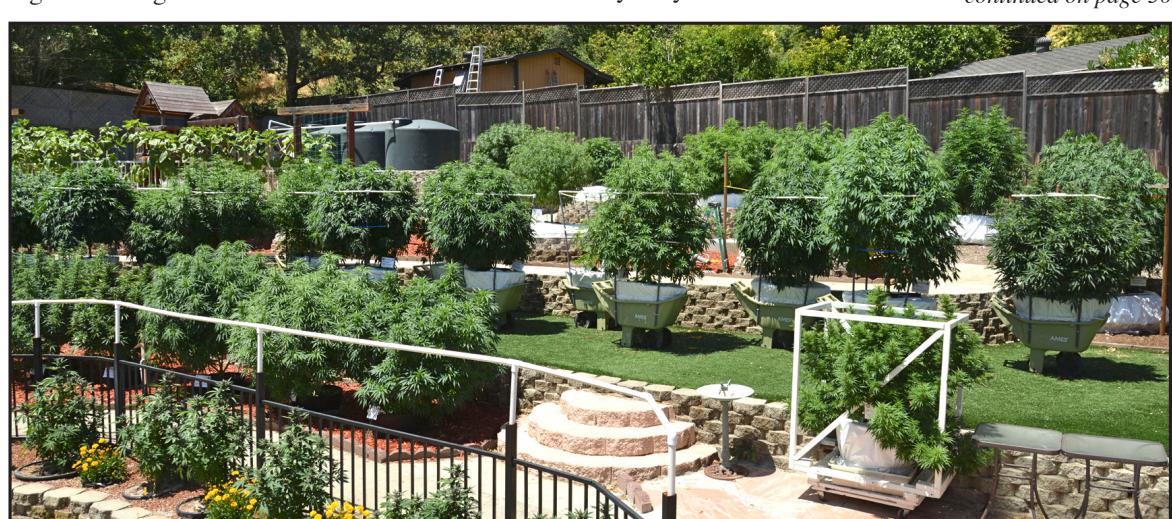
Roger Pertwee and colleagues at the University of Aberdeen reported in 2005 that

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.

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 mini-

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

mum 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.

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.

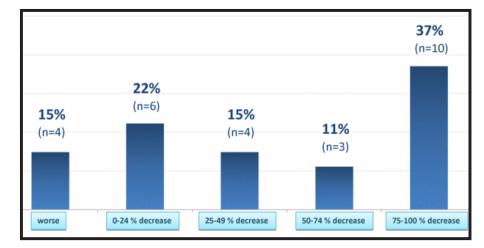
"Randomized controlled trials are warranted," the researchers concluded, "and we are pleased to report that these are now ongoing."

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.



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 Encephalopathy, 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 pre-clinical work that cannabidiol will address a number of these different issues, not just one."

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Cannabidiols:

POTENTIAL USE IN EPILEPSY & OTHER NEUROLOGICAL DISORDERS

FRIDAY, OCTOBER 4, 2013

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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.



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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



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.

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...

"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 de-scheduled, 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 milliliters.

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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

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.

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



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 Uruguayan 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

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 Adjuvant 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 Multidisciplinary 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?

Figi: 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?

Figi: 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?

Figi: 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?

Figi: 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?

Figi: 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?

Figi: 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 marijuana, 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. McCARTIN, 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 jurisdiction of the committee concerned:

A BILL

To amend the Controlled Substances Act to exclude cannabidiol and cannabidiol-rich plants from the definition of marijuana, 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 MARIJUANA.

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 Committees. 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 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 Pensacola 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

**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".

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.

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 is 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 Liszewski is government affairs director for Americans for Safe Access.

Hemp closer to *indica*

Sativa / Indica Genetics Gap Quantified

It has long been assumed that the difference between plants considered by cultivators to be *Cannabis sativa* and plants considered *C. indica* was the result of differences in the genes determining cannabinoid content. But the differences are spread throughout the genome, according to a new study by Canadian plant geneticists.

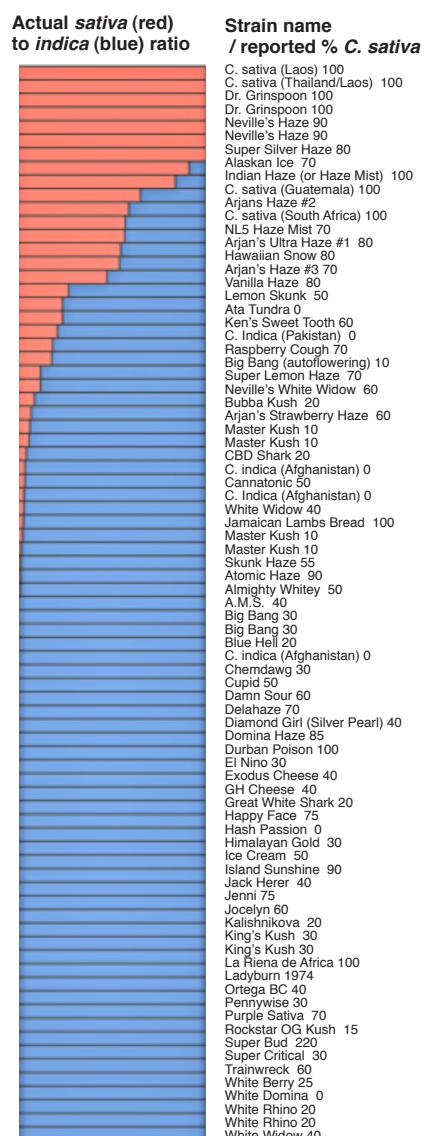
The researchers analyzed 81 marijuana and 43 hemp samples and found that "marijuana and hemp are significantly differentiated at a genome-wide level, demonstrating that the distinction between these populations is not limited to genes underlying THC production."

The study, published August 26 on PLOS1, developed "evidence that hemp is genetically more similar to *C. indica* type marijuana than to *C. sativa* strains."

The authors concluded that there is a "moderate correlation between the genetic structure of marijuana strains and their reported *C. sativa* and *C. indica* ancestry." They also found that "marijuana strain names often do not reflect a meaningful genetic identity" —confirming what Dr. Jeffrey Raber and other chemists have concluded.

The reported ancestry of the 124 plants analyzed was determined via online database searches, seed companies and licensed cultivators. Co-author Darryl Hudson (DOC Solutions in Ontario) estimated the identity of 26 strains for which no online information was available. Only three strains were found to actually be 100% Sativa: Dr. Grinspoon, Neville's Haze, and Super Silver Haze.

The graphic at right lists the strains tested and the ratio of Sativa (left hand part of each horizontal bar, in red) to Indica genetics (right hand part, blue). How inaccurate the commonly used names can be is illustrated by the total absence of Sativa genetics in Durban Poison, Jamaican



Lambs Bread and La Riena de Africa —all reputed to be 100% Sativas.

Lead author Jason Sawler is with Anandia Labs in Vancouver and Dalhousie University's Agriculture Faculty. The study was planned by Sean Myles, also of Dalhousie, and Jonathan Page of Anandia Labs and the University of British Columbia Botany Department.

2015 harvest

Thousands of acres of hemp grown in Kentucky, Colorado and Tennessee

In 2015 the Tennessee Department of Agriculture licensed 47 farmers to plant hemp on 1,595 acres, and allowed importation of 38,180 pounds of seed for them (almost all from Canada). But, as reported by Clay Duda in the *Knoxville Mercury*, "One shipment that arrived in Memphis was sent back to Canada after the carrier, FedEx, discovered the package contained hemp seed, which the company considered a narcotic... Other delays were attributed to the DEA slow-walking necessary paperwork to import the seeds."

So instead of planting in April and May —when fast-growing hemp would have shaded out weeds— Tennessee farmers were planting in June and July and their *Cannabis* had to compete with weeds. (The University of Tennessee had a one-acre hemp plot on which 15 herbicides and pesticides were tested.)

FedEx —but not the DEA— was also responsible for blocking hemp seed deliveries from Canada to Kentucky farmers. The Kentucky Agriculture Department licensed some 1,700 acres but only about 800 were planted, according to Eric Steenstra of the Hemp Industry Association. Heavy sprintime rains also impeded planting.

In Colorado 166 farmers were licensed to plant 3,657 acres of hemp in 2015. Some 2,300 acres were planted, availability of seeds being the main limiting factor. Colorado's Agriculture Department also licensed 571,000 square feet of space for indoor hemp cultivation.

Most of the crops are going towards CBD production. "Colorado tested 52% of the acres this year and only 8% were above 0.3% THC," Steenstra says. Plants in only one field were found to contain more than 1% THC. "Given the lack of certified seed,

that level of compliance is really quite good," Steenstra observes

Bill Polyniak is a Kentucky farmer who considers the hemp program "an absolute success." Originally involved because he has a son with epilepsy, Polyniak now sees hemp as a way to "revitalize" individuals' lives and the overall economy.

In 2015, Polyniak grew hemp in three Bluegrass Country locations —two dedicated to CBD oil production, one to seeds for planting in the future. "I'm thinking about 2025," he says. "These children are going to need oil all their lives."

After a CO2 extraction process in Kentucky, a portion of Polyniak's CBD-rich oil is trucked to South Carolina, where it is further refined, bottled and sold by a company called Palmetto Harmony —"created after a collection of parents with special children ran out of options using modern medicine," the website says. Palmetto Harmony CBD products are sold at healthfood stores in South Carolina.

Polyniak and his wife have developed their own brand of CBD-rich oil, "Genesis Blend," available through their Kentucky Cannabis Company & Bluegrass Hemp Oil websites. The 2014 harvest enabled Polyniak to get the price per milligram of CBD below a dime. The 30 ml bottle holds 300 milligrams of CBD oil and provides 10 milligrams per full dropper. (The dropper holds 30 milliliters.) A stronger extract of 1500 mg per bottle provides 50 mg of CBD per dropper-full. Both strengths are available in larger 4 ounce bottles.

Polyniak has applied for licenses to cultivate 20 acres of hemp in 2016. The goal of the breeding program is to maximize CBD content, seed production and fiber quality and quantity.

When Hemp Reigned in Kentucky

In 1900, Macmillan published "The Reign of Law: a tale of the Kentucky Hemp Fields," by James Lane Allen. If published nowadays it would probably be shelved among the romance novels. The heroine, Gabriella, comes from a wealthy family (even though they've lost their slaves). She is a devout young woman, takes the Bible literally. The hero, David, is the son of a devout hemp farmer. David goes off to college and learns about evolution. He comes home, gets expelled from the church founded by his great grandfather, and feels the wrath of his father and the disappointment of Gabriella. He gets pneumonia and is near death. He pulls through. He decides to go back to college and study the physical sciences. Gabriella, though her faith in Christianity is unwavering, will go with him.

The first chapter, "Hemp," is a florid paean to its subject. Some excerpts follow:

The Anglo-Saxon farmers had scarce conquered foothold, stronghold, freehold in the Western wilderness before they became sowers of hemp—with remembrance of Virginia, with remembrance of dear ancestral Britain...

Hemp in Kentucky in 1782—early landmark in the history of the soil, of the people. Cultivated first for the needs of cabin and clearing solely; for twine and rope, towel and table, sheet and shirt. By and by not for cabin and clearing only; not for tow-homespun, fur-clad Kentucky alone. To the north had begun the building of ships, American ships for American commerce, for American arms, for a nation which Nature had herself created and had distinguished as a sea-faring race. To the south had begun the raising of cotton. As the great period of shipbuilding went on—greatest during the twenty years or more ending in 1860; as the great period of cotton-raising and cotton-baling went on—never so great before as that in that same year—the two parts of the nation looked equally to the one border plateau lying between them, to several counties of Kentucky, for most of the nation's hemp.

It was in those days of the North that the CONSTITUTION was rigged with Russian hemp on one side, with American hemp on the other, for a patriotic test of the superiority of home-grown, home-prepared fibre; and thanks to



"Let these men be the strongest."

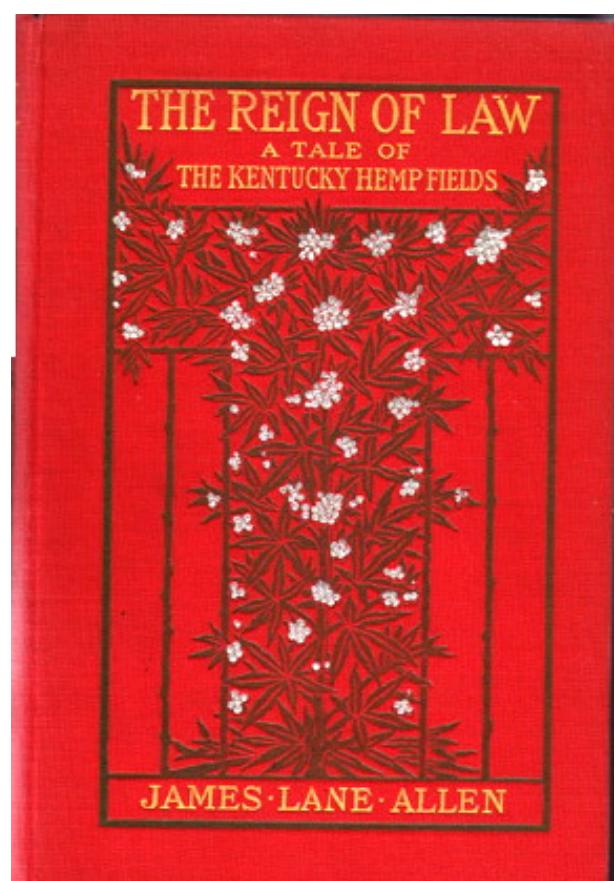
the latter, before those days ended with the outbreak of the Civil War, the country had become second to Great Britain alone in her ocean craft, and but little behind that mistress of the seas. So that in response to this double demand for hemp on the American ship and hemp on the southern plantation, at the close of that period of national history on land and sea, from those few counties of Kentucky, in the year 1859, were taken well-nigh forty thousand tons of the well-cleaned bast.

What history it wrought in those years, directly for the republic, indirectly for the world! What ineffaceable marks it left on Kentucky itself, land, land-owners! To make way for it, a forest the like of which no human eye will ever see again was felled; and with the forest went its pastures, its waters. The roads of Kentucky, those long limestone turnpikes connecting the towns and villages with the farms—they were early made necessary by the hauling of



"Then the fields are as the camp of an army."

the hemp. For the sake of it slaves were perpetually being trained, hired, bartered; lands perpetually rented and sold; fortunes made or lost. The advancing price of farms, the westward movement of poor families and consequent dispersion of the Kentuckians over cheaper territory, whether they carried the same passion for the cultivation of the same plant,—thus making Missouri the second hemp-producing state in the Union,—the regulation of the hours in the Kentucky cabin, in the house, at the rope-walk, in the factory,—what phase of life went unaffected by the pursuit and fascination of it. Thought, care, hope of the farmer oftentimes throughout the entire year!



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no longer at risk of losing a field because of one bad test result. Also, if we were to have crops wiped out by hail—we're dealing with Mother Nature, after all—we would have a back-up."

Joel said he had no idea what share of the market for CBD-rich oil is now being served by companies like Dixie and Bluebird that have been purveying CBD extracted from hemp grown overseas—"anywhere from 5 to 50 percent" was his guess. Starting with the 2015 harvest, he expects, some of these companies will be extracting from CBD-rich plants grown in Colorado and Kentucky.

"I think those companies are planning to do things similar to what we're doing," he says. "I can't believe it's cheaper to extract CBD from industrial hemp than from plants grown specifically for CBD content."

Hemp Oil Importers

Among those attending the Hemp Industry Association convention in Lexington, Kentucky in late September was Stuart Titus, head of a company called MJNA that has been a leading importer / distributor of hemp oil extracted overseas. We asked if checking out the situation in Kentucky presaged a new approach for his company.

Titus was forthright in response: "In Kentucky the seed arrived late into the planting season and the weather was not ideal later into the summer, so the crop was not as robust as was hoped for."

"In Europe, it was a good hemp season and we expect our usual annual crop and a good amount of hemp-based CBD oil to be available to our distribution channels."

"Our overseas efforts with hemp production, and product sales / development efforts are expanding."

CannaVest is another major importer of hemp oil. "We believe that we are the largest supplier of low-THC CBD oil in the world," says their website.

The production chief is Chris Boucher, who has been in the industry since 1990, when he started importing hemp goods from China. In 1992 Boucher founded a trade group, the True Hemp Industries Association, predecessor to the current HIA. In 1994 he grew hemp at the US Department of Agriculture research center in Brawley, California. The USDA was okay with cannabis containing less than 0.3% THC, but Governor Pete Wilson was not. The state overruled the feds.

As explained by Chris Boucher, the oil arrives in San Diego in 25 kilogram buckets as a thick tar, so dark green it looks black. Some of this "raw" oil is sold directly to customers. It contains chlorophyll, cellulose and waxes, and is "about 15% CBD(A)," depending on the crop from which it was extracted, says Boucher. It wholesales for "about three cents per milligram of CBD."

Most of the oil CannaVest imports gets decarboxylated in vacuum ovens at a production facility in San Diego. It is then processed, Boucher says—distilled into "gold oil," which is about 25% CBD and costs about 5¢ per milligram.

Boucher estimates that CannaVest will supply "close to 250 kilograms" of CBD oil to clients such as Medical Marijuana,

Inc., Dixie Elixirs, Bluebird Botanicals, Oasis, and CannaPet. These companies reformulate the raw material—oil or paste—provided by CannaVest. "They re-texturize it and refine it" Boucher says, "using their own proprietary methods." Then they repackage and relabel it in tinctures, edibles, vape pens—even waxes for dabbing—under their own brand names.

More than 150 dispensaries and 180 health food stores "carry our products in some form or another," Boucher says. Cannavest also sells direct to consumers through its website—a sideline accounting for less than 10% of sales.

Founded in 2013, the company has corporate headquarters in Las Vegas run by CEO Michael Mona. A partner in Dusseldorf coordinates the shipments from Europe.

In October we asked Boucher if Cannavest was going to make use of the CBD-rich hemp grown in the U.S. "Our focus this year was on research," he said. The company gave a \$47,000 grant to the University of Kentucky and \$10,000 to Murray State, enabling agronomists (and grad students) to study the optimal layout of hemp fields grown to maximize CBD production, analyze fiber content, and evaluate harvest methods.

"The federal law says 'research and development' and that's exactly what we're doing. Researching what it costs to make it, researching what it costs to sell it, researching what it costs to distribute it across 50 states."

"If you're growing for fiber, are you going to throw that CBD in the flowers away? If you grow hemp for seeds, why throw that CBD away? That's money for the farmer."

"Many farmers are doing 'dual harvest,'" Boucher explained. "If you're growing for fiber, are you going to throw that CBD in the flowers away? If you grow hemp for seeds, why throw that CBD away? That's money for the farmer."

Boucher credits Senators Mitch McConnell and Rand Paul and Kentucky Ag Commissioner James Comer for intervening in 2014 when the Drug Enforcement Administration confiscated seeds before they could reach hemp farmers. David Bronner, head of Dr. Bronner's Magic Soap Company, paid for the lawyers who got the crucial injunction that ended the confiscation.

"McConnell made them back down last year and this year the DEA didn't interfere at all," says Boucher. "They were helpful, in fact."

It was politically shrewd of McConnell, the Senate Republican leader (and faithful shill for the mine owners) to support the hemp industry because he was facing a serious challenge from a Democrat in November 2014. According to an observer of Kentucky politics, "He would go to town meetings and rallies, and the first question—the first three questions—would always be about hemp. And he's like, 'Wait a second, this is a litmus test for the farmers. If this is what they want, I've got to get

behind this.' And it was funny, after about the second or third rally he would say 'Watch this, I bet you the first question is going to be about hemp.' And of course it always was."

Kentucky farmers made three times more per acre growing hemp in 2015 than growing tobacco (which used to be government-subsidized), according to Boucher; and 10 times more than they would have growing corn.

He said hemp companies were paying "anywhere from \$1,800 a ton, dry weight—that's barrel-bottom price—for the top 2.5 feet of their plants."

Companies purchasing hemp stalks plan to make a wide range of products, from horse bedding to fine textiles. Cannavest donated seeds to the Growing Warriors, a veterans group that is making American flags from hemp. "They process it the old-time way," Boucher says. "They watered down the fibers, use an old hemp brake, take the fiber to hand weavers."

Boucher expects to be scaling up in the period ahead. He foresees a market of 40 to 50 million Americans for cannabis, and a large subset looking for CBD. Cannavest will make tinctures and capsules marketed as nutritional products, depending on directives (or signals) from the DEA. "That's where everything's kind of in limbo," he adds.

Boucher says there are misconceptions about the warnings sent by the FDA earlier this year to companies that made claims attributing curative properties to CBD, and lied on their labels about how much CBD their products contained. The warning was not a blanket injunction against distribution of CBD-rich oil, according to Boucher, but an outing of companies making false claims. And Cannavest was blameless.

"We sell to hundreds of different companies, and some of those third parties were making claims. When we sell to people, we specifically tell them in the sales agreement that you cannot make claims and we're not liable if you start making claims."

The Cannavest lab and processing facilities in San Diego have been inspected by Dr. Jahan Marcu, Boucher says, and they're awaiting Patient-Focused Certification, having done the "minor things" Marcu said they needed to do to comply with all the relevant laws and codes.

Marcu says that in mid-December he is planning to inspect a farm growing hemp for Cannavest in northern Germany. "They're very conscientious about testing every batch, and they pay for the service—unlike almost everybody else in the industry," Marcu said with a trace of bitterness in a late November phone interview.

Waiting for Data

The Kentucky harvest was beginning at the time of our interview, and Boucher estimated that Cannavest would be producing "Quite a few hundred kilos." It will depend on how efficient the innovative extraction technology turns out to be and variables like how tightly farmers pressed the plant material.

"Unfortunately," he adds "we can't ship a 1:1 ratio across state lines. Technically, we can ship a 25:1 because the THC level is so low. I almost feel like 1994 when I was growing hemp at the USDA research center in California. Everyone came after me, said 'you can't do this, this is illegal.' And I had a contract with the USDA, written and signed by the research center."

"But I think this time everybody's going to move forward because, watch out, there's some big players that are going to jump in this game. They're just sitting and waiting for everybody to burn up all their R&D money, develop the product, see how the market responds, and then jump in the game."



CHRIS BOUCHER WITH DEA PERMITS authorizing Cannavest to import hemp seed from Germany destined for farmers in Kentucky.

Noting that GW Pharmaceuticals had opened an office in proximity to his in San Diego, Boucher said: "I think they're going to move their growing operations here. At the end of the day, I think the whole import model might close down... The way this thing's playing out in Kentucky, it could be that they can't stop it because a lot of investment is going into it and there's a lot of political power behind it."

Boucher says he gets from two to 10 phone calls a day from California farmers asking about their prospects for growing hemp. State Attorney General Kamala Harris has said that private farmers cannot engage in research and development—that's the province of the Department of Food and Agriculture (CDFA) or institutions of higher learning, according to Sacramento attorney Patrick Goggin.

The CDFA "does not have the resources or interest in leading a project," Goggin told O'Shaughnessy's. "They are going to leave it up to the University of California and Cal State systems."

Cannavest's Boucher says, "Kentucky will have a huge lead. California could miss out. I think there's a lot more opportunities here for farmers than anywhere else. But, that's my opinion."

It will be "several years," Boucher projects, before hemp grown stateside will replace foreign hemp as the main source of Cannavest's CBD oil. "This year we're testing production methods, [determining] how many kilos we're going to get per dried ton. As soon as we have that, we'll know how to scale up next year."

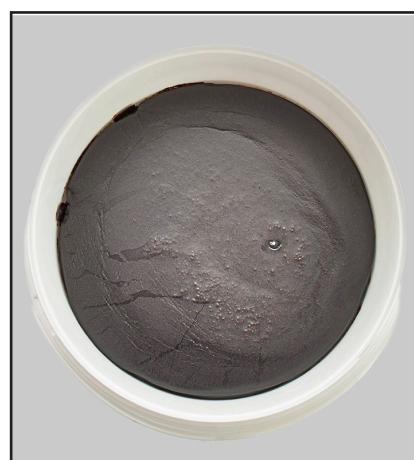
Other companies selling oil made from foreign hemp were also buying hemp grown in Kentucky—and in Colorado and Tennessee—in 2015. "We're getting offers right now at eight or nine cents a milligram, coming out of Colorado," Boucher said in October 2015. "There's definitely going to be a lot of oil."

Cannavest faces competition from companies selling a crystalline form of CBD that—extracted with hexane—that is 99% pure. "Powder is a formulator's dream," Boucher says. "All you've got to do is sprinkle the powder into what you're making instead of putting this thick, gooey oil in. But with 99% pure you lose the entourage effect and have to provide a much higher dose of CBD. Also, it takes a lot of hexane to make a kilo of powder."

Boucher says Cannavest makes its powder by mixing CBD-rich oil with rice powder and heating until dry.

Some dispensaries in California and other states carry products made with CBD oil extracted from foreign-grown industrial hemp. Imported by wholesalers like Cannavest, Endoca, and Elixinol, this high-CBD/low-THC oil is marketed primarily through internet storefronts and nutraceutical start-ups.

The Biosynthesis Pharma Group (BSPG) and Hempdiol are among the leading wholesale distributors of CBD in the form of a (nearly) pure, single-molecule powder derived from industrial hemp. CBD as an isolate lacks the therapeutic synergies conferred by whole plant cannabis oil, but it may be an easier pill for THC-phobic regulatory agencies to swallow.



HEMP EXTRACT IS SHIPPED FROM GERMANY TO SAN DIEGO on pallets weighing about a ton. The cannabinoid-laden substance is then refined in myriad ways.

Amy Farrah Weiss contributed to this article.