**CMCR hosts meeting on the future of MCR (Medical Cannabis Research) By Dale Gieringer**

_Cannabis and Health_ was the stated theme of a conference held June 8 at the Center for Medicinal Cannabis Research on the UC San Diego campus. Benefit, not harm, is the new focus. $10 million in tax revenue collected from cannabis consumers and providers will be allocated to research by the State of Cannabis Control. The looming questions are: what research to fund, and which researchers.

The conference drew about a hundred attendees from every facet of the field. Sherry Yafai, MD, represented the Society of Cannabis Clinicians. She was articulate, positive and passionate in defense of her practice. She only began practicing after Prop 64 on January 1, 2018, and only takes physician referrals.

“I’m not a new kid in the block. Yafai described her patient population, which ranges from age 2 to 100 (1), and the various indications—mainly cancer and mood disorders. Most had tried marijuana in their youth and most don’t want inhaled medicine. Yafai added that patients decrease use of other medications, including opiates, other controlled substances, and blood pressure drugs. She works with a “High Street” or prescription-smokable cannabis to treat drug addiction. Her patients—long-term addicts—are given medical cannabis to replace THC-rich oils to get off drugs. She said she had successfully treated four long-term opioid addicts, helping them get entirely “clean” in 10 days using nothing more than cannabis oil.

Yafai noted that high-potency products are used in cancer treatment and formulations for epilepsy and drug abuse.

_A French addiction specialist in the audience questioned her claim_. Yafai said she would soon have data to present. (Earlier in the session she had taken the mike to respond to a presenter who questioned the evidence of cannabis benefit.)

The conference began with a lucid presentation by Dr. Piomelli on the history of medical cannabis, the cannabinoid receptor system, endocannabinoids, and the National Academy of Sciences, Engineering & Medicine (NASEM) report. Piomelli said he wanted to work on specific agonists, antagonists, and FAAH inhibitors. “I don’t think cannabis is really a good drug,” he said. “I think we can have better drugs.” He remains concerned about the premature exposure to cannabis, not because of the lower birth weight, which can be explained by smoking, but by possible effects on fetal stem cells, which haven’t been investigated. (Overall though he is pro-cannabis and anti-prohibition.)

Ziva Cooper from Columbia University presented her research on pain treatment with cannabis and opioids. Subjects given sub-clinical doses of oxycodone and cannabis to treat cold-pressor-induced pain showed no response; but when the two drugs were combined, they were effective. Conclusion: cannabis increases analgesia but not intoxicating effects of opioids.

Marcel Bonn-Miller of University of Pennsylvania and Tilray discussed the lack of research regarding cannabis and PTSD. Surveys of patients at SPARC et al show widespread use of cannabis amongst PTSD patients. They prefer high THC to CBD. Early results of an ongoing study of cannabis use by Bonn-Miller: only minor reductions in PTSD symptoms, but a high association with problematic use.

Doris Trauner of UCSD has received a grant from Insys and the Nournda Foundation to study cannabis in autism. She cited a recent study finding that 61% of parents reported behavioral improvements in autistic kids using CBD-rich cannabis.

Iain McGregor of University of Sydney, GW and Tilray, has received $33 million from the Lambert family to study cannabis in Gervas syndrome. Australian GPs are more accepting of cannabis than specialists, he said. Quality control of CBD products is a big problem. The placebo effect is strong. In a survey of epileptic children treated with cannabis, many samples tested “effective” turned out to contain no CBD or CBDA. Surprisingly, driving performance tests found that patients given a mixture of 50-50 CBD/THC were no less impaired than those given pure THC.

Staci Gruber of McLean Hospital noted that studies on cannabis and cognition have focused mainly on young recreational users, not the older medical population. Patients exposed to cannabis before age 16 tend to score significantly poorer on cognitive tests, but those not exposed later.

Research suggests that cannabis can help reverse age-related cognitive decline. Her studies of older medical users found reductions in opioid and drug use, reductions in depression, improvement in sleep, improvement in executive function, but the usual memory impairment.

Tom Marcotte of UCSD gave a good presentation on cannabis and driving ability. Some signs of impairment observed in driving studies, but may be offset by subjects’ awareness of their condition. No apparent increase in accidents in Colorado post-legalization; more drivers are being screened for drugs than before. THC less impairing than anti-depressants, hypnotics, alcohol. Need to look at effects of oral dosing.

Alan Budney of Dartmouth apologized for being the one addiction specialist at the forum. His presentation was disorganized, informal and lacking in data. His bogey man: the “popular myth that cannabis is good for everything.”

Yafai was part of the “Real World Cannabis Use” panel. Ryan Vandyck of John Hopkins and Insys spoke on “What’s in a real-world cannabis?” He was the first speaker to bring up terpenes and flavonoids, which remain totally unstudied. He complained about the general lack of standardization in current products, poor testing quality control, inadequate labeling, questionable contaminants, etc.

Mahmoud ElSohly spoke about his drug development at the University of Mississippi. He showed pictures of the O’Miss farm, which features both indoor and outdoor gardens. ElSohly’s surveys show a substantial increase over the last year in THC:CBD ratio of cannabis grown in the US—despite the legalization of CBD. This could be because ElSohly samples confounded by law enforcement, not legal products from medical states. He is working on suppositories. He said that THC by itself is useless in pain, and terpenes and tannins, it needs to be in modified form of THC-hemiscuminate in order to penetrate. He is also working on glaucoma formulations with longer activity than inhaled/ingested THC, which wear off too quickly. He has a promising formulation that is active for four hours and is seeking to extend it to eight hours.

ElSohly is also doing research on CBD and opioids. He has found that CBD combined with a sub-active dose of oxycodone produces analgesic effects. I asked him about the many cannabis topicals, creams, lotions, etc. on the market. He wasn’t sure about CBD, but THC can’t penetrate the skin, he said. Topicals and suppositories claiming to provide THC are “fakes.” (A representative from Mary’s Medicinals told me they sell epidermal patches that use a patented carrier to help THC penetrate the skin.)

_Tilray has applied to FDA to do clinical trials._

Three manufacturing companies were invited to discuss their activities. Tilray-Devin of Cannabric, Lynn Honderd of Mary’s Medicinals, which specializes in transdermal patches, and Catherine Jacobson of Tilray, which is working on childhood epilepsy and has applied to FDA to do clinical trials. Jacobson previously worked with Dr. Chabner’s Epilepsy Lab, which should be approved by FDA in the next month or so. After that the DEA must still grant it a special schedule.

The last session featured government officials talking on regulations and barriers to research. Dominic Chiapperino of the FDA Controlled Substances Office described the agency’s role in cannabis regulation. The FDA oversees the “k-factor analysis” that is required for rescheduling. Chiapperino pointed to the need for larger clinical trials, alternatives to smoked marijuana (e.g., vaporizing), and evaluation of long-term chronic use. He mentioned that his agency sent 20 warning letters to CBD manufacturers who had nationally marketed products and were making egregious health claims.

Lori Ajax of California’s Bureau of Cannabis Control outlined her agency’s ongoing efforts to implement state regulations. The emergency regulations have been extended to Dec 31, but can’t be extended again; they will shortly be issuing their final rules. Ajax addressed the many concerns expressed at the forum about the quality of existing products, Ajax said that state-regulated products are quality tested and labeled so as to meet requisite standards for product control. There is still a shortage of li- censed labs: just 31 out of a statewide goal of 100.

Steve Gust from NIDA spoke about the agency’s cannabinoid research program. Most of the projects are non-marijuana: $15 million for CBD research; another $13.9 million for cannabinoid research, $62 million for endocannabinoids, and $36 million for therapeutic research. Altogether, some 70 projects.

Ellen Auriti, an attorney from the University of California’s Office of the President, gave an overview of the many legal challenges to conducting research. Schedule I licenses must be had from DEA; state approval by the Research Advisory Panel of California (conveniently reorganized from CRAP) is still needed. Industrial hemp can only be researched under an agricultural pilot program that hasn’t yet been developed in CA. CBD from hemp is illegal under DEA’s latest rules, upheld by the 9th Circuit Court of Appeal. A Schedule 1 license is needed to work with CBD. UC must comply with the Drug Free Schools and Communities Act, which requires standards of conduct that clearly prohibit illicit drugs (including CBD). Also, the Drug Free Workplace Act.

Everyone at the forum— including Gust of NIDA—agreed that there was a need for additional sources of cannabis for research. Igor Grant wondered aloud what CMCR could do. Apply for a DEA license? Expensive and uncertain (a bill to authorize CMCR to apply for a DEA license was killed by the Assembly Appropriations Committee this year.)

Work with a private company? But what private company would be willing to invest in FDA drug development, given that so many companies were already able to market their products legally in CA and other states. Given all of the difficulties, Grant ventured that CMCR’s best alternative might be to import products from other countries.

“We’d love to work with you,” Devitt said. Cannacraft sold two million units last year, and would gladly provide products to researchers conducting clinical trials. She also offered to share the information that the company has collected via surveys— for example, people using cannabis to treat Asperger’s Syndrome showed a preference for 4:1 CBD-THC ratio.

Despite promise to add sources: **O’Miss still lone supplier of cannabis for research**

In August 2016 —towards the end of the Obama era— the Drug Enforcement Administration said it would license more cultivators of cannabis for research purposes. Two years later, after accepting 26 applications from would-be suppliers, DEA has licensed none. It has stopped taking applications. Mahmoud Elsohlly, PhD, at the University of Mississippi, retains his monopoly status.

Supervising the stall is the Dixie Pixie, US Attorney General Jeff Sessions. “It’d be better to have some more competition in the supply, but I’m sure we don’t need 26 new suppliers,” he twirled.

Lyle Craker, a professor at the University of Massachusetts at Amherst, has been applying for a DEA license to cultivate cannabis for research since 1999! Craker is among the 26 who haven’t heard back as we go to press in September 2018.

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**MAHMOUD ELSOHLY (RIGHT) SHOWS SANYU GUPTA the walk-in safe where cannabis grown on the O’Miss campus under contract with NIDA is stored. GALLERY FROM CNN.**