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Determining Medicine through Science: Clinical Approach to Cannabidiol Studies Can Result in Positive Outcomes for Patients

The Honorable Carlton E. Turner, Ph.D., D.Sc.

There is a growing movement in the United States to legalize an extract of the C*annabis sativa* L. plant known as "Charlotte's Web" (CW) for medicinal purposes. Legislation for this purpose has been introduced in several states. Parents, with children suffering from severe forms of epilepsy, are applying intense political pressure. The parents believe that CW will help their children and should be legalized. Since CW comes from a fiber type *Cannabis* plant and is not *smoked*, some legislators believe passage of a bill to legalize CW would not be legalizing "medical marijuana." However, a United Nations working group, at the University of Mississippi, determined that the genus and species of all types of *Cannabis* is simple *Cannabis sativa* L.; thus, legalizing CW is simply legalizing pot. In reality, by passing a bill to legalize CW, the legislators are making sick children guinea pigs for commercial pot growers.

The current extract known as "Charlotte's Web" is produced only in Colorado in a non-certified and unregulated production environment. This extract is produced by Joel Stanley and his brothers, who own a large marijuana growing operation in that state. They are reported to have 52 acres, 16,000 sq. ft. of greenhouses and at least 4 "medical marijuana dispensaries." They started a non-profit foundation called "The Realm of Caring" to promote and provide marijuana therapy to patients. It appears that their goal is to sell marijuana for profit without regard to international treaties, federal laws or the U.S. Food and Drug Administration (FDA) drug approval process.

Cannabidiol (CBD), a non-psychoactive compound from the *Cannabis* plant, has shown promise in reducing the number of seizures in some children with severe forms of epilepsy. The Stanley brothers produce CW that contains not only CBD, but also tetrahydrocannabinol (THC), which is the mind-altering component of marijuana. No government certified lab has analyzed samples of CW. So the statements from Stanley that CW contains ratios between 15 and 50 to 1 of CBD to THC are not proven. Because the plant is used as grown, each batch of CW will have its unique ratio of CBD to THC.

Any state legislature authorizing a medicine created from an untested substance is a dangerous move. Science has shown that marijuana can cause permanent brain damage and other health problems. There may be other dangers that are not yet known. For elected officials to knowingly bypass the FDA and the very safeguards that keep the public safe is ludicrous. Charlotte's Web has never been clinically tested and there is no data that documents the side effects or problems that may be encountered through its interaction with other drugs.

To make CW legal in states where legislation is pending, *Cannabis sativa* L. would have to be grown in those states. Thus, those state legislatures would be, in effect, "legalizing marijuana as medicine." In order to make CW, the crude drug marijuana would have to be produced from *Cannabis* rich in CBD, extracted with a chemical solvent, concentrated, and then mixed with some vegetable oil. That process yields a crude drug that can be given orally but does not meet federal manufacturing requirements for human drugs. Additionally, it will take several months to obtain seeds, legally or illegally, and grow *Cannabis* plants in those states for the production of CW.

Crude *Cannabis* plant material (marijuana) is unstable and will not have a consistent batch to batch composition. Also, of concern about "Charlotte's Web", there are possible contaminates from pesticides and herbicides. The chemical solvents used to make CW are critical. Clinically, who will determine the appropriate therapeutic ratio of CBD to THC, the mind altering substance in pot that can induce seizures? Who will be available to assist patients with bad reactions to this crude drug?

There is a solution for parents desperate to help their sick children. Rather than pushing for unregulated, untested and unsafe strains of crude marijuana extracts, grown and produced under unknown conditions that will put children more in harm's way, state legislators can establish and fund treatment programs that protect sick children and provide the best clinical care available.

CBD now has orphan drug (pharmaceutical agent developed specifically to treat a rare medical condition) status with the FDA and is called Epidiolex™. It is a natural and pure drug that has a known potency and is controlled by regulatory agencies and administered in clinical settings providing maximum medical support. Epidiolex™ can be provided through investigational new drug (IND) research at no cost to participating patients. Additionally, onsite medical specialists support the medical needs of all patients.

Epidiolex™ is produced by GW Pharmaceuticals (GW) founded in 1998 and listed on both the NASDAQ Global Market (GWPH) and AIM, a market of the London Stock Exchange. GW is licensed by the United Kingdom Home Office to work with a range of controlled drugs for medical research purposes. The group's lead program is the development of a product portfolio of cannabinoid prescription medicines to meet patient needs in a wide range of therapeutic indications. One, Sativex® oral spray, is on the market in 11 countries for spasticity due to multiple sclerosis and

in development for cancer pain and neuropathic pain of various origins and Epidiolex™ for childhood epilepsy.

GW has assembled a large in-house team with extensive experience in developing cannabinoids, medicines containing controlled substances, as well as plant-based prescription pharmaceutical products. They maintain in-house control over all aspects of the cannabinoid product development process including botanical research, extraction technology, formulation into drug delivery technologies, clinical trials and regulatory affairs. GW follows current good manufacturing practices (cGMP) for pharmaceutical products for clinical trials and commercial purposes.

GW has filed a Drug Master File (DMF) as required by FDA that provides data from pre-clinical animal studies to rule out birth defects including a detailed composition of matter of their drug (each dose will be same as previous or future doses), how the drug is manufactured in order to be used in humans, stability of the drug, metabolism profile and other data. The compilation of a DMF costs millions. *Epidiolex™, unlike CW, contains only trace amounts of THC.*

Rather than having innocent children used as guinea pigs by commercial marijuana producers, states facing this type of legislation can demonstrate their true compassion for sick children by funding clinical treatment programs at recognized medical facilities. A **truly compassionate approach** would be to make the experimental CBD-based drug Epidiolex™ or pure CBD available to patients through clinical treatment trials under a compassionate IND (expanded access IND's) protocol. The treatment of sick children in a comprehensive clinical environment is the proper approach. It is ethical to allow our existing scientific process to guide us in determining safe and effective

medicines. This is a medical/health issue and should not be treated as an unethical, irrational and political/legislative approach that treats our sick children as medical guinea pigs.

About The Author

The Honorable Carlton E. Turner, Ph.D., D.Sc. was a full research professor at the University of Mississippi (UM), School of Pharmacy and Director of its Research Institute of Pharmaceutical Sciences (RIPS). While at UM, he was the Director of the Marijuana/Cocaine project funded by the National Institute on Drug Abuse. One of his post-doctoral students currently is the director of the UM Marijuana Project.

Dr. Turner has authored over 100 peer reviewed research papers ranging from analytical data to chapters in psychiatric text books. He was an author of “Marihuana: An Annotated Bibliography” Volume I and II and annual addendums. He has served as a consultant to the United Nations (UN), Canadian and American Senates, various state legislatures and foreign governments.

He served on President Reagan’s White House staff as Special and Deputy Assistant to the President and Director of The Drug Abuse Policy Office. He held cabinet rank and assisted Mrs. Reagan with her “Just Say No” campaign. He developed the concept of The First Lady to First Lady Drug prevention/awareness campaign and chaired The First Lady to First Lady Conferences at the UN and the White House.

In 1981, Dr. Turner was given the responsibility to develop a program to rid the U.S. Military of illicit drug users. The modern drug testing program used today is based on the testing program he implemented in the military.

He has been the president/CEO of clinical laboratories and biotech companies (public and private) and has developed and overseen drug development programs for pure drugs, biologic drugs and vaccines. He knows the FDA procedure for drugs and neutraceuticals from the Investigative New Drug Application (INDs) through Phase I safety, Phase II efficacy, Phase III dosage and subsequent drug approval though the New Drug Application (NDA) process.