APPENDIX C

Whitepaper:

Defining Full Spectrum CBD

Dan Kennedy, csa December 10, 2019

As there is a need to properly classify the various types of CBD products, one of the categories being addressed in the USDA proposed 2019 industrial hemp rules is "full spectrum" CBD. As the name suggests, full-spectrum means a "full range". For industrial hemp, full spectrum refers to the plant's chemical contents. From the 100 phytocannabinoids to the multitudes of terpenes, alkalines, and more, what constitutes full-spectrum has varied wildly in current, consumer products. We will try to analyze the purpose of full-spectrum claims and then address [at least some of] the requirements for a product to be considered full-spectrum and make recommendations.

A "Whole" Health Agenda:

To properly define full spectrum requires an understanding of the intent / purpose of the phrase. According to Collins Dictionary, full spectrum is defined as:

"Showing a complete range of typical or possible elements: comprehensive.1"

Using this definition, one must understand that the purpose of a "full spectrum" extract from Cannabis Sativa L. industrial hemp is not to actually consume the plant itself, but to encompass a comprehensive set of chemicals from the plant; more specifically: chemicals with a positive, biological effect. In the world of industrial hemp cannabidiol (CBD), to maintain legality, a plant, for example, may extract some of the Tetrahydrocannabinol (THC) chemicals, as long as the Δ^9 -THC chemical (that causes intoxication), does not exceed the legal threshold. Thus, there must be some "adjustments" to how full spectrum is defined. We can also conclude from recent studies in the herbal extracts of Panax Ginseng (where the polysaccharides help augment the efficacy of the positive chemical effects over elemental extracts of purified ginsenosides²), that there is a benefit to a full spectrum product vs an extracted product (with concentration). This is similar to studies on St. John's Wort that have demonstrated the benefits of flavonoids in augmenting its clinical performance. Although industrial hemp compromises a large amount of chemicals, patents already exist that use 1 or 2 compounds together (rather than multichemical formulations) for medical purposes such as GW Pharmaceuticals, Sativex³.

While a medical formulation such as Sativex may be based upon singular, or even multi-compound purified extracts, they are still purified and extracted separate from the other chemicals present in industrial hemp for the purpose of augmenting their concentrated doses. In this case, they do not qualify for the definition of full spectrum. Furthermore, given their uniquely high concentrated doses, they are not mere "nutritional" extracts as they provide a specific, direct medical benefit (structure function). Nutritional elements, such as vitamins, herbs, and similar extracts contain much smaller doses and although they can be concentrated for use in medication, their purpose is supplemental health support to the human body, albeit limited. Often times, the consumption of one vitamin is typically

¹ Collins Dictionary, 2019 [Link]

² Draco, 2019 [Link]

³ GW Pharmaceuticals, 2013 [Link]

enhanced by the consumption of another at the same time. Failure to do so can actually reduce the efficacy of the vitamins⁴. Some vitamins can also impede the effectiveness of prescription medications (and usage is always referred to a medical professional and/or pharmacist prior to consumption).

It is clear that at the medication level, and nutrition level, there are benefits to the combination of certain chemicals as they augment one another. In the case of industrial hemp, where CBD counters the uptake of THC, the combination of both, unless provided for at medical dosages, would be one case where the chemicals can also conflict. Fortunately, for industrial hemp formulations that emphasize CBD, this is also a desired result as it reduces the uptake potential of Δ^9 -THC. However, Cannabis Sativa L. is a very unique plant in that it contains hundreds of individual chemicals and the majority of them have very positive effects, many of which complement one another (Figure 1) and are already recognized by the U.S. Food and Drug Administration ("FDA") as beneficial. Many of the terpenes, for instance, are already published in the European Pharmacopoeia, 6th Edition (2007), and the terpenes listed in Figure 1 are already generally recognized as safe, by the FDA as food additives.

Just like Centrum™ offers a full spectrum vitamin regimen that provides a "whole health" boost (which the American Medical Association recognizes the benefits of⁵), the multitudes of chemicals in industrial hemp appear to have that same multi-functional potential. There are even studies (which we highlight further on) that demonstrate the augmented benefits of a full-spectrum CBD product at below medical dosage levels due to the interaction of chemicals.

From this high-level analysis we have assessed that the intent / purpose of a "full spectrum" product is to provide a generalized, total positive biological benefit from the interaction of the full spectrum of Cannabis Sativa L chemicals that are not at the "medical" grade of prescription drugs nor do they qualify as a quasi-medical over the counter (OTC) drug such as acetaminophen (which is a concentrated extract of chemicals). To be a full-spectrum chemical, industrial hemp oils, however used, must be extracted in a way that does not artificially concentrate /augment individual chemicals (not changing the natural ratio more than 5%) in the same manner as distillation, isolates, or other "extraction" that artificially isolates and concentrates chemicals. To quantify this, we will first look at the chemical constituents of industrial hemp.

Chemical Contents of Cannabis Sativa L:

<u>Phytocannabinoids</u>: Of the 483 compounds identified in industrial hemp, the 66 cannabinoids are almost unique to Cannabaceae plants. The terpenes, however, are widespread in the plant kingdom⁶. Cannabinoids represents a group of C_{21} terpenophenolic compounds found in Cannabis Sativa L^7 . These are known as phytocannabinoids⁸ (of which 100+ were identified). For the purposes of this analysis, we evaluated the most prevalent active ingredients available in the current, scientific literature that we were able to access (which, with their citations, has included more than 250 studies). The main active

⁴ Consumer Labs, 2019 [Link]

⁵ AMA, 2019 [Link]; recognizing the research of Fairfield and Fletcher, 2002.

⁶ ElSohly, 2019

⁷ Note that synthetic cannabinoids such as nabilone (<u>Ward and Holmes, 1985</u>), HU-211 [dexanabinol (<u>Burstein, 1992</u>), or ajulemic acid [CT-3] (<u>Mechoulam, 1990</u>) do not qualify under full spectrum in this analysis, as will be discussed further on]

⁸ Pate, 1999

ingredients (those that provide a positive, biological benefit) in Cannabis Sativa L., of interest are as follows (this list may be expanded as is scientifically validated and appropriate):

LIST 1

Phytocannabinoids:

- 1. CBG: Cannabigerol (from CBGA \rightarrow from Δ^9 -THC)
- 2. CBC: Cannabichromene (from CBCA)
- 3. CBD: Cannabidiol (from CBDA) / CBDV
- 4. Δ^9 -THC: Δ^9 -Tetrahydrocannabinol (from THCA) / THCV (a propyl analogue of THC)
- 5. Δ^{8} -THC: Δ^{8} -Tetrahydrocannabinol (from THCA)
- 6. CBL: Cannabicyclol (from CBLA → from CBC)
- 7. CBE: Cannabielsoin (from CBEA and CBEB)
- 8. CBN: Cannabinol / CBND: Cannabinodiol (from THC and CBD respectively)
- 9. CBT: Cannabitriol (exists in the form of both isomers and racemate)
- 10. Miscellaneous: dehydrocannabifuran / cannabifuran, cannabichromanon / cannabiripsol

<u>Terpenes</u>: Terpenoids give Cannabis its unique scent. Terpenoids may be acyclic, monocyclic, or polycyclic hydrocarbons with substitution patterns including alcohols, ethers, aldehydes, ketones, and esters. The post-harvest drying process can significantly reduce terpene concentration. Over 200 terpenes have been reported. Their yield is less than 1% in most cannabis assays, but may represent 10% of trichome content⁹. The terpenes of interest include:

- 1. Limonene (major terpene)
- 2. Linalool (major terpene)
- 3. β-Myrcene (major terpene)
- 4. Trans-caryophyllene (major terpene)
- 5. α-pinene (major terpene)
- 6. Trans-ocimene, (major terpene)
- 7. α -terpinolene (major terpene)
- 8. α -humulene (major terpene).
- 9. α -terpinene (minor terpene)
- 10. sabinene (minor terpene)
- 11. cineole (eucalyptol) (minor terpene)
- 12. pulegone (minor terpene)
- 13. y-terpinene (minor terpene)
- 14. terpineol-4-ol (minor terpene)
- 15. bornyl acetate (minor terpene)
- 16. α-copaene (minor terpene)
- 17. alloaromadendrene (minor terpene)
- 18. viridiflorene (minor terpene)
- 19. β-biabolene (minor terpene)
- 20. y-cadinene (minor terpene)
- 21. *trans*-β-farnasene (minor terpene)
- 22. trans-nerolidol (minor terpene)
- 23. β-bisabolol (minor terpene)

<u>Hydrocarbons</u>: There are 50 known hydrocarbons in Cannabis and consist of n-alkanes ranging from c_9 to c_{39} , 2-methyl-, 3-methyl-, and some dimethyl alkanes. The most prevalent of these are:

1. *n*-C₂₉ alkane nonacosane

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⁹ Potter, 2009

- 2. heptacosane
- 3. 2,6-dimethyltetradecane
- 4. Pentacosane
- 5. Hexacosane
- 6. Hentriacontane.

<u>Nitrogen Constituents</u>: There are more than 70 nitrogen-containing constituents, with the most prevalent being:

- 1. 2 spermidine type alkaloids
- 2. Quartenary bases:
 - a. Choline
 - b. Trigonelline
 - c. Muscarine
 - d. Isoleucine betaine
 - e. Neurine
- 3. Amides:
 - a. N-tran-feruloyltyramine
 - b. *N-p*-coumaroyltyramine
 - c. N-trans-caffeoyltyramine
- 4. Lignanamide derivatives: Cannabisin A, B, C, and D
- 5. Amines:
 - a. Piperidine
 - b. Hordenine
 - c. Methylamine
 - d. Ethylamine
 - e. Pyrolidine
- 6. Proteins
 - a. Edestin
 - b. Zeatin
 - c. Zeatinnucleoside
- 7. Enzymes:
 - a. Edastinase
 - b. Glucosidase
 - c. Polyphenoloxydase
 - d. Peptidase
 - e. Peroxidase
 - f. Adenosine-5-phosphate

<u>Amino Acids</u>: There are also 18 amino acids which are a structure common for plants. The carbohydrates of interest are:

- 1. Monosaccharides
 - a. Fructose
 - b. Galactose
 - c. Arabinose
 - d. Glucose
 - e. Mannose
 - f. Rhamnose
- 2. Disaccharides
 - a. Sucrose
 - b. Maltose

- 3. Polysaccharides
 - a. Raffinose
 - b. Cellulose
 - c. Hemicellulose
 - d. Pectin
 - e. Xylan
- 4. Sugar alcohols and cyclitols
 - a. Mannitol
 - b. Sorbitol
 - c. Glycerol
 - d. Inositol
 - e. Quebrachitol
- 5. Amino sugars
 - a. Galactosamine
 - b. Glucosamine

<u>Flavonoids</u>: There are 23 commonly occurring flavonoids identified in Cannabis with cannflavins A and B unique to Cannabis. Of interest are:

- 1. Apigenin
- 2. Luteolin
- 3. Quercetin
- 4. Kaempferol.
- 5. Major flavonoid glycosides:
 - a. Orientin
 - b. Vitexin
 - c. Luteolin-7-O-glucoside
 - d. Apigenin-7-O-gkucoside

<u>Fatty Acids</u>: In the oil of Cannabis seeds, there are 33 different fatty acids, mostly being unsaturated fatty acids. Of interest:

- 1. Unsaturated fatty acids
 - a. Linoleic acid
 - b. Linolenic acid
 - c. Oleic acid
 - d. y-linolenic acid
 - e. stearidonic acid
 - f. eicosanoic acid
 - g. cis-vaccenic acid
 - h. isolinolenic acid
- 2. Saturated fatty acids
 - a. Palmitic acid
 - b. Stearic acid
 - c. Arachidic acid
 - d. Behenic acid
 - e. Myristic acid
 - f. Lignoceric acid
 - g. Caproic acid
 - h. Heptanoic acid
 - i. Caprylic acid
 - j. Pelargonic acid

- k. Capric acid
- I. Lauric acid
- m. Margaric acid
- n. Isoarachidic acid

Phenols: There are 34 noncannabinoid phenols. Of interest:

- 1. Spiro-indan-type structure
 - a. Cannabispiran
 - b. Isocannabispiran
- 2. Nine dihydrostilbenes (e.g. cannabistilbene-I, -II)
- 3. Three dihydrophenanthrenes (e.g. cannithrene-1, -2)
- 4. Six phenols, phenol methylethers, and phenolic glycosides (phloroglucinol glucoside)

Others: Additional contents of interest:

- 1. Alcohols
 - a. Methanol
 - b. Ethanol
 - c. 1-octene-3-ol
- 2. Aldehydes
 - a. Acetaldehyde
 - b. Isobutyraldehyde
 - c. Pentanal
- 3. Ketones
 - a. Acetone
 - b. Heptanon-2
 - c. 2-methyl-2-heptene-6-one
- 4. Acids
 - a. Arabinic acid
 - b. Azealic acid
 - c. Gluconic acid
- 5. Phytosterols
 - a. Campesterol
 - b. Ergosterol
 - c. B-sitosterol
 - d. Stigmasterol
- 6. Vitamin
 - a. Vitamin K
- 7. Pigments
 - a. Carotene
 - b. Xanthophylls
- 8. Other elements:
 - a. Na
 - b. K
 - c. Ca
 - d. Mg
 - e. Fe
 - f. Cu
 - g. Mn
 - h. Zn
 - i. Hg

Positive Biological entourage effects evaluated:

The following tables are not intended to validate whether or not there is a positive, biological benefit to the use of the chemical constituents of industrial hemp. The literature has more than validated this fact (and the benefits listed herein are linked to their studies). This is a partial list of studies, adapted from modern scientific analysis, that were investigated to determine that there is, in fact, a biological benefit to the consumption of the chemical constituents of industrial hemp and that there is evidence of an entourage effect by way of chemical interaction between multiple components of industrial hemp (thus quantifying the nutraceutical definitions of full spectrum).

Effect	THC	CBD	References			
Receptor/nonreceptor effects						
CB1	++	±	Rhee, 1997; Iwamura, 2001; Hayakawa, 2008			
CB2	+	±	Rhee, 1997, Showalter, 1996			
Anti-inflammatory	+	+	<u>Juknat, 2011</u>			
Immunomodulatory	+	+	Costa, 2007			
CNS Effects						
Anticonvulsant	+	++	<u>Wallace, 2001</u>			
Muscle relaxant	++	+	Lakhan and Rowland, 2009			
Anxiolytic	±	++	Zuardi and Guimaraes, 1997; Crippa, 2009			
Psychotropic	++	-	Russo, 2001; D'Souza, 2004; Borgwardt, 2008			
Antipsychotic	-	++	Zuardi, 1995; Moreira and Guimaraes, 2005			
Short-term memory problems	+	-	Hayakawa, 2008; Morgan, 2010			
Distortion of perception of time	++	-	Karniol and Carlini, 1973; Anderson, 2010			
Neuroprotective antioxidant	+	++	<u>Juknat, 2011</u>			
Antiemetic	++	++	Parker, 2011			
Sedation	+	-	Nicholson, 2004; Russo, 2007			
Cardiovascular Effects						
Bradycardia	-	+	Benowitz and Jones, 1981			
Tachycardia	+	-	Gorelick and Heishman, 2006			
Hypertension	+	-	Batkai, 2004			
Hypotension	-	+	Gorelick and Heishman, 2006			
Appetite/GI/Metabolic						
Appetite	+	-	Pertwee, 2009			
GI Motility (slowed)	++	+	Di Marzo and Piscitelli, 2011			
Metabolic / diabetes	+	-	<u>Di Marzo, 2011</u>			
Anticarcinogenesis						
Glioma (Apoptosis)	+	+	<u>Torres, 2011</u>			
Lung Cancer	+	++	Athanasiou, 2007; Ramer, 2012			
Opthalmological						
Intraocular pressure (reduced)	++	+	Green, 1998			

Table 1: Updated biological effects of CBD^{10,11}

¹⁰ Atakan, 2012 (adapted)

¹¹ Russo and Guy, 2006

Phytocannabinoid Structure	Selected pharmacology (reference)	Synergistic terpenoids
i i	Analgesic via CB ₁ and CB ₂ (Rahn and Hohmann, 2009)	Various
	Al/antioxidant (Hampson et al., 1998)	Limonene et al.
ОН	Bronchodilatory (Williams et al., 1976)	Pinene
	↓ Sx. Alzheimer disease (Volicer et al., 1997; Eubanks et al., 2006)	Limonene, pinene, linalool
	Benefit on duodenal ulcers (Douthwaite, 1947)	Caryophyllene, limonene
	Muscle relaxant (Kavia et al., 2010)	Linalool?
delta-9-tetrahydrocannabinol (THC)	Antipruritic, cholestatic jaundice (Neff et al., 2002)	Caryophyllene?
	Al/antioxidant (Hampson et al., 1998)	Limonene et al.
	Anti-anxiety via 5-HT _{1A} (Russo et al., 2005)	Linalool, limonene
ОН	Anticonvulsant (Jones et al., 2010)	Linalool
	Cytotoxic versus breast cancer (Ligresti et al., 2006)	Limonene
	↑ adenosine A _{2A} signalling (Carrier <i>et al.,</i> 2006)	Linalool
	Effective versus MRSA (Appendino et al., 2008)	Pinene
OH OH	Decreases sebum/sebocytes (Biro et al., 2009)	Pinene, limonene, linalool
cannabidiol	Treatment of addiction (see text)	Caryophyllene
OH	Anti-inflammatory/analgesic (Davis and Hatoum, 1983)	Various
	Antifungal (ElSohly et al., 1982)	Caryophyllene oxide
	AEA uptake inhibitor (De Petrocellis et al., 2011)	-
cannabichromene	Antidepressant in rodent model (Deyo and Musty, 2003)	Limonene
l óh	TRPM8 antagonist prostate cancer (De Petrocellis et al., 2011)	Cannabis terpenoids
	GABA uptake inhibitor (Banerjee et al., 1975)	Phytol, linalool
	Anti-fungal (ElSohly et al., 1982)	Caryophyllene oxide
H0 H0	Antidepressant rodent model (Musty and Deyo, 2006); and via 5-HT _{1A} antagonism (Cascio <i>et al.</i> , 2010)	Limonene
	Analgesic, α-2 adrenergic blockade (Cascio et al., 2010)	Various
	↓ keratinocytes in psoriasis (Wilkinson and Williamson, 2007)	adjunctive role?
cannabigerol	Effective versus MRSA (Appendino et al., 2008)	Pinene
	Al/anti-hyperalgesic (Bolognini et al., 2010)	Caryophyllene et al
OH OH	Treatment of metabolic syndrome (Cawthorne et al., 2007)	-
___\	Anticonvulsant (Hill et al., 2010)	Linalool
tetrahydrocannabivarin	Inhibits diacylglycerol lipase (De Petrocellis et al., 2011)	-:
OH OH Cannabidivarin	Anticonvulsant in hippocampus (Hill et al., 2010)	Linalool
T	Sedative (Musty et al., 1976)	Nerolidol, myrcene
ОН	Effective versus MRSA (Appendino et al., 2008)	Pinene
	TRPV2 agonist for burns (Qin et al., 2008)	Linalool
	↓ keratinocytes in psoriasis (Wilkinson and Williamson, 2007)	adjunctive role?
	↓ breast cancer resistance protein (Holland <i>et al.</i> , 2008)	Limonene
cannabinol (CBN)	re 1: Phytocannahinoid Activity Table 12	

Figure 1: Phytocannabinoid Activity Table 12

 $^{^{12}}$ Russo, 2011 (adapted): see [Link] for a detailed table focused on empirically established terpene biological impacts. All referred studies are in the Woks Cited section.

Some further examples of the beneficial biological results of the chemicals within Cannabis Sativa L include:

- 1. β -Myrcene is the most abundant monoterpene and has analgesic, anti-inflammatory, antibiotic, and antimutagenic properties¹³.
- 2. β-Caryophyllene is the most common sesquiterpene and has anti-inflammatory, cytoprotective (gastric mucosa), and antimalarial activity.
- 3. As a flavonoid, Apigenin has a well-known range of biological effects.
- 4. Heptacosane has been discovered to have potential inhibitory effects against the growth of tumor cells¹⁴.
- 5. Choline supports DNA synthesis, health nervous system and is required to make acetylcholine, an important neurotransmitter.
- 6. Amines support metabolic and physiological functions.
- 7. Enzymes are essential for healthy digestion.
- 8. Monosaccharides are an important, natural sugar that should not be taken in excess, but is a simple sugar that is good for the body. This includes di- and polysaccharides¹⁵.

And, of course, this list could go on. There are sufficient studies in the medical field highlighting some positive biological benefit from the various chemicals available in industrial hemp. For a product to be full-spectrum, there has to be some level of inclusion of these (and all other) chemicals and how they are subtracted and/or supplemented into final formulations.

Defining "Full-Spectrum":

It would seem that almost every individual producer of CBD-based oils that claims full spectrum also claims to have their own, unique, plant-to-oil conversion method. After reading several hundred descriptions, this method can vary from infusion, to extraction, to chemical isolation and re-mixing to a specified balance. Whatever the method, the only way to test for its efficacy as a "full spectrum" product is to analyze the resulting oils and determine if, in fact, enough of the plant's chemicals remain in-tact to qualify as "full-spectrum".

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¹³ McPartland and Russo, 2001

¹⁴ American Chemical Society, 2017

¹⁵ Lovegrove, 2017

Cannab ino id Name	ш	Weight %	Conc. mg/g
Cannabichromenic Acid	CBCA	ND	ND
Cannabicyclol	CBL	ND	ND
Cannabidiol	CBD	1.355	13.55
Cannabidiolic Acid	CBDA	ND	ND
Cannabidivarin	CBDV	0.021	0.21
Cannabidivarinic Acid	CBDV A	ND	ND
Cannabigerol	CBG	0.044	0.44
Cannabigerolic Acid	CBGA	ND	ND
Cannabichrome ne	CBC	ND	ND
Cannabinol	CBN	ND	ND
Cannabinolic Acid	CBNA	ND	ND
Δ9-Tetrahydrocannabinol	Δ9-THC	ND	ND
Δ8-Tetrahyrirocannabinol	∆8-THC	ND	ND
Tetrahydrocannabinolic Acid A	THCA-A	ND	ND
Tetrahydrocannabivarin	THCV	ND	ND
Tetrahydrocannabivarinic Acid	THCV A	ND	ND
Total	Camabinoids Total THC*	1.420 ND	14.20 ND

Figure 2: Example - Full spectrum phystocannabinoid product lab analysis¹⁶.

In Figure 2 the manufacturer is advertising a full-spectrum phytocannabinoid product based on the phytocannabinoids (CBD, CBDV, and CBG). There was no data we could identify regarding the other chemicals found in Cannabis Sativa L. PureKana¹⁷ asserts full spectrum to mean the range of phytocannabinoids having applied an interpretive analysis to a 2005 study¹⁸ in which the entourage effects were compared against isolated effects, but no terminology was used to suggest that phytocannabinoids were the substance of full spectrum.

This trend of relying upon cannabinoids as the definition of full spectrum is prevalent throughout the internet. Restart™ claims that all cannabidiol oils must include THC¹9, and Quicksilver Scientific²0 that refers to several studies also referred to in this paper for "full spectrum" (attempting to delineate it from broad spectrum) while not providing any other information about contents (of their own). Koi oils²¹ is one of the few companies we found that claimed a full spectrum product and provided laboratory results identifying 4 cannabinoids and at least 2+ terpenes (and impressively, a full mycotoxin report which we have seen a very alarming lack of in the industry), but nothing else.

For the purposes of this paper, we are not relying upon the totality of phytocannabinoids as the defining factor of what constitutes "full spectrum" CBD oil (or other limiting factor based on current market/industry claims). It would be scientifically inaccurate to make this assumption and after considerable research on the internet appears to be one of the methods that multitudes of companies have been using that may be a key to misleading consumers (emphasizing the need for regulations that definitively quantify the meaning of "full spectrum"). Therefore, we turn, once again, to our original interpretation of full spectrum:

¹⁶ NaturesPlus.com, 2019 [Link]

¹⁷ PureKana, 2019 [Link]

¹⁸ Gallily, 2015

¹⁹ Restart, 2019 [Link]

²⁰ Quicksilver, 2019 [Link]

²¹ Koi Oils, 2019 [Link]

"... the intent / purpose of a "full spectrum" product is to provide a generalized, total positive biological benefit from the interaction of the full spectrum of Cannabis Sativa L chemicals that are not at the "medical" grade of prescription drugs nor do they qualify as a quasi-medical over the counter (OTC) drug such as acetaminophen (which is a concentrated extract of chemicals). To be a full-spectrum chemical, industrial hemp oils, however used, must be extracted in a way that does not artificially concentrate /augment individual chemicals (not changing the natural ratio more than 5%) in the same manner as distillation, isolates, or other "extraction" that isolates chemicals."

Based on our contextual research, it is our understanding that the botanical / nutraceutical industry already has existing definitions / interpretations of full spectrum products and they appear to all be in agreement with one another:

"Full-Spectrum Extracts contain all the active chemical constituents of whole herbs ... most closely mimic the effects of whole herbs because full-spectrum extracts contain the same balance of chemical constituents and the same complex interactions between chemical constituents as whole herbs. The Full Spectrum Extraction keeps a plant as close to its natural makeup as possible. Extracting the whole part of the herb containing the plant's active ingredients -- the whole leaf, whole root, or whole stem, for example -- maintains the plant's natural integrity and balance, enhancing its overall therapeutic effects and keeping the extract as close to the original plant as possible.²²"

"A full-spectrum extract is made with an herbaceous plant's part(s), tinctured in a menstruum of alcohol for a product that includes the highest percentage of all the plant's chemicals and compounds, without affecting the natural ratio of these constituents present in the plant.²³"

"In the Nutritional Supplement Industry, "full spectrum" almost universally refers to "the entire range of chemical compounds or constituents that are naturally occurring in a certain part of a particular species of plant.²⁴"

Whether or not a full spectrum extract is actually more beneficial than a non-full spectrum product is not the subject of this paper (only that it refers to the positive, biological effects of the multitudes of chemicals within Cannabis Sativa L., whether or not that benefit can be defined as a structure function claim, or not²⁵). However, the definition based on our analysis and the industry standard remains very clear: full spectrum means as many of the "active" (active meaning that the chemical participates in causing a positive, biological effect) / desired chemical contents of a plant as possible, in their most natural ratio possible, that provide a presumption of supplemental, positive biological effects (that do not reach the level of quantifying the dosage as prescription medical or OTC medical). Based on our research, the following quantifications should be considered as part of the definition for full spectrum CBD oil:

LIST 2

- 1. Full Spectrum CBD oil must contain:
 - a. At least 1 or more phytocannabinoids with CBD being the primary chemical*.

²² Tianjangus.com [Link]

²³ Beneficial Botanicals [Link]

²⁴ Draco Natural Botanicals [Link]

²⁵ FDA, 2019 [Link]: As of the date of this paper, the FDA does not authorize structure function claims by CBD dietary supplements / nutraceuticals.

- i. Δ^9 -THC and THC-a concentrations must be below the legal limit.
- b. At least 1 or more terpenes from the included list (herein)*.
- c. A natural extraction of hydrocarbons in the precise concentration existing in the current plant from which an oil extract is being made.
 - Some hydrocarbons will be lost in the extraction process, and unless there
 are no other hydrocarbons present in the oil batch, no hydrocarbons may be
 supplemented.
- d. Nitrogen constituents must include at least 1 or more chemical from each of the following categories:
 - i. Alkaloids,
 - ii. Quaternary bases,
 - iii. Amides,
 - iv. Lignamides,
 - v. Amines,
 - vi. Proteins, and
 - vii. Enzymes.
- e. Amino Acids should include at least 1 or more chemical each from the following categories*:
 - i. Monosaccharides,
 - ii. Disaccharides,
 - iii. Polysaccharides,
 - iv. Sugar alcohols and cyclitols, and
 - v. Amino Sugars.
 - 1. It should be noted that the extraction of sugars (or other amino acids) may be necessary for some nutritional formulations, but this alters the "full spectrum" nature of the plant and should not be advertised as full spectrum, but may use a variant of the title to indicate the health benefits of zero sugars (or other chemical).
- f. At least 1 or more of the flavonoid chemicals*.
- g. At least 1 or more of the fatty acids.
 - i. Although there may be some situations whereby unsaturated or saturated fatty acids are excluded (such as dietary reasons), this alters the "full spectrum" nature of the plant and should not be advertised as full spectrum, but may use a variant of the title to indicate the health benefits of zero saturated fats (or other chemical).
- h. At least 1 or more of the phenols.
- i. And, at least 3 of any combination of the following chemicals:
 - i. Alcohols (naturally occurring),
 - ii. Aldehydes,
 - iii. Ketones,
 - iv. Acids,
 - v. Phytosterols,
 - vi. Vitamin K*,
 - vii. Pigments, and
 - viii. And any 1 or more of*:
 - 1. Na
 - 2. K
 - 3. Ca

- 4. Mg
- 5. Fe
- 6. Cu
- 7. Mn
- 8. Zn
- 9. Hg
- 2. Full Spectrum by way of chemical isolation is only permissible if:
 - a. The isolated chemical is diluted prior to re-introduction into an existing solution and mixed so that it becomes evenly distributed. The final concentration level cannot exceed the natural chemical concentrations from the whole plant had the isolated chemical not been isolated.
- 3. Missing ingredients from LIST 2 may be substituted (unless otherwise indicated), as long as the isolated chemical being substituted does not exceed the natural chemical concentrations from the whole plant had the isolated chemical not been isolated.
- 4. Any full-spectrum formulation which substitutes / supplements a chemical must include on the front of the label: Full Spectrum + Supplemented, or other verbiage to indicate that it is a "simulation" of an all-natural full spectrum formulation. All substituted ingredients needed to reach full-spectrum status must come from Cannabis Sativa L. and contain the necessary onlabel or web-link reference information to match batch numbers to suppliers.
- 5. Only oil extractions that do not have supplemental ingredients (other than added flavors, extraction chemicals, etc.) may use the term: "All Natural Full Spectrum" on their labeling, to distinguish their product.
- 6. Full spectrum products may contain higher concentrations of certain chemicals by diluting the remaining chemicals. This allows for specializing full-spectrum formulas to concentrate on specific biological functions.
- 7. The use of "organic" in labeling should continue to be restricted under USDA guidelines and we have recommended (elsewhere) that the USDA use a combination of "hops" and custom pesticide profiles for rating industrial hemp as organic.
- 8. To protect full-spectrum formulations, the only individually listed components that need be identified by title (not quantity), are those that have an asterisk at the end of their name (LIST 2). This will also specifically provide protection for individuals with allergies, diabetes, or other medical condition that may be impacted by the use of a full spectrum product.

While not necessarily comprehensive, LIST 2 is a base-line guide for "full spectrum". Not every formulation will be the same and not every formulation will be able to contain every chemical. Therefore, we also recommend a grading scale "guideline" for consumers (that may be refined as needed / over time through empirical evidence):

	Chemical Contents	Type I	Type II	Type III	Type IV
	Phytocannabinoid CBD +				
	None	Χ	Χ	Χ	Χ
7	CBG	+/-	+/-	+/-	+/-
egol	THC (-A, -V)*	+/-	+/-	+/-	+/-
Category	CBC	+/-	+/-	+/-	+/-
	CBN	+/-	+/-	+/-	+/-
	Other	+/-	+/-	+/-	+/-

Category 2	Terpenes [†] 4 – 23 3 or less	X X	X X	X X	- X
Category 3	Hydrocarbons ^{††} Complete Partial to none	X X	X X	- X	×
Category 4	Nitrogen Constituents 1+ Alkaloids 3+ Quartenary 0-2 Quartenary 1+ Amides 1+ Lignamide 3+ Amines	X X - X X	X - 2 X X	X - X X X	- X X
Cate	1-2 Amines 3+ Proteins 1-2 Proteins 3+ Enzymes 1-2 Enzymes	- X - X	2 - 2 - 2	X - X - X	X - X - X
Category 5	Amino Acids 3+ Monosaccharide 1-2 Monosaccharide 1+ Disaccharide 3+ Polysaccharide 1-2 Polysaccharide 3+ Cyclitols 0-2 Cyclitols 1+ Amino Sugars	X - X X - X	2+ - X 2+ - 2+ - X	- 2 X - 2 - 1+ X	- X - - X -
Category 6	Flavonoids 3+ non-glycosides 1-2 non glycosides 3+ glycosides 0-2 glycosides	X - -X	2+ - -2+	- X - 1+	- X - X
Category 7	Fatty Acids 6+ Unsaturated 4-5 Unsaturated 3-4 Unsaturated 1-2 Unsaturated 6+ Saturated 4-5 Saturated 3-4 Saturated 1-2 Saturated	X X - - X X	- X X - - X X	- X X - - X	- - X - - X

Category 8	Phenols 4+ 2-3 0-1	X X -	X X X	- X X	- - X
Category 9	Natural Alcohols 2+ 0-1	X -	1+	- X	- X
Category 10	Aldehydes 2+ 0-1	X -	1+ -	- X	- X
Category 11	Ketones 2+ 0-1	X -	1+	- X	- X
Category 12	Acids 2+ 0-1	X -	1+	- X	- X
Category 13	Phystoserols 2+ 0-1	X -	1+ -	- X	- X
Category 14	Vitamin K	Х	Х	Х	+/-
Category 15	Pigments 2+ 0-1	X -	1+ -	- X	- X
Category 16	Minerals 4+ 2-3 1+	X X X	- X X	- X X	- - X

Table 2: Full Spectrum Grading Guide (baseline recommendation)

Table 2 is not meant to be an "absolute" whereas ranges have been provided across multiple categories with the understanding that some plant species, or even individual crops (depending on factors such as high soil nutrients which result in reduced terpenes), may not be inclusive of all of these chemicals.

^{*}within legal threshold

[†] Because not all terpenes are present in every strain of Cannabis Sativa L., the augmenting effects of even a few of the terpenes can still be effective and are therefore recommended across multiple grades

^{††} Hydrocarbons may appear not present in some concentrations as the scrubbing of chemicals used in extraction could equally remove naturally occurring chemicals like heptacosane and hexacosane.

No percentages or ratios are offered here as it is anticipated that each formulation will be unique to the producer.

However, without a solid definition for "full spectrum" that is agreed upon by the entire nutraceutical community for industrial hemp, this provides a volatile and unfair market of misinformation for consumers. In the case of Table 2, certain resellers may apply to the USDA for some relief in meeting some of the requirements (or may grade some formulations as (for example): Type II/III, or Type III+, where a product falls between two grades). Additionally, to qualify as a full spectrum product²⁶, this means that more tests than are normally conducted will have to be performed. Given the consumer cost per unit of industrial hemp full-spectrum oil, a single test per batch is certainly not financially overwhelming and should not be a breaking-point for the market. Furthermore, once the FDA provides approval for industrial hemp in food products, their stricter labeling requirements will force makers of CBD-infused consumables to perform more thorough testing.

Another important consideration of Table 2 is that it provides a comprehensive list of chemicals for consumer protection. While terpenes should be listed out (at least through a consumer on-line portal), for the purposes of identifying potential, and to some people, deadly allergens, on-label ingredients do not require a complete reveal (sometimes pertaining to which ingredients or in what quantities/mixture these ingredients are present), protecting formulations. LIST 2 provides a recommendation of which chemicals have to be individually referenced (whether on-label or through an on-line portal), by way of an asterisk (this is also necessary for consumers to identify other potential reactionary issues including, but not limited to: diabetes, hypoglycemia, prescription medication interaction, etc.).

In discussion with agricultural producers, oil producers, and product sales, this list seems daunting and unattainable. However, these sources also revealed that they had never tested for said ingredients and were more concerned about the effects of extraction chemicals either exempting them from full spectrum (by extracting too many of the baseline chemicals) or causing them to be in a lower grade. We should be clear: the grading system is not for the purposes of quality. In fact, the grading system is actually beneficial to producers (thus, we selected the word "Type" over "Grade" and a numerical category vs an alphanumeric such as "A, B, C, etc"). Where some individuals may have allergies to certain parts of industrial hemp (ie. some of the minor / more rare terpenes), or where a Type I (for example) full spectrum CBD oil could interfere with prescription medication, a lower grade oil / different "Type" may be necessary, while still offering many of the entourage benefits of full spectrum chemical interaction. This concept is not all that different from the various "specialty" brands offered by Centrum, whereby their multi-vitamin supplements are modified to meet the individual needs of men, women, children, and the elderly.

Finally, we have addressed supplementing chemicals back into an extraction to meet the full-spectrum definition. Already, there are terpene and flavonoid retailers providing these extracted chemicals so that extraction techniques which have stripped more chemicals than desired may substitute the missing elements. It would be our recommendation that these supplemental ingredients also be sourced from Cannabis Sativa L. However, there may be cases where supplemental flavors and other formulations naturally complete the full spectrum ratio / balance.

²⁶ In regard to a final, full-spectrum form product, this refers to an oil, or a powder, that meets the included definition of full spectrum. For the purposes of this paper, based on our research, we do not differentiate "oil" from "tincture" and have, to date, quantified no difference between the two terms.

Additional Note:

As an additional note to this study: we did not sustain or confirm the empirical evidence regarding the medical suitability of the chemical constituents of Cannabis Sativa L. However, it is clear from the literature that not only are there a significant amount of studies going back long before pharmaceuticals applied for FDA licensing, but the studies on the individual components and some of the entourage effects have been reproduced, verifying both a medical-grade and non-medical-grade value. There are certain structure function claims which may be a misinterpretation of effects (such as CBD's effect as an anti-inflammatory also being the same as reducing pain), which could be easily rectified in subsequent analysis if determined such analysis is needed²⁷.

Conclusion:

There is enough information that can be drawn from the botanical nutraceutical (dietary supplement) market and the assumed intentions of having a full spectrum product to rely upon the final conclusions in this white paper:

A full spectrum industrial hemp oil must contain a minimum number of elements from the 16 major categories of identified chemicals in order to qualify as a "full spectrum" botanical extract (product) and must be extracted and/or supplemented in such a manner that does not change the natural, pre-extraction ratio of any one chemical more than 5%.

Since formulations and extraction methods will all be different, a baseline guide should be provided (Table 2) to ensure uniform consistency among oil producers for qualifying, full spectrum products. It is our recommendation that the term "full spectrum", be limited to products that fit within the guideline recommendations herein (or as may be amended). Based on our research, the term "broad spectrum" does not provide qualified information for consumers and should not be a qualifying, stand-alone term similar to full spectrum. "Full Spectrum" may be associated with a unique set of sub-chemicals (such as terpenes, phytocannabinoids, etc.), but that definition guideline is not part of this paper (and not recommended at this time).

²⁷ Future Systems is available to perform this analysis for any qualified agency, but that is a separate matter which will require additional medical scientific input and costs. Please contact us if interested.

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