Douglas MacKay, ND: Defining the Regulatory Landscape for Hemp-based Supplements

Interview by Dick Benson

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Alternative therapies in Health and Medicine **(ATHM):** How do you think the change in FDA commissioners will affect the regulatory pathway for hemp?

Dr MacKay: We understand that the new acting FDA commissioner, Ned Sharpless, MD, intends to continue to clarify a regulatory path forward for food-based, hemp-derived CBD products. Everything we are hearing in Washington DC from the agency, as well as from insiders that have met with the agency, is that regulating cannabis products is a priority. Congress continues to apply pressure on the agency and we know that Congress influences FDA priorities because they provide FDA funding. Gottlieb has made various public statements where he committed to holding public meetings and developing a task force to address issues surrounding *Cannabis*. In my opinion, Dr Sharpless will stay the course and continue progress where Gottlieb has left off.

***ATHM*:** What intrigued you about the hemp-CBD market and the regulatory change happening there?

Dr MacKay: I have worked in Washington, DC with dietary supplement issues for the past 10 years. I have observed the hemp-CBD sector grow, despite the legal and regulatory questions. Being part of several high-level meetings and getting to know the industry, I realized that unique circumstances created a new—and this is probably not the best term—Wild West! You have unprecedented consumer demand driving a rapidly growing hemp-CBD food and supplement marketplace that exists in a regulatory gray area. These activities are coinciding with the first cannabis-based FDA prescription drug approval—Epidiolex—as well as a patchwork of changing state laws related to using *Cannabis*—not the same as hemp—for its intoxicating effects—aka recreational use. Then, consider all the pressure to get these new markets regulated: pressures from Congress, pressures from consumers, and from retailers who express urgency to have high-quality hemp-CBD products that are complaint with FDA regulations for food and supplements, while avoiding products that FDA would consider prescription drugs, or worse that the DEA would consider a controlled substance. It's a perfect storm.

Over the last 10 years working in the food and supplement policy space with science and regulations, I was already participating in the conversation—and it was really an exciting conversation. It had so much to do with the intersection of all the things that interest me within botanical medicine. We have this incredibly dynamic plant, *Cannabis sativa,* that was once taboo, that is now at the foundation of different policy discussions. Everyone is talking about how to use *Cannabis* safely and appropriately as a food, supplement, prescription drug, or adult recreational use. These are distinct regulatory categories that this plant can land in; the various swim lanes, if you will. Each category has a different intended use that will govern the type and scope of cannabis product that is allowed in the category. You have drug development, you have food and supplements, and then you have this whole emerging recreational market in some states. Each of these have different end users, whether it's as a nonintoxicating hemp-based supplement to help support the endocannabinoid system, as a compared to a cannabis drug-cultivar derived prescription drug intended for epilepsy or another serious condition. These are different products, with different

intended uses, and different risk/benefit profiles—different swim lanes.

Over the last 10 years, I've recognized that the regulatory paradigms that exist, while not perfect for each of these categories, are based on rational public health and public policy rational. For example, a lot of people in the food and supplement space, particularly integrative health care practitioners, are very excited about the notion of having different foods and drinks with purified CBD—we'll call it *isolated CBD* because it's concentrated—and you can put large amounts in them.

We also know that isolated CBD is already an approved prescription drug for two serious forms of epilepsy. Supplement marketers need to respect the significant science and specificity it takes to develop a drug and to prove the product is safe and effective for a particular condition. The supplement industry should immediately stop trying to imply that foods and supplements are the same as drug products—they are not. The supplement industry needs to recognize the risk in undermining future investment in research to find new applications where cannabinoids could be used by physicians in serious medical conditions. If we don't, we may never fully answer whether there other seizures that CBD or other cannabinoids might be good for, can cannabinoids treat cognitive conditions, and might there be other areas where it provides neuroprotective effects?

To invest scientific resources needed to answer those scientific questions with certainty, we need to honor the fact that the FDA drug approval process is the way to do that. If we listen to the CBD advocates in the supplement industry and allow highly purified or isolated CBD to be sprinkled in foods, drinks, and dietary supplements, there will be no financial incentive for companies to invest in future research.

At CV Sciences, we believe that food and supplements should be derived from hemp extracts, as opposed to low-THC, drug-type, cannabis cultivars. These are the kinds of products that are appropriate to be consumed as foods and dietary supplements: derived from real hemp, extracted in ways that are typical for dietary supplements, and provide a full spectrum of cannabinoids and other constituents.

These are the types of products we envision the FDA will allow as dietary supplements. FDA will understand why people might want to supplement their diet with hemp to support their health. FDA is going to be very hesitant to say, "Yes, you can use isolated CBD or highly purified CBD in supplements," because there is already a prescription drug in this form.

This is nuanced health policy that requires a lot of long-term thinking, and that is the kind of thing I am interested in: sitting in on those long policy meetings where people are using data to make a case for what these markets should look like. I say it's about 3 to 5 years of work to get this all worked out, and so I'm excited to be part of it.

***ATHM*:** A lot of education is needed. I was listening to a program on Saturday talking about CBD with two doctors, and it was an *ask the doctor* format. One of them asked the other, "Aren't you afraid of people getting high?" I thought: "Doesn't he know what CBD is?" THC is the euphoric psychoactive in *Cannabis*, not CBD. And CBD is often derived from hemp, which by legal definition contains only trace amounts of THC.

Dr MacKay: That is an interesting observation. If we talked to Stuart Tomc, CV Sciences, vice president of human nutrition, who manages education, today, he'd say: "When I first started at CV Sciences, the number one thing I had to explain was, 'You can't get high from CBD.'" Most informed consumers have moved past that level of knowledge, but it is going to be a long time before the mainstream consumers and medical doctors understands even that basic information. There will always be an old-fashioned mentality, "Oh, that's related to pot," but we both know scientifically that's just a distraction and that eventually hemp-derived CBD products will be mainstream.

I was just at a meeting last week of the Food, Drug, and Law Institute. Frank Yiannas, the deputy commissioner of foods, was there. He said, "We have to figure out the appropriate type of hemp-derived CBD products for foods and supplements. Consumers want it, Congress wants it." He gets it. FDA knows that there is no risk of getting high with products derived from true food-fiber hemp.

That does bring up a very important point: The USDA is writing its proposed rule that allows people to grow hemp over the next year. Congress passed hemp farming legislation in the 2018 farm bill. Now, it's USDA's job to issue regulations. One of the things CV Sciences is advocating for is that USDA should be careful to mandate farming of real industrial food-fiber hemp. The spirit of the hemp provision in the farm bill was to grow food-fiber hemp, to bring back hemp as an agricultural commodity. Therefore, we should honor the intent and we should be growing real hemp.

In other countries, like Germany, that have growing programs for industrial hemp, they require certain seeds that are known to be genetically industrial hemp: very tall, full of fiber, and low in resins. These are the only cultivars allowed to be grown. The farmers are required to plant licensed and registered seeds. The licensed seed list changes because some cultivars will begin to produce too much THC, and without USDA keeping ahead of this, hemp farming can become drug-type cannabis growing. At the source, we think it is important that USDA uses a seed licensing and registration scheme to foster food-fiber hemp farming for use in food and supplements.

Seed distinction will be important because there is going to be a separate farming industry for growing cannabis drug cultivars, for recreational or drug-development, which is very different than hemp. Drug-type *Cannabis* requires a different amount of water, is often done indoors, and involves different cultivars of *Cannabis* with different levels of CBD and THC. I am not against the emerging cannabis drug-type industry; it is going to be a very exciting industry on the

growing side as well as in product development. But it is important to keep these lanes separate and very inappropriate to consider hybrids of drug-type cultivars as appropriate for food and dietary supplement products.

***ATHM*:** One person recently said to think of the differences between the plants as striving for a beautiful flower to develop THC in cannabis drug-cultivars versus hemp, where the uglier the plant, the better.

Dr MacKay: Again, a lot of people are going to struggle with this because CBD itself isn't going to be different in those kinds of products. But to respect how food and farm policy go, we need to create a healthy market for the food-fiber hemp farmer who will be able to sell product for textiles and paper as well as to make old-school hemp oil with a lot of fatty acids, hemp proteins, and hemp flowers from the seeds, as well as hemp extracts that are known to be naturally absent of THC. Food and supplement products derived from food-fiber hemp are, however, going to have a different phytocannabinoid profile. Then, there will be a separate market where different cultivars of *Cannabis* are grown to make these different recreational as well as medical products. This is CV Sciences vision of the future we will continue to advocate for this future.

CV Sciences is investing in developing a better understanding how hemp extracts can be different and beneficial in different ways than CBD isolates. When you look at the chemistry of hemp extracts, there's a full profile of cannabinoids, fatty acids, and terpenes. Differences exist when you take a full-spectrum, hemp CBD product. CV Sciences is conducting analytical science and clinical trials to better understand the unique products we deliver to the consumer and how they act as a food that feeds the endocannabinoid system.

***ATHM*:** Before you were at the Council for Responsible Nutrition, or CRN, you were at Nordic Naturals. Do you see the emergence of CBD as similar to what happened with fish oils?

Dr MacKay: Well, yes. My choice is not by accident. Nordic Naturals is a category leader in an area with strong science. When I joined Nordic, the fish oil category was expanding and I wanted to be part of something that has that kind of horsepower, if you will. That was a valuable experience at a great company, managing their science portfolio, helping it grow, and helping it with regulatory compliance. That led me to the Council for Responsible Nutrition, CRN. CRN was just another platform, a bigger platform, to do similar things.

More recently, as I watched the CBD explosion, I had a very similar feeling. It was very nostalgic. I was sitting in meetings at NIH listening to legacy scientists open up about their interest in researching cannabinoids. I was seeing progress with cannabis drug-development. I thought, "This could be another omega-3 scenario." Cannabinoids and the human endocannabinoid system are things that scientists have known relatively little about. Now, it's emerging that we have this remarkable endocannabinoid system (ECS) and plant-based bioactive compounds that interact with the ECS. The ECS is involved in regulating a variety of functions including sleep, appetite, pain and immune system response. I want to be part of unwrapping all of this, helping hemp-derived CBD products come to maturity, and be part of the supplement economy." I believe in it and it's easy to work hard at the intersection of science and regulatory-policy when you believe in something.

***ATHM*:** Much like omega-3s, CBD right now is at the point where it's pretty much good for anything. I don't want to be flippant about it, but it seems to affect almost every condition—anxiety, sleep, relaxation, all different types of chronic issues that we have.

Dr MacKay: The science on cannabinoids and CBD are rapidly evolving. We have learned about the ECS and how phytocannabinoids interact with the ECS, what receptors are involved, and what those receptors do, however we should manage expectations with supplement products. There have been a lot of ingredients that, when we first learned how they work, it generated a lot of excitement about potential impact on physiology and health conditions. Then, when you start doing human clinical trials and really getting it out there, we learn that sometimes the impact is more moderate than we thought. The reason people say it is good for everything is because of how the endocannabinoid system works. So, you can start to argue "Yes," but the question is: "Will the user experience all those things?"

With fish oil for example, we learned that omega-3 fatty acids are in every cell membrane in the body and help with cell membrane fluidity. It's easy to assume the benefit of optimal cell membrane fluidity will translate to specific health benefits. So we assume, fish oil must do all these amazing things, but then you do the human clinical trials and you say, "Oh, well, it looks like it's good for you, it looks like it's protective, but at the same time it's not a magic bullet." I think it goes back to integrative medicine in the sense that changes in diet lead to changes the biochemistry in your body that have a moderate, but a lasting, impact on your health. As opposed to taking a drug, which has very acute and intense effects, but again, not necessarily long-acting, physiology-changing effects. A drug may be able to knock out a fever, but it doesn't really make you healthier.

***ATHM*:** Do you think that CBD will evolve like omega-3s, where they are now combined with other ingredients to target specific conditions?

Dr MacKay: It is important to remember the way we're looking at it: The ingredient itself is a hemp extract. The hemp extracts are going to have CBD as a constituent of the whole. The question is: "When FDA gets a hold of this, what level of CBD will be allowable in said hemp extract?"

I personally do not think that isolated CBD is going to be allowed at all in food or supplements. The reason I say that is isolated CBD would probably be easier to mix and match into different formulas because it won't take up a whole lot of room; it won't be in an oil form. If you were making an anxiety formula, you'd be able to add CBD to tablets and capsules, and it would be easy to do from a manufacturing standpoint. If industry is required to work with true food-fiber hemp extracts, like I think FDA will require, you have some limitations. You have a larger set of constituents in hemp extracts that provide a certain amount of CBD, and formulating with it becomes a different story, if you will.

But yes, absolutely, there is an opportunity to mix hemp extracts with ingredients such as curcumin or omega-3s and put together formulas. I'll have to underscore, again, I have a regulatory sensitivity and any of these products would be considered by FDA as New Dietary Ingredients, or NDIs. The firm that would make them would have to make sure that their ingredients and combinations of ingredients will be safe based on the intended use. When you develop your own extract of hemp, like CV Sciences has, best practice calls for performing GRAS affirmation, which requires conducting and publishing toxicology studies to make sure that the product is safe when consumed as directed.

***ATHM*:** Doesn't hemp extract contain other phytocannabinoids besides CBD?

Dr MacKay: Correct. Say, for example, the pharmaceutical data that is out there shows that CBD isolate is safe when used as a drug; that data cannot be used for hemp extracts because that hemp extracts are entirely different and contain many more cannabinoids and other bioactive constituents.

***ATHM*:** What about the impact of toxin exposure through fertilizers or weed and pest control on hemp crops going forward?

Dr MacKay: Any plant-derived material will include trace amounts of environmental chemicals, this is even true for organic crops. However, hemp-derived dietary supplements should not contain more than ultra-trace amounts of environmental chemicals because of the manufacturing and testing requirements. Responsible manufacturers test incoming raw material and finished products for pesticides and heavy metals.

***ATHM*:** Michael Murray, ND, stresses the need for research. Anecdotal information is great, but we need to see research, we need to see case reports, things like that. What's your feeling in that area?

Dr MacKay: We agree completely with Dr Murray. CV Sciences recently published a retrospective study of 72 cases involving our Gold formula for sleep and anxiety as an adjunct to conventional treatment. CV Sciences is also supporting a randomized, placebo-controlled clinical trial—details coming soon. In addition, we are evaluating several other opportunities to invest in research that will expand our understanding of our hemp-derived CBD products.

In general, the past DEA scheduling of hemp as a controlled substance significantly limited scientific research until 5 to 10 years ago. It was just too difficult for researchers to get materials and the necessary IRB approvals. This has all changed. We now have published studies and many more on the way. In addition to following the emerging published research, CV Sciences is investing in understanding the benefits of its own products. I want to underscore that having your own evidence tied to your own extract is an important thing for everyone in this industry to do.

The regulatory blockade on conducting clinical research is lifting. Now, it is easier for a university to say, "Hey, CV Sciences, can you send us product and placebo? We want to run a clinical trial." When before, they were worried they were dealing with a controlled substance. If you go to http://www.clinicaltrials.gov, a lot of trials have been registered and are recruiting, so we are going to learn a whole lot about hemp, including CBD in the next 5 to 10 years.

***ATHM*:** What about hemp as a crop? Do you think that it could exceed expectations in industrial purposes and make it hard to source for supplement purposes?

Dr MacKay: Oh, no. In fact, I do think that the major use of hemp is going to be industrial and fiber products. The aerial parts of the plant can be extracted for foods and supplements, but the stalks can be used as fibers. The seeds could be used to make fatty acid-rich oils. In the spirit of the 2018 Farm Bill, we want to see the United States farmers growing thousands and thousands of acres of hemp. There is a benefit to sequestering carbon from the atmosphere and getting farmers back to growing a profitable crop. There are going to be lots of product categories for food-fiber hemp to go into. Supplements will be one small part of what is derived from this new and exciting agricultural commodity. Parallel to hemp farming, there will be a separate drug-type cannabis growing industry growing a variety of cannabis cultivars with varying levels of THC and CBD to support state-based recreational products.

***ATHM*:** What do you see happening in the next 18 months?

Dr MacKay: The next 18 months are critical. Regulations will be put into place and come companies will have to pivot or be gone. USDA is developing regulations right now that will further define what can be planted and called hemp and how it is managed. USDA just held two listening sessions, they're getting input from the farm community, they're trying to figure out how it will issue its regulations for legal growing of hemp in the United States. USDA is committed to allowing farmers to get plants in the ground in the 2020 growing season. That's all going to happen in the next year. Then, FDA

will determine what it is going to do about companies that sell hemp-derived products as food or dietary supplements. FDA has indicated that it will go through a proposed rulemaking process. The FDA process will involve a series of meetings, stakeholder feedback, and opportunities for industry input. Congress could decide FDA is not moving fast enough and step in with new legislation, but that process in not predictable.

***ATHM*:** On the legislative side, how well are the lawmakers' teams educated about CBD and hemp?

Dr MacKay: Lawmakers are very educated on CBD and hemp. What they weren't so educated on is the fact that the Farm Bill did not automatically give consumers access to CBD. Members of Congress were not aware that FDA authority to regulate food and supplements was another obstacle for CBD. Congress thought that removing hemp from the Controlled Substance Act would be enough to make highly purified CBD legal to sell in food and supplements, and they overlooked that fact that it is already a drug. Stakeholders are having to educate Congress on how FDA policies still need to be resolved and that FDA needs to clarify a pathway for food and supplements. Many members of Congress have said, "We thought we already took care of CBD in the farm bill." There has been a lot of education to do in that area.