



U.S. Department of Justice

Office of Legislative Affairs

Office of the Assistant Attorney General

Washington, D.C. 20530

June 23, 2015

The Honorable Charles E. Grassley
Chairman
Senate Caucus on International Narcotics Control
United States Senate
Washington, DC 20510

The Honorable Dianne Feinstein
Co-Chairman
Senate Caucus on International Narcotics Control
United States Senate
Washington, DC 20510

Dear Mr. Chairman and Co-Chairman Feinstein:

This responds to your letter to the Attorney General and Secretary Burwell, dated May 13, 2015, regarding regulations governing research involving marijuana and its constituent, cannabidiol (CBD). This also supplements our January 5, 2015, response to your October 20, 2014, letter on this issue. Your May 13th letter asks that the Department of Justice (the Department) work with the Department of Health and Human Services (HHS) to determine additional ways to support and facilitate research with marijuana and CBD.

Per your written request, the Drug Enforcement Administration (DEA) will work with HHS to evaluate CBD under section 201 (a) – (c) of the Controlled Substances Act (21 U.S.C. 811(a)-(c)). To accomplish this, DEA will initiate the review of CBD and request a scientific and medical evaluation and scheduling recommendation for CBD from HHS. Please be advised, although CBD products are currently being evaluated under Investigational New Drug Applications, additional scientific studies may need to be initiated and conducted to assess CBD's abuse liability. Scheduling recommendations are evidence-based, and DEA will provide any assistance necessary to aid HHS in its collection of information critical to its scientific and medical evaluation and formulation of a recommendation.

The Department, including DEA, is fully committed to supporting lawful research involving marijuana and CBD by ensuring compliance with the Controlled Substances Act and the Single Convention on Narcotic Drugs. DEA will continue to review the relevant regulations to ensure they are consistent with supporting lawful research. If this review determines that amending the existing regulations governing the Schedule I researcher registration process is necessary to accomplish these goals, DEA would initiate the process to do so. DEA will also

continue to work with HHS to streamline the Schedule I researcher registration process and identify new opportunities for improvement.

To date, DEA has not denied any research application that has met the CSA requirements. In fact, the number of authorized Schedule I researchers, including CBD researchers, continues to grow.^[1] Between November 2014 and June 4, 2015, the number of researchers approved to conduct research with CBD on human subjects has increased from 16 to 41. As of June 4, 2015, there are 399 active researchers registered with DEA to conduct bona fide research with Schedule I controlled substances. Of these 399 Schedule I researchers, 265 active researchers are registered with DEA to conduct bona fide research with marijuana and marijuana extracts that include CBD, and 41 researchers are approved to conduct research with CBD on human subjects. Each of these 41 researchers is approved to conduct or supervise an investigation with at least one study subject with synthetic or plant-derived CBD. In furtherance of our ongoing efforts to support CBD research, DEA will continue its policy of expediting these applications.

In your letter dated May 13, 2015, you put forward specific questions related to the review of the Schedule I researcher registration process. Following are the responses to your enumerated questions.

1. Based on the response to our letter, it appears that DOJ has already concluded that none of the regulations regarding this research should be altered. Is this correct?

Response: As noted above, DEA is amenable to changes to the existing regulations governing the Schedule I researcher registration process, if necessary. We remain committed to working with HHS and Congress on this issue.

2. Our letter also outlined concerns with regulatory requirements governing changes to the quantity of marijuana needed for approved research. DOJ's response suggests that additional quantities of controlled substances can be purchased and used for research purposes as soon as DEA returns the receipt. Is this so? If not, what additional steps are required?

^[1]As of November 17, 2014, there were approximately 237 active Schedule I researchers registered with DEA. Of those researchers, 166 were approved to perform bona fide research with marijuana, marijuana extracts, and marijuana derivatives such as CBD and cannabitol. Of these 166 researchers, 16 were approved to conduct research with CBD on human subjects. As of February 25, 2015, there were 372 active researchers registered with the DEA to conduct bona fide research with Schedule I controlled substances. Of these 372 researchers, 247 active researchers were registered to conduct bona fide research with marijuana and marijuana extracts that include CBD. As of June 4, 2015, there were 399 active researchers registered with the DEA to conduct bona fide research with Schedule I controlled substances; of these 399 researchers, 265 active researchers were registered to conduct bona fide research with marijuana and marijuana extracts.

Response: According to regulations under 21 C.F.R. 1301.18 (c), upon return of receipt from DEA, the registrant is authorized to purchase the additional quantity of the controlled substance or substances specified in the request. To conduct research with the additional quantity, the researcher is required to wait until DEA has communicated the Food and Drug Administration's (FDA's) concurrence with the protocol modification. During this review process, the previously approved protocol remains active and the researcher may continue to conduct research under this protocol.

3. We understand from staff at the Food and Drug Administration that it takes approximately nine months for federally-funded research on marijuana to be approved. Existing regulations stipulate that if the approved protocol changes, a supplemental protocol must be submitted and is processed in the same manner as the original protocol.
 - a. If a researcher amends their protocol, is it correct that all work must stop until the supplemental protocol is approved, which could take as long as nine months?

Response: The Schedule I researcher registrant is allowed to continue research using the previously approved protocol until DEA and FDA take the final action regarding the supplemental protocol. Under current DEA regulations, when a researcher who is in the midst of an ongoing, approved study seeks to increase the quantity of the Schedule I controlled substance being used for the research, the researcher must submit to DEA an amendment to the approved protocol. 21 C.F.R. § 1301.18(c). "Upon return of the receipt, the registrant shall be authorized to purchase the additional quantity of the controlled substance or substances specified in the request." *Id.* DEA forwards this information to HHS, and HHS "shall approve or deny the request as an amendment to the protocol." *Id.* Submission of an amendment does not stop research with the previously approved protocol, which remains active. The researcher may continue to conduct research pursuant to the previously approved protocol.

DEA's role in the process is to ensure that there is accurate accounting and security for the increase in material. From a diversion control standpoint, DEA needs to be informed of any changes in the quantity of Schedule I controlled substance to ensure that there continue to be effective procedures to guard against diversion of all such controlled substance material. Further, in some instances, the Schedule I drug that is used in the clinical trial is imported. In such cases, where the researcher seeks to use more material than indicated in the original protocol, 21 C.F.R. § 1301.18(c) allows the increased amounts to be legitimately used in research, thereby providing the basis for allowing the increased amount to be imported pursuant to 21 U.S.C. § 952(a)(2)(C) (authorizing the import of Schedule I substances if in limited quantities for research uses).

Such quantity changes might impact the scientific merit of the research; therefore, the regulations require the researcher to provide to DEA and FDA notice of the additional quantities of controlled substances that the researcher wishes to procure. FDA reviews the proposed increase in quantity to ensure that the protocol remains scientifically sound and meritorious, and safe for human research subjects.

If an approved researcher intends to deviate from the previously approved research protocol other than quantity of controlled substance (e.g., if a researcher were to seek to expand the subject group to include pediatric patients, to include patients with different diagnoses or suffering from life-threatening ailments, or to change the method of delivery of the drug), the researcher must submit a supplemental protocol to DEA. DEA forwards the supplemental protocol to FDA for review and approval. These types of changes might raise significant new questions concerning the scientific merits of the protocol. Close review is important because material deviations in the research protocol could potentially alter the scientific merit of the research and have impacts on the health and safety of the human research subjects. For this reason, protocol changes noted in 21 C.F.R. § 1301.18(d) – unlike the quantity changes in 21 C.F.R. § 1301.18(c) – are reviewed in the same manner as an original protocol. As previously noted, the Schedule I researcher may continue research using the previously approved protocol until DEA and FDA take the final action regarding the supplemental protocol.

It is important to act expeditiously on applications for Schedule I research. The timeframes for DEA's and FDA's processing of Schedule I research applications are specified in the regulations. DEA forwards complete Schedule I research protocols to FDA within seven days of receipt; FDA notifies DEA of its determination regarding the merits of the protocol within 30 days; and DEA issues a certificate within 10 days of receiving the FDA's notice. 21 C.F.R. 1301.32(a) and (c). It should be noted that although many clinical researchers may be subject to a standardized protocol, thereby streamlining the process, some researchers must also meet institutional and State requirements prior to approval. DEA works closely with researchers to assist with the expeditious completion of their protocol submission and registration application.

- b. Does DOJ believe that it would be beneficial to amend its regulations to include a timeframe by which a secondary approval will be granted or denied? If not, why not?

Response: We agree it is important to act expeditiously on applications for supplemental protocols. According to 21 C.F.R. 1301.32(e), the supplemental protocols are processed in the same manner as original protocols. The time frames are: seven days after the receipt of protocol for DEA to forward to FDA; 30 days for FDA to notify DEA about its determination; 10 days after the receipt of FDA's notice for DEA to issue the replacement certificate.

The Honorable Charles E. Grassley
The Honorable Dianne Feinstein
Page Five

We hope this information is helpful. Please do not hesitate to contact this office if we may provide additional assistance regarding this or any other matter.

Sincerely,

A handwritten signature in blue ink, appearing to read "PKA", written in a cursive style.

Peter J. Kadzik
Assistant Attorney General