U.S. Department of Justice

Office of Legislative Affairs

Office of the Assistant Attorney General

Washington, D.C. 20530

January 5, 2015

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

Dear Chairman Feinstein:

This responds to your letter to the Attorney General and Department of Health and Human Services (HHS) Secretary Sylvia Burwell dated October 20, 2014, regarding research involving marijuana and its derivatives, particularly cannabidiol (CBD). You requested a review of regulations pertinent to research related to marijuana, particularly CBD. We are sending an identical response to Co-Chairman Grassley, who joined in your letter.

As you know, both the Department of Justice (the Department) and HHS, through the Food and Drug Administration (FDA), have statutory roles related to this issue. We are committed, consistent with the Federal Food, Drug, and Cosmetic Act (FDCA) and the Controlled Substances Act (CSA), to assisting the healthcare needs of patients. In this regard, the Department and FDA appreciate the importance of supporting the efficient and scientific assessment of marijuana and its constituents in connection with new drug development, and believe the regulations and procedures currently in place do so consistent with the underlying law. The FDCA and the CSA contain provisions that are specifically designed to allow for both clinical research with, and treatment uses of, unapproved drugs, provided certain steps are taken to protect the rights, safety, and welfare of human subjects. FDA's drug approval process, as established by Congress, represents the best way to ensure that safe and effective new medicines are available as soon as possible for the largest numbers of patients. To date, the Drug Enforcement Administration (DEA) has not denied an application that has met the requirements. As of November 2014, there were 236 active researchers registered with DEA to perform bona fide research with marijuana, marijuana extracts, and marijuana derivatives.

Currently, there are a number of researchers around the country who are looking into the possible medicinal benefits of CBD. Because no drug products containing CBD are approved for marketing under the FDCA, no clinical investigation involving CBD may be conducted under the FDCA unless the sponsor of the investigation has submitted to FDA an investigational new drug application, which must be in effect before any human subjects can be enrolled in such investigations. Also, CBD derived from marijuana is a Schedule I controlled substance. Accordingly, to conduct research with marijuana-derived CBD, a researcher must obtain a

registration from DEA by submitting a research protocol that DEA forwards to HHS for review. Once HHS determines that the research protocol is scientifically meritorious and that the researcher is qualified, DEA will grant the registration, provided the researcher will have in place effective controls against diversion. This process is not unique to CBD research, but rather is applicable to any research involving potential medicinal benefits of any Schedule I substance.

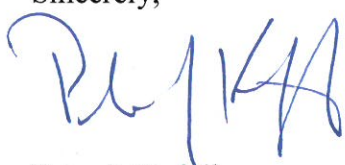
We support research involving CBD and its potential capacity to treat multiple conditions. In June 2014, FDA granted Fast-Track designation to the investigational CBD product, Epidiolex, for study in the treatment of a rare form of childhood epilepsy. FDA has also authorized the use of Epidiolex under expanded access, which is designed to facilitate the availability of investigational drug products to patients while those drugs are being studied for approval. We support the use of expanded access, which provides access to treatments for patients with serious or immediately life-threatening diseases or conditions, while preserving important protections for those patients. GW Pharmaceuticals, the maker of Epidiolex, has publicly announced that there are over 300 patients being treated through this program, including many pediatric patients with seizure disorders.

You indicated in your letter that, under current regulations, where a researcher who is in the midst of an ongoing study seeks to increase the quantity of the Schedule I controlled substance being used for the research, the researcher must submit to DEA a new request that "essentially [puts the researcher] back to square one." It is important to clarify that the procedure in these circumstances, as required under 21 C.F.R. § 1301.18(c) and (d), only requires the researcher to provide to DEA notice of the additional quantities of controlled substances that the registrant wishes to procure. "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.*

However, if the researcher plans to deviate from the previously approved research protocol (other than quantity of controlled substance), the researcher must submit to DEA a supplemental protocol for approval. Consistent with Federal law, DEA forwards this additional documentation to HHS for approval. This review is important, particularly with respect to research with Schedule I controlled substances 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.

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 mater.

Sincerely,



Peter J. Kadzik
Assistant Attorney General

U.S. Department of Justice

Office of Legislative Affairs

Office of the Assistant Attorney General

Washington, D.C. 20530

January 5, 2015

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

Dear Co-Chairman Grassley:

This responds to your letter to the Attorney General and Department of Health and Human Services (HHS) Secretary Sylvia Burwell dated October 20, 2014, regarding research involving marijuana and its derivatives, particularly cannabidiol (CBD). You requested a review of regulations pertinent to research related to marijuana, particularly CBD. We are sending an identical response to Chairman Feinstein, who joined in your letter.

As you know, both the Department of Justice (the Department) and HHS, through the Food and Drug Administration (FDA), have statutory roles related to this issue. We are committed, consistent with the Federal Food, Drug, and Cosmetic Act (FDCA) and the Controlled Substances Act (CSA), to assisting the healthcare needs of patients. In this regard, the Department and FDA appreciate the importance of supporting the efficient and scientific assessment of marijuana and its constituents in connection with new drug development, and believe the regulations and procedures currently in place do so consistent with the underlying law. The FDCA and the CSA contain provisions that are specifically designed to allow for both clinical research with, and treatment uses of, unapproved drugs, provided certain steps are taken to protect the rights, safety, and welfare of human subjects. FDA's drug approval process, as established by Congress, represents the best way to ensure that safe and effective new medicines are available as soon as possible for the largest numbers of patients. To date, the Drug Enforcement Administration (DEA) has not denied an application that has met the requirements. As of November 2014, there were 236 active researchers registered with DEA to perform bona fide research with marijuana, marijuana extracts, and marijuana derivatives.

Currently, there are a number of researchers around the country who are looking into the possible medicinal benefits of CBD. Because no drug products containing CBD are approved for marketing under the FDCA, no clinical investigation involving CBD may be conducted under the FDCA unless the sponsor of the investigation has submitted to FDA an investigational new drug application, which must be in effect before any human subjects can be enrolled in such investigations. Also, CBD derived from marijuana is a Schedule I controlled substance. Accordingly, to conduct research with marijuana-derived CBD, a researcher must obtain a

registration from DEA by submitting a research protocol that DEA forwards to HHS for review. Once HHS determines that the research protocol is scientifically meritorious and that the researcher is qualified, DEA will grant the registration, provided the researcher will have in place effective controls against diversion. This process is not unique to CBD research, but rather is applicable to any research involving potential medicinal benefits of any Schedule I substance.

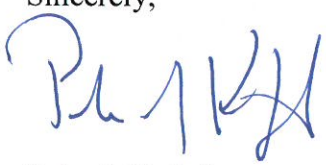
We support research involving CBD and its potential capacity to treat multiple conditions. In June 2014, FDA granted Fast-Track designation to the investigational CBD product, Epidiolex, for study in the treatment of a rare form of childhood epilepsy. FDA has also authorized the use of Epidiolex under expanded access, which is designed to facilitate the availability of investigational drug products to patients while those drugs are being studied for approval. We support the use of expanded access, which provides access to treatments for patients with serious or immediately life-threatening diseases or conditions, while preserving important protections for those patients. GW Pharmaceuticals, the maker of Epidiolex, has publicly announced that there are over 300 patients being treated through this program, including many pediatric patients with seizure disorders.

You indicated in your letter that, under current regulations, where a researcher who is in the midst of an ongoing study seeks to increase the quantity of the Schedule I controlled substance being used for the research, the researcher must submit to DEA a new request that "essentially [puts the researcher] back to square one." It is important to clarify that the procedure in these circumstances, as required under 21 C.F.R. § 1301.18(c) and (d), only requires the researcher to provide to DEA notice of the additional quantities of controlled substances that the registrant wishes to procure. "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.*

However, if the researcher plans to deviate from the previously approved research protocol (other than quantity of controlled substance), the researcher must submit to DEA a supplemental protocol for approval. Consistent with Federal law, DEA forwards this additional documentation to HHS for approval. This review is important, particularly with respect to research with Schedule I controlled substances 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.

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 mater.

Sincerely,



Peter J. Kadzik
Assistant Attorney General