



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

The Honorable Mark E. Souder
Chairman
Subcommittee on Criminal Justice,
Drug Policy, and Human Resources
Committee on Government Reform
House of Representatives
Washington, D.C. 20515-6143

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Dear Mr. Chairman:

Thank you for the letter of April 12, 2004, containing follow-up questions from the April 1, 2004, hearing entitled, "Marijuana and Medicine: The Need for A Science-Based Approach." We have restated your questions below with our response for the record.

1. Legislation has been introduced in Congress to allow states to bypass the FDA process and allow marijuana to be promoted and sold as a medical therapy – without being proven to be safe and effective as required by federal law. Do you believe patients are well served by such political efforts or is the health of patients and the public best served when science is used by the FDA to demonstrate the safety and effectiveness of all drugs including marijuana?

The Food and Drug Administration (FDA or the Agency) believes that all drugs considered for medical use, including marijuana, should be proven safe and effective for their intended indication(s). The Federal Food, Drug, and Cosmetic (FD&C) Act requires that new drugs be shown to be safe and effective for their intended use before being marketed in this country. This statutory provision affords patients the most effective protection against untested and unproven products. FDA's drug approval process requires well-controlled clinical trials that provide the necessary scientific data upon which FDA makes its approval decisions. The disciplined, systematic, scientific conduct of such trials is the best means of obtaining the data documenting the safe and effective use of a drug so that it will have the most beneficial effect.

2. If pharmaceutical companies wished to bring new or even existing medical product to market and chose to bypass the FDA approval process by using ballot initiatives or state legislative approval, would the FDA take any action? If so, what would the Agency do? For example, if a company tried to pass a state referendum allowing oxycodones or hydrocodones to be "recommended" by a doctor for any condition whatsoever, would the FDA take action? If so, what action would the agency take?

The type of state laws you discuss would not change either the Federal prohibition on the sale of an unapproved new drug under the FD&C Act or the restrictions placed on a controlled substance under the Controlled Substances Act (CSA). FDA is the sole governmental agency that approves drug products as safe and effective for particular indications, and efforts that seek to bypass the FDA drug approval process would not serve the interests of public health. Physician recommendations of approved prescription drug products for indications other than those indications approved by FDA (off-label use) are generally considered to be within the scope of the practice of medicine by FDA and are not regulated by the Agency.

Currently, there are FDA approved oxycodone and hydrocodone products available by prescription for specific indications. If a company promotes their drug for an off-label use, FDA will review the materials related to the promotion and can take action under certain conditions. Merely sponsoring or supporting a referendum, however, is not likely to lead to a violation of the FD&C Act.

3. As a result of the public campaigns of pro-marijuana activists, many Americans erroneously believe that smoking marijuana is a legitimate medical treatment. The FDA was established – and is funded by Congress – to ensure that such confusion does not exist. Will the FDA now consider issuing warning letters to all states and localities that have attempted to approve “medicinal” marijuana use, and to all sellers of “medical” marijuana, explaining that botanical marijuana has not been approved by the FDA for medical use and cannot be advertised as such? Will it consider imposing penalties, as appropriate, on those that continue to illegally promote this dangerous drug as medicine?

The Department of Health and Human Services (HHS) does not support the availability of marijuana for medical use as it has not been proven safe and effective as required by Federal law. In 2001, HHS completed an extensive analysis in response to a request to reschedule marijuana to a less restrictive schedule. After looking at all the relevant data on marijuana, HHS concluded that the weight of the scientific evidence supported the findings that marijuana should continue to be scheduled as Schedule I because it has a high potential for abuse, no currently accepted medical use in the United States, and a lack of accepted evidence about the safety of using marijuana under medical supervision.

As a Department, HHS has been actively involved in the Administration’s effort to educate Americans about the status and dangers of marijuana. FDA is committed to working in cooperation with the Office of National Drug Control Policy (ONDCP), the Drug Enforcement Administration (DEA), the National Institute on Drug Abuse (NIDA), and the Substance Abuse and Mental Health Services Administration (SAMHSA) to inform the public about the dangers of marijuana and that it is not approved for any medical use.

One very successful education campaign that warns against marijuana use is provided by HHS’ NIDA. NIDA has a very comprehensive website (at: www.marijuana-info.org) that includes specific information about the effects of marijuana on health. The information details the physical and neurological effects of marijuana on the brain, lungs, heart and immune responses. There is also information about the effects of marijuana use on pregnancy, learning, social behavior, genetic makeup and the potential for addiction. NIDA is also actively involved in

research on marijuana and in March 2004 published the Marijuana Research and Dissemination Update detailing the research efforts of the institute. FDA works with NIDA and actively reviews all investigational new drug (IND) applications for marijuana. FDA's role is to ensure that the research is conducted in accordance with regulatory requirements of the FD&C Act. HHS' SAMHSA works to bring effective substance abuse prevention to every community nationwide. SAMHSA's Center for Substance Abuse Prevention supports the National Clearing House for Alcohol and Drug Information, the largest Federal source of information about substance abuse research, treatment, and prevention available to the public. SAMHSA is also actively engaged in substance abuse treatment through the promotion of high-quality and available community-based substance abuse treatment services for individuals and families who need them. SAMHSA is on the frontlines in helping programs to treat individuals with addictions to alcohol and drugs, including marijuana.

For the reasons explained below, FDA believes that DEA is the more appropriate agency to continue to lead in taking action against entities that appear to be violating the law by illegally using or distributing marijuana. Under some circumstances, the sale of marijuana would violate both the FD&C Act and the CSA. However, there are considerably more elements to prove to bring an enforcement action under the FD&C Act than under the CSA. To bring a case under the FD&C Act, FDA would need to gather evidence that the marijuana was a drug within the meaning of the FD&C Act. To do so, FDA would have to prove that under the specific facts of the case, it was intended to cure, mitigate, or treat a disease or to affect the structure or function of the body of man. In addition, FDA would need evidence that the marijuana was received or distributed in interstate commerce. FDA would also need either labeling associated with the marijuana sufficient to prove that the marijuana is a new drug or proof that the marijuana is adulterated or misbranded under the FD&C Act.

In addition, the penalties are more significant under the CSA. Assuming FDA was able to prove the elements mentioned above and brought a criminal action against a seller of marijuana who believed that marijuana is effective for medical use, the offense would be a misdemeanor unless there was evidence that the seller either took steps to evade detection by FDA or another government agency or somehow defrauded his or her customers. By contrast, a violation of the CSA related to the sale of marijuana requires fewer elements of proof and would be a felony subject to much higher penalties than those available under the FD&C Act.

We also note that warning letters are a specific regulatory tool sent by FDA when we have evidence that a violation of the FD&C Act has occurred. These letters require corrective action on the part of the recipient and if attempts at corrective action fail to remedy the FD&C Act violation, further enforcement action is pursued.

DEA is the lead Federal agency responsible for enforcing restrictions placed on the sale, distribution and possession of controlled substances under the CSA. DEA has the authority, expertise, and resources to interdict the illegal use of controlled substances and the CSA provides greater penalties and requires proof of far fewer elements to establish a violation. However, FDA still works cooperatively with DEA when necessary on any investigative or enforcement matters that may be appropriate under the CSA and the FD&C Act. For example, FDA's Office of Criminal Investigations (OCI) is responsible for managing and conducting the Agency's criminal

investigations. As a part of its duties, OCI works closely with DEA on criminal investigations involving the illegal sale, use, and diversion of controlled substances including controlled substances sold over the Internet. OCI and DEA have worked together to utilize the full range of regulatory and administrative tools available to them to pursue cases involving controlled substances.

The primary responsibility for implementing the CSA, however, resides with DEA, and FDA generally defers to DEA on criminal enforcement efforts related to violations of the CSA involving Schedule I controlled substances. FDA has not taken independent criminal enforcement action related to the sale, promotion, or marketing of botanical marijuana as medicine. FDA has worked closely with the Department of Justice and DEA on certain legal actions involving marijuana. These cases include Kuromiya v. United States, 37 F. Supp. 2d 717 and 78 F. Supp. 2d 367 (E.D. PA 1999) in which the plaintiffs sought access to marijuana for medical use and the government explained the importance of the drug approval process and the fact that marijuana has not been proven safe and effective for medical use and United States v. Oakland Cannabis Buyers' Cooperative, 532 U.S. 483 (2001), in which the Supreme Court ruled that there was no medical necessity defense to the CSA prohibitions on manufacture and distribution of marijuana. The government briefs in the case clearly spelled out the importance of FDA's drug approval process in making safe and effective medications available to the public.

It is a more efficient use of government resources to allow the agency that has more expertise and stronger penalties for violations of law involving controlled substances to take the lead in such cases. FDA believes that DEA is the more appropriate agency to handle enforcement matters involving Schedule I controlled substances and NIDA and SAMHSA, working through its state partners, are the appropriate HHS component to continue its work educating and informing the public of the health implications of marijuana use. FDA will continue its primary responsibility to review and monitor clinical trials investigating marijuana for medical uses under the IND provisions of the FD&C Act, and will continue to work with DEA, ONDCP, and NIDA to continue to inform the public that marijuana has not been proven effective for any indication.

4. According to a September 25, 2003, letter to this Subcommittee, the FDA stated, "Evaluation indicates that sound scientific studies supporting the claims of marijuana's usefulness are lacking." The FDA letter further states that, "there is some concern that the use of smoked marijuana may be harmful to individuals suffering from the conditions for which it is touted as a safe and effective treatment." The letter also noted, "botanical marijuana has not been approved by the Food and Drug Administration as a safe and effective drug. Will the FDA consider issuing a clear statement to the public clearly stating that smoked marijuana has not been proven to be useful as medicine and may actually be harmful? Will the FDA undertake a public educational and awareness campaign on this subject, similar to those it has undertaken for obesity and herbal supplements?"

FDA's April 1, 2004, Statement to this Committee, which can be found on FDA's website, <http://www.fda.gov/ola/2004/marijuana0401.html>, clearly states that FDA has not approved marijuana for medical use in the U.S. From the perspective of Federal law, there currently is no medical marijuana. Above, we highlighted several other forums where HHS agencies have publicly posted information on marijuana's abuse potential, health effects, and status as an

unapproved drug. As noted previously, marijuana is a Schedule I drug and Schedule I substances are defined as having a very high potential for abuse, no accepted medical use in the U.S., and lacking accepted safety data for use under medical supervision. Nevertheless, Schedule I substances can still be the subject of an IND under the FD&C Act, although the conditions for their use are more restrictive. As noted in our statement, there has been considerable interest in the use of marijuana for the treatment of a number of conditions, including glaucoma, AIDS wasting, neuropathic pain, treatment of spasticity associated with multiple sclerosis, and chemotherapy-induced nausea.

HHS and FDA support the medical research community, which intends to and is currently studying marijuana in scientifically valid and well-controlled clinical trials as part of FDA's drug approval process. These clinical trials are the foundation of an objective, science-based approach to evaluating the merits of marijuana for medicinal purposes. Also, as detailed in the response to Question 3, NIDA and SAMHSA, two other components of HHS, are actively involved in a public and educational awareness campaign on the health effects of marijuana use. While there are no proven benefits from marijuana use, there are many short and long-term risks associated with marijuana use. FDA has not approved any drugs for which the preferred form of administration is smoking.

FDA has been involved in both the obesity and herbal supplement campaigns based on FDA's jurisdictional responsibilities. While HHS is the primary sponsor of the obesity educational campaign, FDA has been active in this area based on its statutory responsibility for nutritional labeling. In March 2004, FDA issued a report outlining its action plan on obesity, as part of HHS' comprehensive strategy for combating the epidemic of obesity in the U.S. The report by FDA's Obesity Working Group is focused on providing consumers with accurate, helpful information that allows them to make wise food choices at home, at supermarkets and in restaurants; such nutrition information is within FDA's statutory authority and scientific and regulatory expertise. For example, the report includes recommendations to strengthen food labeling, to educate consumers about using nutritional information to maintain a healthy diet and weight, and to encourage restaurants to provide calorie and nutrition information. It recommends increasing enforcement to ensure food labels accurately portray serving size. The report also recommended revising and reissuing an FDA draft Guidance for the Clinical Evaluation of Weight-Control Drugs and strengthening the coordination of research into obesity and the development of foods that are healthier and lower in calories with other HHS agencies, the U.S. Department of Agriculture, and other public and private sector partners.

FDA's work regarding dietary supplements likewise stems from its primary jurisdiction over the regulation of these products under the Dietary Supplement Health and Education Act of 1994 (DSHEA). Under responsibilities imposed by DSHEA, FDA has conducted a number of public education campaigns on dietary supplements.

FDA regulates smoked marijuana, a botanical product, when it is being investigated for use in the diagnosis, cure, mitigation, treatment or prevention of disease in man or other animals, as a drug, under the FD&C Act. Under the FD&C Act, FDA's primary role is to review and monitor objective data collected in adequate and well-controlled clinical trials regarding the potential merits of marijuana for medical uses.

We do cooperate in many arenas with DEA and with ONDCP on matters that are connected to FDA's jurisdiction. As you may know, on March 1, 2004, the Administration announced a coordinated drug strategy to confront the illegal diversion and abuse of prescription drugs. Director of the White House Office for National Drug Control Policy, John Walters, then-FDA Commissioner Dr. Mark McClellan, DEA Administrator Karen Tandy, Surgeon General Dr. Richard Carmona, and Chairman Tom Davis, Committee on Government Reform, joined together to release the President's National Drug Control Strategy, which outlines the extent of prescription drug abuse in the U.S. and new Federal programs designed to address the problem. FDA will participate in this coordinated program. In addition, FDA directs readers to the NIDA website for information on teens and marijuana:
<http://www.fda.gov/oc/opacom/kids/html/7teens.htm>.

5. The L.A. Times recently reported that researchers are studying the potential uses of nicotine or its derivatives as medicine. If a cigarette manufacturer began claiming in its advertising that cigarettes could be used as treatment for certain medical conditions – such as obesity or attention deficit disorder (ADD) – would the FDA take action? If so, what action would it take?

If a manufacturer were to market a tobacco product for treatment of the conditions you cite -- obesity or attention deficit disorder -- those product claims would render the tobacco product a drug within the meaning of section 201(g) of the FD&C Act. Whether FDA would take action to regulate such a product as an unapproved new drug depends on a variety of factors, and FDA generally makes enforcement decisions on a case-by-case basis.

In general, FDA employs a risk-based enforcement approach with respect to marketed unapproved drugs. This approach includes efforts to identify illegally marketed drugs, prioritization of those drugs according to potential public health concerns or other impacts on the public health, and subsequent regulatory follow-up. Some of the specific actions the Agency has taken have been precipitated by evidence of safety or effectiveness problems that has either come to our attention during inspections or was brought to our attention by outside sources. FDA has issued a draft Compliance Policy Guide (<http://www.fda.gov/cder/guidance/5704dft.pdf>) for comment that provides the Agency's current thinking on its enforcement policies for unapproved drugs. Scarce resources prevent the Agency from taking many legally supportable actions against products that meet the legal definition of unapproved drugs. The particular example above differs from physician recommendation of marijuana in several important respects. First, the drug product identified is not a controlled substance, much less one designated as Schedule I, which Congress has defined as the top enforcement priority for DEA under the CSA. Second, the example involves a direct connection between the sale and promotional activities, which is generally a necessary prerequisite to trigger drug approval requirements. Third, the example implies a large-scale manufacturing and promotional enterprise that would not usually raise jurisdictional questions involving interstate commerce.

6. In a letter to this Subcommittee dated March 31, 2004, the FDA says it has not taken a strong role in discouraging the promotion of marijuana as medicine because it is the agency's practice to refer "matters involving controlled substances" to the DEA. Just last week, the FDA issued new regulations on generic versions of oxycodones, which is a

controlled substance. Please explain why FDA has chosen to regulate one controlled substance – oxycodone – while failing to regulate another, namely marijuana?

FDA's primary mission as defined in the FD&C Act is to help ensure that only safe and effective medical products, including drugs, are marketed in the U.S. The Agency carries out this mission by administering the regulatory system under which drugs are evaluated, and determining when drugs have been shown to be safe and effective for their intended use. FDA's regulatory authority is usually triggered when a manufacturer submits an application either to study or to market a drug, including a drug scheduled as a controlled substance under the CSA. Thus, FDA regulates the controlled substance oxycodone because manufacturers submitted applications to FDA for approval of this drug for marketing for a medical use under the FD&C Act. FDA's recent action on oxycodone was a result of the submission of a number of applications to market generic versions of the drug. The FD&C Act requires the Agency to approve generic applications once all statutory requirements are met. FDA is also regulating marijuana because sponsors have submitted IND applications to study marijuana for a variety of medical uses. FDA would take appropriate regulatory actions with respect to approval of marijuana if FDA received an application to review for the approval of that drug.

As noted previously, FDA regulates controlled substances when applications are submitted to the Agency seeking approval for their study or marketing. In addition, the CSA gives HHS a role in determining the proper scheduling of a substance. When questions arise regarding the sale, distribution, or possession of marijuana as a Schedule I controlled substance, then the provisions of the CSA are triggered and DEA has primary authority to take action under that statute. As discussed above, enforcement actions are deferred to DEA because that Federal agency is best suited to enforce the CSA particularly when the substance at issue is a Schedule I controlled substance.

7. The Washington Post reported this morning that the FDA has begun to regulate health claims for walnuts. Similar health claims for other nuts are being reviewed by the FDA. Yesterday, another report appeared indicating that FDA will begin "scrutinizing" ultrasound imaging of unborn children, despite any real record of negative health effects. Why does FDA have the time and resources to review health claims of nuts and to scrutinize ultrasound but not to review the health claims of marijuana?

Under the FD&C Act, FDA is the primary Federal agency tasked with regulating radiological health and food, other than certain meat, poultry, and egg products. FDA is the primary agency tasked with the review of pending INDs evaluating botanical marijuana for the treatment of various conditions. As long as marijuana is a Schedule I controlled substance, FDA will defer to DEA on enforcement actions related to the illegal distribution or manufacture of marijuana. FDA is committed to working with the ONDCP, DEA, and NIDA to convey to the public the Administration's position on the use of marijuana.

8. In your testimony, you state that FDA defers to DEA to take the lead in regulating controlled substances like marijuana. This feeds a perception in the pro-marijuana movement and in the public at large, however, that the federal government is only interested in the law enforcement problems of marijuana – not the medical or health problems created

by marijuana. Wouldn't you agree that it's about time for the FDA to provide some assistance to DEA to avoid creating that misconception?

As discussed in the above responses, FDA has provided assistance to DEA in certain legal actions as well as investigations. More importantly, two other HHS component, NIDA and SAMHSA, have primary responsibility for educational and public awareness efforts related to the health effects of marijuana use. These efforts complement the efforts of ONDCP and DEA with respect to marijuana use. FDA has also made a number of public statements, including through congressional testimony, that marijuana has not been approved by the Agency as safe and effective for any medical use and that its use may be harmful to health. These statements are posted on FDA's website, www.fda.gov. Further, FDA will actively cooperate with the ONDCP, DEA, and NIDA in alerting the public about the current status of marijuana.

9. We are very puzzled about how silent FDA has been in the face of state laws that bypass FDA regulations and permit marijuana to be used for "medical" purposes. If the FDA continues to do so little, this will encourage other special interest groups to seek similar state laws for other popular drugs. It appears to us that this will not just undermine FDA's authority – it will destroy it. Is FDA at all concerned about this trend? What, if anything, will FDA do to counteract it?

FDA has not been silent in these matters. FDA has worked closely with DEA and has provided active assistance, when it has been requested, in certain legal cases and investigations involving the illegal use of marijuana. FDA's authority has not been affected or pre-empted by these state actions. Approval of marijuana as a drug for specific medical indications still remains within the purview of FDA. Several states have passed referenda making marijuana available for a variety of medical conditions, but these laws are in conflict with the CSA and often with the FD&C Act. Our position continues to be that these ballot measures send the wrong message to the public– too many of whom do not recognize the dangers of marijuana – and that these measures are inconsistent with our efforts to ensure that approved medications have undergone rigorous scientific scrutiny and FDA's approval process.

FDA will continue to state, as it did in its Congressional testimony, that marijuana is not an approved drug and that only the disciplined, systematic, scientific conduct of clinical trials can establish whether there is any medicinal value to marijuana, smoked or otherwise. As with other efforts attempting to pre-empt FDA's authority, FDA will evaluate and address the effort in accordance with its priorities and in the most efficient use of limited government resources. In this circumstance, in which the primary jurisdiction of a Schedule I controlled substance, a substance with no approved medical use, rests with DEA, and for which there are significant criminal penalties and easier elements of proof under DEA's jurisdiction, FDA will continue to defer to DEA for appropriate enforcement action.

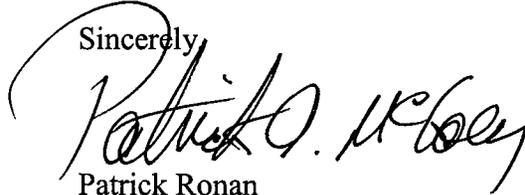
FDA will work with the ONDCP, DEA, and NIDA to convey to the public the Administration's position on the use of marijuana. 1) FDA has not approved marijuana for any indication, 2) DHHS' current evaluation indicates that sound scientific studies sufficient to support claims of marijuana's usefulness as a medication are lacking, despite anecdotal claims to the contrary, and

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3) there is a lack of accepted safety for use of smoked marijuana, the known risks of which are not outweighed by any potential benefits.

Thank you again for contacting us concerning this matter. FDA appreciates the opportunity to testify before the Subcommittee. Please let us know if there are further questions.

Sincerely,



Patrick Ronan
Assistant Commissioner
for Legislation



cc. DEA
NIDA
SAMHSA