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United States Senate

September 29, 2016

VIA ELECTRONIC TRANSMISSION
The Honorable Charles P. Rosenberg
Acting Administrator
U.S. Drug Enforcement Administration
8701 Morrissette Drive
Springfield, VA 22152

Dear Acting Administrator Rosenberg:

We write with concern about your agency's proposed regulatory action to place mitragynine and 7-hyroxymitagynine, key constituents of the kratom plant, into Schedule I of the Controlled Substances Act (CSA) without undertaking a robust process of stakeholder input and discussion of medical, public safety, and scientific considerations. Specifically, we would like the Drug Enforcement Administration (DEA) to delay its scheduling decision on kratom, and extend the public comment period for stakeholders to weigh in on this proposed regulatory action.

On August 31, 2016, the DEA posted notice in the Federal Register that it was going to place kratom into Schedule I within 30 days. We are concerned that the 30-day comment period for such a proposed regulatory action is not a sufficient amount of time for public comment on a drug that, according to recent scientific studies, may actually be an effective substance to help combat the opioid epidemic. While we understand there are times when public safety demands that your agency act quickly on scheduling decisions, we believe that in this instance additional time for the scientific community, public health officials, and other members of the public to comment is warranted and may prove to be in the interest of public health and safety.

As you know, Schedule I of the CSA is reserved for substances that have a high potential for abuse and that have no currently accepted medical use. An increasing body of research has shown kratom's potential value as a treatment for a number of conditions. On September 2, 2016, eleven scientists from well-respected research institutions in the U.S. wrote an open letter to Congress expressing "grave concern" about the agency's proposed action and expressed their opposition to any efforts to designate kratom as a Schedule I controlled substance of the CSA.[1] In their letter, the scientists wrote:

> [T]here are a significant number of individuals using kratom as a treatment for numerous medical conditions, including chronic pain, depression, and weaning addictions to other, more dangerous opioids. Although instances of self-medication are concerning to us in the medical community, the majority of such patients so far report that they achieve therapeutic benefits with few side effects, while occurrences of serious abuse or dependence remain infrequent.

[1] Letter attached from Andrew C. Kruegel, PhD, et al., to Congress (Sept. 2, 2016).

Given that we are in the midst of a drug crisis and there is promising evidence of kratom's potential medical benefits, including the possibility of new, safer medications for the treatment of pain, we believe that placing kratom in Schedule I without adequate time for experts to weigh in via public comment may have unintended consequences.

Furthermore, since 1980, our federal prison population has exploded by nearly 800 percent. This increase is a result of draconian drug policies that continue to place nonviolent drug offenders behind bars. We should not, in haste and without adequate opportunity for comment and analysis, place substances in categories that may be inconsistent with their medical value and potential for abuse.

We believe that your agency can more fully engage consumers, researchers, and other stakeholders in the well-established protocol for significant matters such as this one. Thank you for your prompt attention.

Sincerely,

Cory A. Booker
United States Senator

Kirsten E. Gillibrand
United States Senator

Ron Wyden
United States Senator

September 2nd, 2016

We are writing to express the grave concern of some of us in the scientific community regarding the just-announced Drug Enforcement Administration proposal to place key constituents of the kratom plant, mitragynine and 7-hydroxymitragynine, into Schedule 1 of the Controlled Substances Act. Our laboratories at Columbia University, Memorial Sloan Kettering Cancer Center, and partner institutions are currently engaged in extensive research efforts involving these natural compounds, their synthetic analogs, and other opioid modulators, which we feel will be jeopardized by a prohibition. We seek to understand the actions of this unique molecular class in both cells and animals, and to better evaluate its potential as a starting point for developing new medications. Ultimately, we believe mitragynine analogs may serve as new painkillers that eliminate many of the dangers associated with those opioid analgesics in current use (e.g. morphine and oxycodone).

Research in cells and animals, both in our laboratories and those of others, is consistent with an enhanced safety profile for mitragynine and its analogs. Due to unique properties of their molecular signaling (Kruegel *et al. JACS*, 2016) in the brain, several compounds in this class are effective pain relievers but induce limited respiratory depression in animals; an important point considering that respiratory failure is the key cause of death from opioid overdose. Another semi-synthetic analog in this series also exhibits greatly attenuated tolerance, dependence, and abuse potential in animal models (Váradi *et al. J Med Chem*, 2016). Further, a synthetic drug with similar molecular signaling properties, oliceridine (TRV130), is currently in Phase 3 clinical development and has demonstrated improved respiratory safety in humans, thus exemplifying the clinical potential of mitragynine analogs. **The kratom alkaloids therefore represent a major and unique opportunity to address the opioid crisis that is currently sweeping our nation, through the development of new, safer drugs for pain.**

Hundreds of years of human use worldwide further suggest, albeit in an anecdotal manner, that kratom is typically safe, with no substantiated fatal overdoses from kratom plant consumption alone (in contrast to >18,000 deaths per year from prescription opioids and >10,000 from heroin). In fact, there are a significant number of individuals using kratom as a treatment for numerous medical conditions, including chronic pain, depression, and weaning addictions to other, more dangerous opioids. Although instances of self-medication are concerning to us in the medical community, the majority of such patients so far report that they achieve therapeutic benefits with few side effects, while occurrences of serious abuse or dependence remain infrequent.

In sum, we are strongly opposed to any scheduling efforts directed towards the control of kratom or its molecular constituents at the present time. Although the availability of novel opioid modulators certainly represents a point of concern, there is currently no strong evidence to suggest that kratom use poses a major threat to public health or safety. In fact, the available data instead speaks to a favorable safety profile compared to other drugs in the opioid class. Furthermore, much more research is needed to establish any potential risks associated with use of kratom by the public and to evaluate the medicinal potential of mitragynine and its analogs; work which will be challenging in a prohibition environment. **Placing these compounds into Schedule 1 will erect an enormous barrier to scientific research in this field and will dramatically curtail our work with this exciting plant. Thus, an outright ban of kratom is not the scientific choice at present.**

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