MINNESOTA BOARD OF PHARMACY

Report to the Legislature on Changes the Board Proposes to Make to the Controlled Substance Schedules Maintained by the Board in Minnesota Rules. (In compliance with Minnesota Statutes Section 152.02, Subd. 12)

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COST OF REPORT

Minnesota Statutes §3.197 states that a "report to the legislature must contain, at the beginning of the report, the cost of preparing the report, including any costs incurred by another agency or another level of government". The estimated cost of preparing this report was **$150.00**. That is the approximate value, in terms of salary and benefits, of the time that Board staff spent preparing the report.

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Introduction

The Board of Pharmacy (Board) is submitting this report to the Legislature in compliance with Minnesota Statutes §152.02, subdivision 12. That section states, in part:

> "The state Board of Pharmacy shall annually submit a report to the legislature on or before December 1 that specifies what changes the board made to the controlled substance schedules maintained by the board in Minnesota Rules, parts 6800.4210 to 6800.4250, in the preceding 12 months. The report must include specific recommendations for amending the controlled substance schedules contained in subdivisions 2 to 6, so that they conform with the controlled substance schedules maintained by the board in Minnesota Rules, parts 6800.4210 to 6800.4250."

The Board has not made any changes to the controlled substance schedules found in Minnesota Rules Chapter 6800 during calendar year 2016. However, the Board is in the process of using the expedited rule-making authority granted to it under Minn. Stats §152.02, subd. 8b to add additional substances to Schedule I, specifically synthetic or 'designer" drugs. This report outlines those changes and it makes recommendations to the Legislature for changes to MN Stats. §152.02. Finally, it includes a discussion of kratom, a plant native to Southeast Asia that is being increasingly abused in Minnesota.

Addition of Opioids and Hallucinogens to Schedule I

The Board proposes to place additional substances into Schedule I after finding that they have high potential for abuse, no currently accepted medical use in the United States, a lack of accepted safety for use under medical supervision, and known adverse health effects. Some of these substances have also been added to the federal Schedule I. The Minnesota Bureau of Criminal Apprehension and local law enforcement agencies have notified the Board that some of these substances are available for purchase within Minnesota. All of these substances are available for purchase, by Minnesota residents, from businesses that operate Internet Web sites.

The Board recommends that the Legislature amend MN Stats. §152.02, subd. 2 to add these substances to Schedule I:

- Paragraph (b) – opiates
  - 3,4-dichloro-N-[(1R,2R)-2-(dimethylamino)cyclohexyl]-N-methylbenzamide (U47700)
  - N-phenyl-N-[1-(2-phenylethyl)piperidin-4-yl]furan-2-carboxamide (furanylfentanyl)
- Paragraph (d) – hallucinogens
  - 3-(2-Ethyl(methyl)aminoethyl)-1H-indol-4-yl (4-AcO-MET)
  - 2-Phenyl-2-(methylamino)cyclohexanone (deschloroketamine)

Board staff will draft proposed legislation to address the recommendations listed above and submit it to the Office of The Revisor of Statutes to be prepared for introduction during the 2017 Session.

Information concerning kratom

<u>Background</u>

Kratom, (Mitragyna speciosa korth), is a tropical tree that is in the same family as the coffee tree. It is indigenous to Southeast Asia, where it has been used by the inhabitants as an herbal drug. Kratom has been mostly used as a stimulant by laborers and farmers to deal with the burdens of hard work. The leaves are chewed to boost energy and provide relief from muscle aches and strains. Since kratom can activate opioid receptors at higher doses, it is

also used as a substitute for opium when that drug is not available. In fact, kratom has been used by chronic opioid users to manage opioid withdrawal symptoms.

Kratom appears to produce both stimulant and sedative effects, depending on the dose. At low doses, it produces stimulant effects, such as increased alertness, physical energy, talkativeness and sociable behavior. At high doses it produces opioid-like sedative and euphoric effects. Effects occur within 5 to 10 minutes after ingestion and last for 2 to 5 hours. Acute side effects include nausea, itching, sweating, dry mouth, constipation, increased urination, and loss of appetite. Long-term use of kratom can cause anorexia, weight loss, insomnia, skin darkening, dry mouth, frequent urination, and constipation. Several cases of kratom-induced psychosis have also been reported, with kratom addicts exhibiting symptoms such as hallucinations, delusions and confusion. Kratom consumption can lead to addiction. A withdrawal syndrome has been observed, consisting of symptoms of hostility, aggression, emotional lability, wet nose, achy muscles and bones, and jerky movement of the limbs.

In 1943, the Thai government made planting of the tree illegal and, in 1979, placed kratom (along with marijuana) in Category V of a five category classification of narcotics. Nevertheless, kratom remains a popular drug in Thailand.

In the United States, kratom is widely promoted as a legal psychoactive substance. It can be purchased from Internet Web sites. (A Google search of the phrase "kratom products" yielded 36,700 hits). Forms of kratom available through the Internet include leaves (whole or crushed), powder, extract, encapsulated powder, and extract resin "pies". Seeds and whole trees are also available from some vendors. "Herbal dietary supplements" that contain extracts of Kratom are also available for purchase from health food and nutritional supplement stores. A wide variety of health claims are made by the sellers of kratom (e.g. lowered blood pressure, relief of depression and anxiety, weight loss and enhancement of sexual performance). However, none of these claims has been substantiated by well-designed scientific studies or clinical trials. Neither kratom nor its primary active ingredient (mitragynine) have been approved by the U.S. Food and Drug Administration for medical use.

The United States Centers for Disease Control published an article titled "Kratom (Mitragyna speciosa) Exposures Reported to Poison Centers — United States, 2010–2015" in the Jul7 29, 2016 edition of *Morbidity and Mortality Weekly Report.* According to this article "(d)uring the study period, U.S. poison centers received 660 calls about reported exposure to kratom. The number of calls increased tenfold from 26 in 2010 to 263 in 2015." The report further stated: "(m)edical outcomes associated with kratom exposure were reported as minor (minimal signs or symptoms, which resolved rapidly with no residual disability) for 162 (24.5%) exposures, moderate (non-life threatening, with no residual disability, but requiring some form of treatment) for 275 (41.7%) exposures, and major (life-threatening signs or symptoms, with some residual disability) for 49 (7.4%) exposures." The report concluded: "Kratom use appears to be increasing in the United States, and the reported medical outcomes and health effects suggest an emerging public health threat. Members of the public and health care providers should be aware that the use of kratom can lead to severe adverse effects, especially when consumed in combination with alcohol or other drugs."

Minnesota Considerations

Over the past two years, several law enforcements officials have contacted the Board to express concern about the abuse of kratom. Kratom and products containing kratom extracts are being sold in tobacco shops and one law enforcement agency was contacted by a liquor store that wanted to sell kratom products. For example, it was reported to the Board that a tobacco shop in the Alexandria area was selling a product that contained either kratom or mitragynine. The product was meant to be used to make a tea. Some of the product was taken from a student of an area school by the principal.

During 2014, the Hennepin Regional Poison Center (HRPC) received calls concerning 8 exposures to kratom (six in Minnesota, two in Fargo, ND). Symptoms varied and included muscle spasms, stupor, agitation, and confusion. The individuals involved in five of the Minnesota cases received care in an emergency department. For the first half of 2015, HRPC received 20 calls related to kratom exposure, including calls involving individuals who had symptoms of addiction and withdrawal. The Board is also aware of one case involving a health care professional who became addicted to kratom and then started abusing opiate prescription drugs.

In June of 2015, Twin Cities television station KMSP (Fox9) reported that undercover reporters who had been sent to try to buy kratom where able to obtain it from "head shops, herbal shops, and nutrition stores." The purchased products often had no labeling or no dosage information. The KMSP report also described two suicides linked to kratom use that had occurred in Florida and Georgia.

Regulatory Information

Australia, Thailand, Burma and Malaysia have banned the sale and use of kratom. New Zealand, Finland, Denmark, Germany and Romania have not totally banned the drug but they do have legal controls in place. Wisconsin, Indiana, and Tennessee have made the sale and possession of kratom illegal through legislative action. Vermont regulates kratom by rule. Illinois prohibits kratom from being sold to or possessed by minors. Efforts to regulate kratom in some manner have also occurred in Iowa, Michigan, New Jersey, Louisiana and Oklahoma.

The U.S. Food and Drug Administration (FDA) issued Import Alert 54-15 (Detention without Physical Examination of Dietary Supplements and Bulk Dietary Ingredients that are or Contain Mitragyna Speciosa or Kratom) on December 9, 2015. The alert is that agency's current guidance to its field personnel regarding kratom and products that contain it. The alert allows field personnel to detain products that contain kratom – at least those products manufactured or distributed by certain companies. The alerts states that "FDA has seen an increase in the number of shipments of dietary supplements and bulk dietary ingredients that are, or contain kratom," and "shipments of kratom have come in a variety of forms, including capsules, whole leaves, processed leaves, leaf resins, leaf extracts, powdered leaves, and bulk liquids made of leaf extracts." Per the alert (emphasis added):

> "there does not appear to be a history of use or other evidence of safety establishing that kratom will reasonably be expected to be safe as a dietary ingredient. In fact, the scientific literature disclosed serious concerns regarding the toxicity of kratom in multiple organ systems. Consumption of kratom can lead to a number of health impacts, including respiratory depression, nervousness, agitation, aggression, sleeplessness, hallucinations, delusions, tremors, loss of libido, constipation, skin hyperpigmentation, nausea, vomiting, and severe withdrawal signs and symptoms. In the absence of a history of use or other evidence of safety establishing that kratom will reasonably be expected to be safe as a dietary ingredient, **kratom and kratom-containing dietary supplements and bulk dietary ingredients are adulterated** under section 402(f)(1)(B) of the Act [21 U.S.C. 342(f)(1)(B)], **because they contain a new dietary ingredient for which there is inadequate information to provide reasonable assurance that such ingredient does not present a significant or unreasonable risk of illness or injury**."

On August 30, 2016, the U.S. Drug Enforcement Administration (DEA) announced its "intention to place the active materials in the kratom plant into Schedule I of the Controlled Substances Act in order to avoid an imminent hazard to public safety." However, following pressure from vendors of kratom products, advocates for its use, and some members of Congress, the DEA withdrew its notice of intent on October 12, 2017. Based on the DEA's August 30th notice of intent, the Board added the active ingredients of kratom, mitragynine and 7-hydroxymitragynine, to the original draft of its proposed expedited controlled substances scheduling rule. The Board did so because Minn. Stats. §152.02, subd. 12 states, in part: "If any substance is designated, rescheduled, or deleted as a controlled substance under federal law and notice thereof is given to the state Board of Pharmacy,

the state Board of Pharmacy shall similarly control the substance under this chapter, after the expiration of 30 days from publication in the Federal Register of a final order designating a substance as a controlled substance or rescheduling or deleting a substance." Since the DEA has now withdrawn its intent to schedule these substances, the Board removed them from its proposed rules draft.

Analysis and recommendation concerning kratom

When using its authority under Minn. Stats. §152.02, subd. 8b to add a substance to Schedule I through the use of expedited rule-making, the Board must find that the substance has a high potential for abuse, has no currently accepted medical use in the United States, has a lack of accepted safety for use under medical supervision, has known adverse health effects, and is currently available for use within the state. Applying these factors to kratom, the Board finds:

- *Potential for abuse*. There is evidence that kratom and its active ingredients can be, and have been, abused. The main active ingredient in kratom acts as a stimulant in lower doses and activates opioid receptors in the brain at higher doses. Consequently, kratom can produce both euphoria and sedation, psychoactive effects that are considered desirable by individuals who abuse drugs and other substances. Many individuals have described using kratom to intentionally "get high" on Web sites such as Bluelight and Erowid. Others have posted videos on You Tube, describing their use of kratom to induce euphoria and other psychoactive effects. There is also ample evidence to indicate that the use of kratom can cause addiction. The Hennepin Regional Poison Center (HRPC) has received calls concerning individuals who have displayed signs and symptoms of addiction and withdrawal. A search of the Internet reveals many chemical dependency treatment programs that offer treatment for kratom addiction.
- *Currently accepted medical use in the United States and lack of accepted safety for use under medical supervision.* Notwithstanding the claims of kratom advocates, there is no sound scientific evidence that indicates that the benefits of using kratom, for any medical condition, outweigh the risks associated with its use. The FDA has not approved any drug product containing kratom or its active ingredient for medical use. As noted above, the FDA does not believe that kratom can even be used safely in dietary supplements.
- *Known adverse health effects.* As noted in the FDA Import Alert mentioned above: "Consumption of kratom can lead to a number of health impacts, including respiratory depression, nervousness, agitation, aggression, sleeplessness, hallucinations, delusions, tremors, loss of libido, constipation, skin hyperpigmentation, nausea, vomiting, and severe withdrawal signs and symptoms."
- *Currently available for use within the state.* Kratom and products that contain its active ingredient can be purchased by Minnesotans from a large number of Internet Web sites. In addition, the undercover investigation conducted by KMSP reporters revealed that such products can be purchased from head shops, herbal shops and nutrition stores in the Twin Cities. Reports from law enforcement indicate that tobacco and, possibly, liquor stores sell kratom products.

While probably not as dangerous as drugs such as heroin or methamphetamine, kratom does appear to pose a health risk to users. It can be abused and it does cause addiction. At times, very severe adverse reactions can occur, such as respiratory depression, aggression, psychosis and severe withdrawal. There is no good evidence to suggest that kratom can be safely used for any medical condition. Consequently, the Legislature should consider either placing kratom and its main active ingredients into Schedule I or placing restrictions on the sale of kratom and its main active ingredients, such as not allowing sales to minors and barring the sale of products that are not appropriately labeled.