

United States Senate

WASHINGTON, DC 20510-4802

February 7, 2013

Dr. Margaret A. Hamburg
Food and Drug Administration
Department of Health and Human Services
10903 New Hampshire Ave
Silver Spring, Maryland 20993-0002

Dear Dr. Hamburg,

Thank you for your leadership at the Food and Drug Administration (FDA) and for working closely with my office on issues of concern to West Virginians. I am proud of the drug and medical product safety advances made by the FDA, and I firmly support efforts to promote the safety and integrity of prescription drugs, medical devices, and our food supply. One area of particular interest is FDA safeguards that will keep doctors, patients, and the public at large informed of any risks associated with prescription drugs.

Nationwide, we continue to experience a tragic increase in the number of deaths and overdoses from prescription drugs. The Office of National Drug Control Policy describes prescription drug abuse as the nation's fastest-growing drug problem, and the Centers for Disease Control and Prevention (CDC) has classified prescription drug abuse as an epidemic. West Virginia has the second highest rate of drug overdose deaths in the country, and nine out of ten of the drug related deaths in West Virginia are due to the misuse and abuse of prescription drugs, especially opioid painkillers. The over-prescription, misuse and abuse of controlled prescription drugs threatens the health and well-being of many Americans and adds unnecessary costs to the Medicaid and Medicare programs.

As methadone prescriptions for pain increase, so do methadone related fatal overdoses. According to the CDC, methadone is involved in more than 30 percent of prescription painkiller overdose deaths. Too often in West Virginia, methadone has been the leading substance found in drug related overdose deaths. Despite the FDA's warnings about the risks associated with methadone, the CDC reports that more than 4 million methadone prescriptions were written for pain in 2009 alone.

In 2006, the FDA issued an alert regarding revised labeling for methadone, which included a reduction in the starting dose for the analgesic use in opioid naïve patients to 2.5 to 10 milligrams (mg) every 8 to 12 hours. According to clinical guidelines endorsed by the American

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Pain Society and American Academy of Pain Medicine, a safe starting dose for most opioid naïve patients is 2.5 mg every 8 hours, with dose increases occurring no more frequently than weekly. While I appreciate FDA's concern for the safe use of methadone, the current labeling leaves room for frequent administration in early treatment – the very time when the risk of overdose is the greatest. In addition, the dosing recommendations do not cite any information to suggest the current labeled dosing regimen is appropriate for opioid naïve patients.

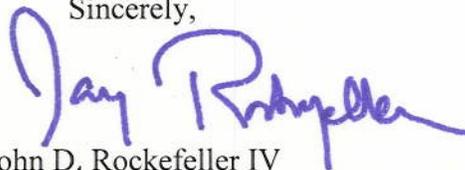
Finally, it is my understanding that the lowest dosage of methadone tablets currently available is 5 mg, although recommended starting analgesic doses are 2.5 mg. The lowest strength tablet for methadone may not be suitable for initiating treatment in many patients and may lead to higher starting doses than are necessary.

As I continue to work with the medical research, pharmaceutical, and prescribing communities to identify solutions to the prescription drug abuse epidemic, it would be very helpful for me to understand the FDA's plans to review and explain its methadone dosage recommendations for opioid naïve patients; make sure lower strength tablets that support FDA's dosage recommendations and that are suitable for gradual titration of dose are available; and communicate in a timely manner the dangers of methadone in labeling information to doctors, pharmacists and others through a "Dear Doctor" letter. Also, since many major clinical references and popular medical information websites contain dangerous information on starting doses of methadone which pose significant threats to patient safety, I would like to know what efforts the FDA can take to correct this proliferation of poor information.

Please know that I am deeply committed to this issue, and look forward to a continued dialogue with you regarding FDA's role in addressing prescription drug abuse. This problem is complicated and growing, and it will take all of us working together to change the landscape.

Thank you for taking the time to respond to this important request and for your sincere efforts to protect the public's health by providing safe and effective drugs to United States consumers. I look forward to receiving your response no later than March 15, 2013.

Sincerely,



John D. Rockefeller IV