DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

The Honorable Tim Murphy
Chairman
Subcommittee on Oversight and Investigations
Committee on Energy and Commerce
House of Representatives
Washington, D.C. 20515-6115

SEP 08 2015

Dear Mr. Chairman:

Thank you for providing the Food and Drug Administration (FDA or the Agency) with the opportunity to testify at the May 1, 2015, hearing before the Subcommittee on Oversight and Investigations, Committee on Energy and Commerce, entitled "What is the Federal Government Doing to Combat the Opioid Abuse Epidemic?" This letter is a response for the record to questions posed by certain Members of the Committee.

If you have further questions, please let us know.

Sincerely,

[redacted]

for Thomas A. Kraus
Associate Commissioner
for Legislation

cc: The Honorable Diana DeGette
Ranking Member

We have restated each Member's questions below in bold, followed by our responses.

The Honorable Michael C. Burgess

1. **While technology has the potential to solve many problems in healthcare, we are hearing similar complaints about PDMPs as we do with EHRs. Some doctors suggest that PDMPs interrupt clinical workflow. The Health IT Policy Committee sought public comment on whether EHR certification could enable and support streamlined access to PDMPs. Because PDMPs are a critical tool for patient care and clinical decision making, ONC suggested in their September 2013 report to Congress that they would explore a PDMP requirement in certification of EHRs. Can anyone speak to further discussion regarding including PDMPs as a requirement for certification of EHRs?**

I refer you to the response provided on behalf of the Department by Assistant Secretary Frank.

The Honorable Larry Buchson

1. **Can you expand a bit on your experience with Vivitrol (aka naltrexone) specifically, and how greater access could be helpful across the nation?**

Vivitrol is an extended-release formulation of naltrexone administered by intramuscular injection once a month. Naltrexone works to block opioid receptors in the brain. It blocks the effects of drugs like morphine, heroin, and other opioids. It was approved in October 2010 for the prevention of relapse to opioid dependence, following opioid detoxification, in patients addicted to opioid drugs.

An oral formulation of naltrexone, under the trade name Trexan, was approved in 1984 for its effect in blocking exogenous opioids, which was intended to support formerly opioid-dependent patients in maintaining a drug-free state. Although its pharmacologic properties are well-established, and its theoretical benefit in preventing relapse to illicit opioid use in detoxified patients is accepted, it was challenging to show that those properties translate into effective relapse prevention in the clinical setting for this oral form of naloxone, perhaps due to poor compliance. Therefore, the development of passive-compliance formulations such as implants, transdermals, and depot injections was a logical extension in the development of naltrexone for treating substance use disorder, and Vivitrol was developed with this in mind.

The safety and efficacy of Vivitrol were studied for six months, comparing Vivitrol injections every four weeks to placebo treatment in patients who had completed inpatient detoxification and who were no longer physically dependent on opioids. Patients were seen weekly for behavioral treatment and provided weekly urine samples for toxicology testing, and also provided self-reports on their illicit drug use. Although many patients did use drugs on some occasions, 36 percent of the Vivitrol-treated patients were able to stay in

treatment for the full six months without using drugs, compared to 23% in the placebo group.

This built upon evidence from a clinical pharmacology study showing that Vivitrol blocked the effects of opioids for a full month, and demonstrated that this blockade translated into clinical benefit by preventing relapses and keeping patients in treatment.

Given these data, Vivitrol represents an important addition to the pharmacologic treatment armamentarium for patients motivated to stay opioid-free after detoxification, which also includes oral naltrexone and the opioid agonist methadone and buprenorphine. Given the complexity of treating substance use disorder, these should all be used as a part of a larger treatment program, including non-pharmacologic and behavioral treatment options.

The Honorable David McKinley

1. **What one thing would you recommend that we could do to try to start reversing this epidemic and this problem?**

We are pleased that this Subcommittee is interested in finding ways that the Congress can have a positive impact on tackling this important issue.

The causes of the current opioid-use disorder epidemic and related overdose deaths in the United States are complex and include an amalgam of medical, social, and economic factors. The consequences are also far reaching, affecting the health, social, and economic welfare of individuals with opioid addiction, as well as their families and the larger community.

Unfortunately, the consensus among experts is that there is no single approach or initiative that will solve this complicated problem. Furthermore, no single organization or entity can address this problem alone; a coordinated, multifaceted response involving the Federal Government, state governments, public health officials, medical and other health partners, and community organizations is required.

Addressing this crisis is a top priority for the Department of Health and Human Services (HHS or the Department) and to do so, the Department has developed an aggressive, multi-pronged initiative that focuses on three priority areas, grounded in the best research and clinical science available, to combat opioid abuse. By leveraging the distinct strengths of the HHS agencies, HHS's three-part plan aims to:

- Improve opioid prescribing practices to address the over-prescribing of opioids;
- Expand the use of naloxone, used to treat opioid overdoses, to help reduce the number of deaths associated with opioid overdose; and
- Expand the use of Medication-assisted Treatment (MAT), a comprehensive treatment model that combines the use of medication with counseling and behavioral therapies to treat substance use disorders.

These priorities represent activities and interventions where evidence suggests that HHS has the greatest opportunity for measureable impact. FDA is working to support these goals where possible.

With regard to assuring that prescribers receive effective training on the safe uses of opioid drugs, the Secretary's initiative includes support for mandatory prescriber education on responsible opioid prescribing practices. As called for by the Administration in the 2011 Prescription Drug Abuse Prevention Plan, and re-emphasized in the 2014 National Drug Control Strategy, mandatory prescriber education is a critical component of the response to the opioid epidemic.

A first step in providing education to providers was taken by FDA through its Risk Evaluation and Mitigation Strategy for Extended-Release/Long-Acting (ER/LA) opioid analgesic products (ER/LA opioid analgesic REMS). The REMS, approved in July 2012, requires manufacturers of ER/LA opioid analgesics to make education programs available to all prescribers of ER/LA opioid analgesics, by providing educational grants to accredited continuing education (CE) providers, who, in turn, offer training to prescribers at little to no cost. These CE activities must cover the content and messages of an education blueprint developed by FDA. Although this training is an important public health measure, FDA continues to support mandatory education for prescribers. By providing effective training, we can help prescribers make better decisions about which patients will benefit from the use of opioids, and when patients could be harmed by them or could benefit from other ways to manage their pain.

The opioid abuse epidemic is a critical issue for HHS, the Administration, and the Nation as a whole, and we know we cannot solve it alone. We look forward to continuing to partner with the Congress, the states, and other stakeholders to continue to make progress on this vital issue and prevent further morbidity and mortality from opioid related overdoses.