April 19, 2018

The Honorable Lamar Alexander
Chairman
U.S. Senate Committee on Health, Education, Labor & Pensions
428 Senate Dirksen Office Building
Washington, DC 20510

RE: Input on S.2680 Opioid Crisis Response Act

Dear Senator Alexander:

We are encouraged by your concern and drive in resolving the Opioid addiction epidemic which is ruining so many lives across our country. Opioid addiction touches so many families in a horrific way. We support your inclusion of unit dose blister packaging as part of your Senate Bill 2680 whereby you are seeking to "Clarify FDA Packaging Authorities" in the amending of Section 505 of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 355-1 (e). by the addition of:

"The Secretary may require a risk evaluation mitigation strategy for a drug for which there is a serious risk of an adverse drug experience described in subparagraph (B) or (C) of subsection (b)(1), taking into consideration the factors described in subparagraphs (C) and (D) of subsection (f)(2), which may include requiring that—"(A) the drug be made available for dispensing to certain patients in unit dose packaging, packaging that provides a set duration, or other packaging system that the Secretary determines may help mitigate such serious risk; or "(B) the drug be dispensed to certain patients with a safe disposal packaging or safe disposal system for purposes of rendering unused drugs non-retrievable (as defined in section 1300.05 of title 21, Code of Federal Regulations (or any successor regulation)) if the Secretary has determines that such safe disposal packaging or system may help mitigate such serious risk and exists in sufficient quantities, in consultation with other relevant Federal agencies with authorities over drug packaging."

We would like to bring to your attention, as well as those of your committee and staff, that unit dose packaging can not only fulfill the CDC's and the FDA's recommendation on limiting initial prescriptions for acute pain with pre-packed doses, but can also address some of the concerns surrounding treating chronic care patients, who have their own set of addiction risks. Managing dose care in chronic care patients is equally important in deterring addiction.

Managing dose care in chronic care patients is equally important in deterring addiction.

According to Dr. Allen Wilson, MD PhD, who has been working in the field of opiate addiction for 30 years, "Approximately 10 to 15 percent of the population is at risk for addiction to drugs: alcohol, benzodiazepines, opiates, barbiturates and stimulants. These individuals, due to a complicated set of factors including the inherited biological response to the effects of such drugs, personality characteristics, and environmental and cultural factors, are at risk to persist in using such drugs for reasons other than the management of physical pain. This addictive potential is not deterministic – it is simply a predisposition.

Many opiate dependent individuals were introduced to these drugs to manage pain (and associated anxiety). The first dose of an opiate reduces the pain, and a dramatic reduction of anxiety quickly follows. As the analgesic effect begins to wear off toward the end of the dosing interval, mild discomfort, but not severe pain, gradually returns. This cues the patient's anxiety to increase disproportionately. The patient has at hand a simple remedy - take the next dose of analgesic before the prescribed interval has passed to reduce the anxiety. Over time, progressive shortening of the interdose interval can result in severe physical dependence and, often, addictive behaviors.

Because the interdose intervals are reduced gradually, by the time the physician or pharmacist recognizes this, the patient may be caught in the addictive cycle, using up a prescription rapidly and perhaps multiple-doctoring or buying medication on the street to avoid breakthrough pain and withdrawal symptoms. Not wanting to leave the patient to withdraw on his own, the physician may engage in this dynamic longer than is desirable, with the result that the patient may become addicted.[1] This cycle of shortened interval doses is noted not just with initial patients for acute pain but with chronic pain patients advises Dr. Wilson, Professor of Psychiatry and Head of Section of Addiction Medicine at University of Ottawa and Director of Substance Use and Concurrent Disorders Program at Royal Ottawa Hospital, as well as an HCPC member.

Utilizing unit dose packaging designed with specific time reminders for doses may help patients better understand the dangers of overdosing and taking doses prior to the regimented time. The unit dose packaging could provide risk reminders through billboard messaging, or through space on which the patient or caregiver records the dispense events directly on the package. In addition, the dispensing events could be coupled with an app that allows for scanning for each dispense event that could notify a medical professional. In addition, digital recording of dispense events via Near Field Communication (NFC) or Radio Frequency Identification (RFID) can be designed into the package for added verification.

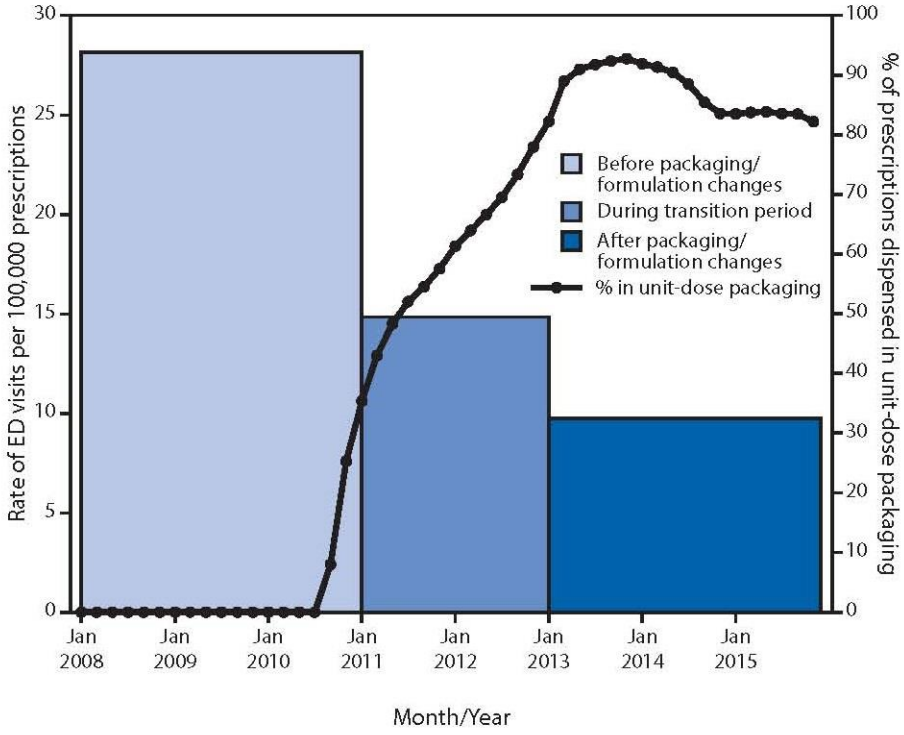
Enhancing child safety in the homes of acute/chronic care patients and patients using addiction treatment drugs

Seeking to provide limited dosing in blister packages for initial prescriptions is certainly a solution for deterring addiction in new patients. We would like to advise the Committee that current chronic care opiates in the antiquated cap and vial still leave children exposed to adverse events and overdosing. These situations exist not just with opiate analgesics but also for addiction treatment drugs. The incidence of hospitalization for prescription opioid poisonings among children and adolescents 1 to 19 years of age increased nearly twofold from 1997 to 2012, with the largest percentage increase occurring among the youngest children, aged 1 to 4 years.[2] This includes the drug Buprenorphine, which the CDC cited as the number one solid dose drug causing hospitalizations by children less than 5 years old. The CDC equated this to "For every 500 adults treated with Buprenorphine, 1 child was hospitalized from 2007 through 2011." This rate changed

[1] Risk Management System for Opioids, Dr. Allen Wilson, MD, PhD.,
[2] https://www.medpagetoday.com/painmanagement/painmanagement/61130, https://jamanetwork.com/journals/jamapediatrics/fullarticle/2571466

when the packaging for buprenorphine was changed to unit dose in 2012. There is a direct correlation to the 65% drop in Emergency Department visits and the change in delivery form. This drop is highlighted in the chart from the CDC.[3]

FIGURE. Estimated rate of emergency department (ED) visits for unsupervised buprenorphine/naloxone ingestions by children aged <6 years per 100,000 dispensed prescriptions, compared with estimates of the percentage of outpatient buprenorphine/naloxone prescriptions dispensed in unit-dose packaging — United States, 2008–2015*



* Estimates of ED visits for pediatric buprenorphine/naloxone ingestions were based on 2008–2015 data from the National Electronic Injury Surveillance System-Cooperative Adverse Drug Event Surveillance project. Estimates of dispensed prescriptions and the percentage dispensed in unit-dose packaging were based on data from the IMS Health National Prescription Audit (2008–2015). Key dates of product changes were as follows: Suboxone buprenorphine/naloxone film in unit-dose packaging available (October 2010); first generic buprenorphine/naloxone products available as tablets in multidose bottles (February 2013); Suboxone buprenorphine/naloxone tablets in multidose bottles discontinued (March 2013); first buprenorphine/naloxone tablets (Zubsolv) available in unit-dose packaging (September 2013).

In addition to protecting young children, unit dose blister packaging can protect tweens, teens and other family members who may be dissuaded from pilfering and diverting a dose for personal use because the packaging would provide an instantaneous indicator that a dose was missing.

[3] **Pediatric Emergency Department Visits for Buprenorphine/Naloxone Ingestion — United States, 2008–2015,** Budnitz, Lovegrove, Sapiano, Mathew, Kegler, Hampp, MMWR / October 21, 2016 / Vol. 65 / No. 41, https://www.cdc.gov/mmwr/volumes/65/wr/mm6541a5.htm

Unit Dose Blisters readily support the DSCSA and keep the serial number intact on the package that reaches the patient

Serialized unit dose packaging would allow better tracking of doses dispensed which would give better visibility to abusive prescribing and dispensing practices. With serialized unit dose blisters, product reaching the street could be tracked back to the patient, pharmacy and prescribing physician which means patterns of abuse would be easier to spot by law enforcement, FDA and DEA.

Serialized unit dose packaging will also aid in the roll out of the Drug Supply Chain Security Act, signed into law in November 2013, by allowing serialized packages to reach patients, ensuring them delivery of a pristine product. The patient can track the source of supply. In addition pre-packed unit dose blisters eliminate repackaging in the pharmacy which reduces the opportunity for filling errors and the introduction of counterfeit drugs.[4] The US accepted practice of bulk packaging in larger bottles (500 or 1,000 count) forces repackaging product in the pharmacy. Bulk packaging is less expensive for the pharmaceutical manufacturer, yet these same manufacturers pack in blisters everywhere else in the world.

Unit dose blister packages can reduce addition, reduce fraud and black market activity and reduce healthcare costs. We applaud the Senate HELP Committee for considering unit dose blisters as part of the solution to this terrible epidemic of opioid addiction and death.

The Healthcare Compliance Packaging Council, (www.hcpconline.org), is a non-profit trade organization comprised of pharmaceutical packaging machinery and materials manufacturers and pharmaceutical contract service companies. We would welcome an opportunity to further discuss with you and your respective staff members the benefits of unit dose packaging and how it can help to reduce healthcare spending by improving the overall health of our US citizens and improve the safety of products in the US supply chain. Our work focuses on unit dose pharmaceutical packaging that improves patient adherence and patient safety by reducing errors in pharmacy, protecting the efficacy of pharmaceuticals, ensuring child safety and enhancing supply chain security.

Sincerely,

Walt Berghahn
Executive Director
Healthcare Compliance Packaging Council

[4]https://psnet.ahrq.gov/resources/resource/28670, http://www.highlighthealth.com/healthcare/pharmacy-errors-avoid-prescription-dispensing-mistakes/