

Exploring Packaging, Storage, and Disposal Solutions to Enhance Opioid Safety

Duke-Margolis Center for Health Policy Conference Center
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Discussion Guide

Introduction

In support of the U.S Food and Drug Administration's (FDA's) efforts to reduce the growing epidemic of opioid abuse, dependence, and overdose in the United States, FDA's "Packaging: Abuse-Deterrent Strategies (PADS)" Task Force is currently exploring whether innovative packaging, storage, and disposal solutions could enhance opioid safety by preventing or deterring misuse, abuse, or inappropriate access to prescription opioids. Identifying key intervention points during opioid use is critical to developing such solutions.

In support of the FDA PADS Task Force's work, the Robert J. Margolis, MD Center for Health Policy is convening this workshop to examine data needs and guiding design principles for developing packaging, storage, and disposal solutions that have the potential to enhance opioid safety and deter misuse and abuse. Key issues to be addressed in the workshop include:

- The potential role of packaging, storage, and disposal solutions in addressing factors that enable prescription opioid abuse and misuse or inappropriate access
- The current landscape of existing packaging, storage, and disposal solutions that may prevent or deter abuse and misuse or inappropriate access of prescription opioids
- Approaches to evaluating the impact of packaging, storage, and disposal solutions to deter misuse and abuse or inappropriate access of prescription opioids
- Considerations for integrating the use of opioid safety-enhancing packaging, storage, or disposal solutions into healthcare and pharmacy systems

This workshop is funded through a cooperative agreement between the U.S. Food and Drug Administration Center for Drug Evaluation and Research (CDER) and the Duke-Margolis Center for Health Policy. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services nor does mention of trade names, commercial practices, or organizations imply endorsements by the U.S. Government.

Background

The Role of Packaging, Storage and Disposal in Enhancing Safety for Prescription Opioids

Opioid analgesics are commonly prescribed for both acute and chronic pain. Approximately 216 million opioid analgesic prescriptions were dispensed from U.S. outpatient retail pharmacies in 2016.ⁱ ⁱⁱ Access to such analgesics is essential to pain treatment and quality of life of the estimated 11.2% of the adult population experiencing chronic pain.ⁱⁱⁱ However, prescription opioids are vulnerable to misuse^{iv} and repeated use of these products is associated with an increased risk of dependence, abuse, and overdose death.^v

Fully addressing the opioid epidemic requires a comprehensive effort amongst Federal and state government, health care practitioners, and community leaders to address root causes contributing to the opioid epidemic including factors that contribute to both excess supply and illicit demand for opioids. Federal and state initiatives include efforts to improve prescribing practices, improving the availability of prescriber education resources, utilization of prescription drug monitoring programs, implementing accessible community take back programs, as well as expanding treatment for substance use disorders and access to naloxone. Given the current widespread availability of opioids, there exist significant opportunities to enhance the safety of legally prescribed opioids through mechanisms such as additional consumer education, improved safe storage and disposal practices, and enhanced packaging and storage options.

GLOSSARY	
Abuse	The nonmedical use of a drug, repeatedly or even sporadically, for the positive psychoactive effects it produces
Dependence	A state of adaptation that is manifested by a drug class specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist
Misuse	The use of a drug outside label direction or in a way other than prescribed or directed by a health care practitioner. This definition includes patients using a drug for a condition different from that for which the drug is prescribed, patients taking more drug than prescribed or at a different dosing intervals, and individuals using a drug not prescribed for them, although for therapeutic purposes

Source: Smith SM, Dart RC, Katz NP et al. J Pain 2013; 154:2287-2296.

Efforts to enhance opioid safety must take into consideration current knowledge about patterns of prescription opioid abuse, misuse, and inappropriate access. Prescription opioid misuse can occur due to a variety of factors, including accidental exposure, non-medical use, use for reward or euphoric effect, compulsive use due to substance use disorders, or other forms of misuse. Given this complexity and range of behaviors, packaging, storage, and disposal interventions may need to target one or more factors relating to prescription opioid use. Such interventions may include:

- Unit-of-use blister packaging to facilitate medication adherence or minimize inappropriate access,
- Solutions that limit unauthorized third-party access through locks or lockout features,
- Solutions that render unused substances inert to reduce the supply of unneeded medications,
- Solutions that employ track and trace technology,
- Solutions that combine multiple features to target more than one aspect of the opioid use continuum,
- Other solutions

While no solution will ever be “abuse proof,” leveraging strategies to support innovative packaging may effectively target misuse and third party access^{vi} while contributing to enhanced opioid safety for legally prescribed opioid products.

Targeting Factors that Enable Opioid Abuse, Misuse, and Unauthorized Access

Improving safe storage and disposal practices

Many prescription opioids are legally prescribed but end up in the wrong hands where they can be abused or misused.^{vii} According to the most recent data from the National Survey of Drug Use and Health (NSDUH), only 1 in 20 individuals 12 years of age and older who had misused pain relievers in the last year purchased them from a stranger, while 53.7 % obtained prescription pain relievers from a friend or relative and one-third misused a prescription from a doctor.^{viii} Given these patterns of access,

FDA is exploring whether there may be opportunities to target solutions aimed at reducing access to the household supply of unused and unwanted prescriptions.

According to a recent study of adults living in households with children, nearly 70% of prescription opioids were reported to be stored in a safe manner. However, prescription opioids were stored in a locked or latched place in only 32.6% of households with young children and 11.7% with older children.^{ix} These statistics highlight the need for more options to ensure the safe storage and disposal of unused prescriptions because young children in households with opioid prescriptions are at an increased risk of accidental exposure and overdose. The initiation of prescription opioid misuse is second only in frequency to initiation of marijuana for adolescents aged 12 to 17.^x

Varieties of initiatives on the public and private levels exist to encourage and educate patients on opioid safety and facilitate safe storage and disposal. FDA maintains a list of consumer recommendations for safely disposing of unused prescription opioids.^{xi} The Drug Enforcement Administration (DEA) supports twice-yearly Drug “Take Back” Days to provide a safe and convenient means of disposing of prescription opioids. Additionally, the *Secure and Responsible Drug Disposal Act of 2010* encouraged both public and private entities to develop an array of methods of collection and disposal in a secure, convenient, and responsible manner.^{xii} Providing consumers with adequate information and a variety of convenient, low-cost options to secure and dispose of unused and unwanted opioids may help to reduce the supply of prescriptions that may be vulnerable to misuse or third-party access, thereby reducing initiation or infrequent use that might lead to higher risk behaviors.

Enhancing compliance with prescribed opioids and reducing the risk of misuse and abuse

Various groups are exploring strategies to facilitate treatment adherence or reduce potential misuse and abuse among patients with legally prescribed opioids. Developing successful strategies to mitigate risks of developing Opioid Use Disorders (OUDs) during pain treatment regimens requires careful monitoring and communication between medical providers and patients, recognition of risk factors for developing substance use disorders, and recognizing key intervention points within the environment of opioid use. For healthcare providers treating patients for acute or chronic pain, packaging or storage solutions may be used to improve treatment by helping patients maintain prescription adherence, monitor use, and address risks related to escalating use or dependence.

Many people initiate use of opioids without developing physical dependence. However, for some users, long term use can increase tolerance to the opioid effect and can lead to physical dependence, escalating dosage and development of opioid-related substance use disorders. While no single approach or technology has the capacity to fully prevent intentional abuse of opioids, packaging and storage solutions offer another tool to support the appropriate use and ensure access to these critical prescription pain relievers. Potential technologies may be tamper-proof, control the flow of opioids, or have the capacity to assist practitioners with monitoring usage. Packaging and storage technologies must work in tandem with efforts to improve treatment of chronic pain and enhanced provider-patient communication regarding the risks of prescribed opioids.

FDA Efforts to Mitigate the Prescription Opioid Abuse and Misuse

In 2016, FDA developed an Opioid Action Plan outlining actionable steps to reduce the impact of opioid abuse on the American public. As part of this plan^{xiii}, the Agency has committed to working more closely with its advisory committees in advance of making critical product and labeling decisions; enhancing safety labeling; requiring new data from postmarketing studies; encouraging the development of abuse deterrent formulations of opioid analgesic products; and seeking to improve treatment of both

addiction and pain.^{xiv} The Agency will simultaneously re-examine the risk-benefit paradigm for opioids and ensure that the Agency considers the wider public health effects.^{xv} Through these steps, the Agency aims to strike a balance between mitigating severe consequences of opioid abuse and ensuring access to safe and effective prescription opioids for patients who need them as part of pain management. The development and utilization of packaging, storage, and disposal technologies can complement the mitigation of risks of opioid misuse and abuse while ensuring access to needed pain relief.

FDA Exploration of Innovative Packaging

FDA’s PADS Task Force was originally created to explore the landscape and application of innovative packaging, storage, and disposal solutions to prevent or deter misuse and abuse of opioid analgesics. Beginning with research efforts in 2013, the Task Force has gathered information on packaging, storage, and disposal solutions technologies through internal data sources, a Lehigh University technology review,^{xvi} a 2014 Federal Register request for comment,^{xvii} and vendor presentations. This preliminary research suggested that, while there were many packaging, storage, or disposal solutions in development or already marketed, they had limited capacity to each address the continuum of factors that contribute to opioid misuse and abuse.^{xviii} Some solutions targeted only a single factor (e.g., charcoal packaging for disposal), while other potential solutions may target more than one factor (e.g. combination locked bottle caps to deter some forms of inappropriate access and accidental child poisonings). Potential solutions intended to target more than one factor with more complex technologies were still conceptual or were in the early stages of development.

Effectiveness of Existing Packaging, Storage and Disposal Solutions

There is currently little evidence to determine the effectiveness of these technologies in deterring misuse, abuse and accidental poisonings. Additional research is needed to better understand both the potential role and effectiveness of packaging, storage, and disposal solutions in enhancing opioid safety as well as any unintended consequences of utilizing these technologies. In 2014, the PADS Task Force sponsored a Lehigh University study exploring the range of packaging and storage solutions used for prescription opioids. The study also reviewed the characteristics of packaging and storage technologies, the development status, and the potential to tackle both unintentional and intentional abuse. The 35 products analyzed were categorized by development status and abuse deterrent features (Table 1).

TABLE 1: Technologies by Abuse Prevention Type		
	Unintentional Misuse or Inappropriate Access	Intentional Abuse
Dispensing Control	3	13
Locking Caps	0	1
Storage	0	1
Blister Packs	6	3
Tracking System Technology	2	3

Source: Babat, O., Gao, H., Katase, K. et al. (2014) *Review of packaging technologies for opioid abuse prevention*. Bethlehem, PA: Lehigh University Department of Systems Engineering.

The study found that technologies such as locking caps, tamper resistant packaging, and pill dispensers were found to deter drug misuse by children and seniors but had limited capacity to effectively prevent intentional abuse.^{xix} Furthermore, technologies that were potentially the most effective in preventing intentional abuse were those that combined multiple features, such as Radio frequency identification (RFID) that enabled real-time tracking of drug use as well as communication and intervention by a healthcare provider.^{xx} Unfortunately, many of these more complex solutions remain in the

developmentstage while many of the solutions on the market are targeted at preventing unintentional misuse.^{xxi} Additional research is needed to understand the effectiveness of differing packaging technologies in deterring or preventing misuse and abuse, as well as the barriers to market and implementation for various technologies. While packaging, storage, and disposal solutions have not yet been a major focus of Federal and state policymakers, some efforts have been put forth on a Federal and state level to explore the feasibility of locking caps and other packaging solutions in pilot studies.

With opioid safety enhancing packaging still an emerging area of development, additional clarity may be needed on how to best to determine the product’s effectiveness at mitigating abuse and misuse, while still ensuring safe access to prescribed medicines. Developers of these new technologies have indicated that providing clarification around types of pre- and post-market data that are most useful for determining whether packaging, storage, or disposal solutions may deter misuse, abuse or accidental ingestions may stimulate/facilitate their development.

Integration of Safety-Enhancing Opioid Packaging, Storage, or Disposal Solutions into Existing Health and Pharmacy Systems

Despite the potential benefits of opioid packaging solutions (in combination with existing strategies to mitigate the risks of opioids), there are practical, evidentiary, and logistical challenges to their successful integration into health systems and pharmacy practice. In particular, increased costs and the lack of reliable evidence about these new technologies undermines the ability for payers, benefit managers and other health care providers to evaluate coverage decisions.

Beyond issues related to the usability and effectiveness of individual solutions in a trial setting, there also may be real-world implications to integrating packaging solutions into healthcare systems and pharmacy practice. The goal of opioid safety-enhancing packaging, storage, and disposal solutions is to deter misuse and abuse without creating barriers to access for patients in pain. To that end, such solutions should be implemented with careful consideration related to their cost-effectiveness, impact on access to opioids as part of a comprehensive pain management plan for patients with pain, and potential for unintended consequences. Additional input and discussion is needed to determine the impact of these solutions on health and pharmacy systems, as well as the cost for patients and caregivers.

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ⁱ Quintiles IMS, National Prescription Audit. Data extracted March 2017.

ⁱⁱ Excludes injectable formulations

ⁱⁱⁱ Nahin RL. Estimates of pain prevalence and severity in adults: United States, 2012. *J Pain*. 2015;16(8):769-780.

^{iv} <https://www.samhsa.gov/atod/opioids>.

^v Dowell, D., Haegerich, T.M., Chou, R. CDC guideline for prescribing opioids for chronic pain — United States, 2016. *MMWR Recomm Rep* 2016;65(No. RR-1):1–49.

^{vi} Alexander, G.C., Frattaroli, S., Gielen, A.C., et al. The prescription opioid epidemic: an evidence-based approach. Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland: 2015.

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- ^{viii} Hughes, A., Williams, M.R., Lipari, R.N., et al. Prescription drug use and misuse in the United States: results from the 2015 National Survey on Drug Use and Health. NSDUH Data Review. (2016; Accessed January 25, 2017 at <https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR2-2015/NSDUH-FFR2-2015.htm>).
- ^{ix} *Ibid.*
- ^x *Supra*, viii
- ^{xi} Shah, A., Hayes, C.J., Martin, B.C. Characteristics of initial prescription episodes and likelihood of long-term opioid use — United States, 2006–2015. MMWR Morb Mortal Wkly Rep 2017;66:265–269.
- ^{xii} See DEA Disposal Act Fact Sheet. (2016; Accessed February 2 2017 at https://www.deadiversion.usdoj.gov/drug_disposal/fact_sheets/disposal_public.pdf).
- ^{xiii} See FDA Opioids Action Plan. (2016; Accessed January 15, 2017 at <https://www.fda.gov/NewsEvents/Newsroom/FactSheets/ucm484714.htm>).
- ^{xiv} *Ibid.*
- ^{xv} *Ibid.*
- ^{xvi} Internal FDA documents provided to the Duke-Margolis Center
- ^{xvii} Federal Register Docket No. FDA-2014-N-0233. Accessible at <https://www.federalregister.gov/documents/2014/07/08/2014-15809/center-for-drug-evaluation-and-research-use-of-innovative-packaging-storage-andor-disposal-systems>
- ^{xviii} Internal FDA documents provided to the Duke-Margolis Center
- ^{xix} Babat, O., Gao, H., Katase, K. et al. (2014) *Review of packaging technologies for opioid abuse prevention*. Bethlehem, PA: Lehigh University Department of Systems Engineering.
- ^{xx} *Ibid.*
- ^{xxi} *Ibid.*