Packaging, storage, and disposal options to enhance opioid safety: Target Problems and Labeling Considerations

Irene Z. Chan, PharmD, BCPS
Deputy Director
Division of Medication Error Prevention and Analysis (DMEPA)

Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)
Disclaimer

The views and opinions expressed in this presentation represent those of the presenter, and do not necessarily represent an official FDA position.

Reference to any marketed products is for illustrative purposes only and does not constitute endorsement by the U.S. Government, the Department of Health and Human Services, or the Food and Drug Administration.

Any labeling statement examples in this presentation reflect preliminary considerations and are included to generate scientific discussion. They do not represent FDA recommended labeling statements.
Overview

- Accidental Exposure
- Misuse
- Third Party Access
- Excess Supply
Approach to Development

Identify Target Problem(s) and Associated Behaviors

- What labeling claim(s) are being pursued?
- Is the goal to address one problem or multiple problems?

Develop Design

- What design features or technologies are needed to target the problem(s) we are trying to address?

Collect Data

- What data will be needed?
- Data will drive the labeling
Identifying Problems

- Accidental Exposure
- Excess Supply
- Misuse
- Third Party Access
Accidental Exposure

‘The Pills Are Everywhere’: How the Opioid Crisis Claims Its Youngest Victims

By JULIE TURKEWITZ  SEPT. 20, 2017

When Penny Mae Cormani died in Utah, her family sang Mormon hymns — “Be Still My Soul” — and lowered her small coffin into the earth. The latest victim of a drug epidemic that is now taking 60,000 lives a year, Penny was just 1.

Increasingly, parents and the police are encountering toddlers and young children unconscious or dead after consuming an adult’s opioids.

“These kids aren’t making a choice because they are trying to get high on a substance. It’s that the pills are everywhere.”

Accidental Exposure

Findings: “This retrospective analysis of 13,052 national hospital discharge records found that pediatric hospitalizations for opioid poisonings increased nearly 2-fold from 1997 to 2012. Hospitalization rates were highest in older adolescents, but the largest percentage increase in hospitalizations over time occurred among the youngest children (toddlers and preschoolers)”

Accidental Exposure

There were significant associations between adult medication use and exposures and poisonings in children...These associations were generally twice as strong for opioids as other drug classes and strongest among children 0 to 5 years of age across drug classes.


www.fda.gov
Accidental Exposure

Why do accidental ingestions continue to occur?

• Improper use of child-resistant closures
  – Leaving container open
  – Incompletely closing container
  – Transferring contents of one bottle to another container
• Availability of non-special packaging, on request, for prescription medication
• Inadequate quality control by manufacturers leading to defective closures
• Violations of the law by the pharmacist and/or the dispensing physician

www.fda.gov
Accidental Exposure

Where might we focus interventions?

- Decrease available supply that children can access
- Make it more difficult for children to access the available supply
- Other?
Accidental Exposure

• Example
  – Parent leaves bottle of XXX on table or counter and has not properly twisted the cap back on. Toddler finds the bottle and easily opens the top and eats the medicine. Toddler is subsequently hospitalized for massive overdose of XXX.

• Labeling Considerations*
  – *The packaging has characteristics expected to lower the risk for accidental pediatric exposure of XXX. However, pediatric accidental exposure of XXX is still possible.*

* Any labeling statement examples in this presentation reflect preliminary considerations and are included to generate scientific discussion. They do not represent FDA recommended labeling statements.
“Roughly 21 to 29 percent of patients prescribed opioids for chronic pain misuse them.”

Vowles KE et al. PAIN 2015; 156(4): 569-576
Misuse

Each day more than 1,000 people are treated in emergency departments for not using prescription opioids as directed

Image: The University of Texas at Austin, http://www.texasenterprise.utexas.edu/2013/10/10/innovation/reinventing-er-hospital-takes-cues-assembly-lines
Misuse

Unintended Misuse*

- Example
  - Patient forgets to take medication
  - Patient doesn’t understand how often to take medication

Intended Misuse

- Example
  - Therapeutic use of drug by a person other than the intended patient that may result from sharing of medication (e.g., giving a friend a Vicodin tablet for her migraine)
  - Intended patient uses more drug than prescribed to self-treat increasing or breakthrough pain
  - Intended patient retains leftover opioid in case of future pain (contributing to excess available supply which could potentially be accessed by a third party)

*The use of the term “unintentional misuse” in this context is not to be confused with the definition of misuse as the intentional therapeutic use of a drug product in an inappropriate way that specifically excludes the definition of abuse.
Misuse

• Could contribute to accidental overdose of an opioid
• Could be a sign of developing addiction
• Could contribute to excess available supply that is susceptible to access by a third party
• Could contribute to individuals not seeking necessary care from a healthcare provider
Misuse

• Labeling Considerations*
  – *The packaging has characteristics that improve patient compliance with labeled directions for use.*
  – *The packaging has characteristics that will destroy XXX after ## days of use, eliminating excess supply of XXX.*
  – *The packaging has characteristics expected to discourage the sharing of XXX.*

* Any labeling statement examples in this presentation reflect preliminary considerations and are included to generate scientific discussion. They do not represent FDA recommended labeling statements.
“Primary prevention of nonmedical use of prescription opioids in late childhood may prevent the onset of more severe types of drug use such as heroin at later ages.”


Third Party Access

Figure 3. Drug overdose death rates for adolescents aged 15–19, by type of drug involved: United States, 1999–2015

Drug overdose deaths involving opioids

Deaths per 100,000 adolescents aged 15–19

Cocaine

Benzodiazepines

Psychostimulants with abuse potential

www.fda.gov

NCHS Data Brief No. 282, August 2017
Third Party Access - Inpatient

Health Care–Associated Hepatitis C Virus Infections Attributed to Narcotic Diversion

Walter C. Hellinger, MD; Laura P. Bacalis, RN; Robyn S. Kay, MPH; Nicola D. Thompson, PhD, MS; Guo-Liang Xia, MD, MPH; Yulin Lin, MD; Yury E. Khudyakov, PhD; and Joseph F. Perez, DrPH

Background: Three cases of genetically related hepatitis C virus (HCV) infection that were unattributable to infection control breaches were identified at a health care facility.

Objective: To investigate HCV transmission from an HCV-infected health care worker to patients through drug diversion.

Design: Cluster and look-back investigations.

Setting: Acute care hospital and affiliated multispecialty clinic.

Patients: Inpatients and outpatients during the period of HCV transmission.

Measurements: Employee work and narcotic dispensing records, blood testing for HCV antibody and RNA, and sequencing of the N558 gene and the hypervariable region 1 of the E2 gene.

Results: 21 employees were recorded as being at work or as retrieving a narcotic from an automated dispensing cabinet in an area where a narcotic was administered to each of the 3 case patients; all employees provided blood samples for HCV testing. One employee was infected with HCV that had more than 95% N558 sequence homology with the HCV strains of the 3 case patients. Quasi-species analysis showed close genetic relatedness with variants from each of the case patients and more than 97.9% nucleotide identity. The employee acknowledged parentral opioid diversion. An investigation identified 6132 patients at risk for exposure to HCV because of the drug diversion. Of the 3929 living patients, 3444 (87.7%) were screened for infection. Two additional cases of genetically related HCV infection attributable to the employee were identified.

Limitation: Of the living patients at risk for HCV exposure, 12.3% were not tested.

Conclusion: Five cases of HCV infection occurring over 3 to 4 years were attributed to drug diversion by an HCV-infected health care worker. Studies of drug diversion and assessments of strategies to prevent narcotics tampering in all health care settings are needed.

Primary Funding Source: None.

For author affiliations, see end of text.
Third Party Access - Inpatient

Third Party Access

• Example
  – Outpatient
    • Adolescents in a household who might be curious or experimenting with opioids
  – Inpatient
    • Healthcare professional withdraws injectable opioid product from vial for self administration and replaces the removed content with saline

• Labeling Considerations*
  – *The packaging has characteristics expected to reduce use by persons other than the intended patient.*

* Any labeling statement examples in this presentation reflect preliminary considerations and are included to generate scientific discussion. They do not represent FDA recommended labeling statements.
Excess Supply

“...leftover prescription opioids from previous prescriptions account for a substantial source of [nonmedical use of prescription opioids] among high school seniors in the U.S.”


Excess Supply

Accidental Exposure

Misuse

Third Party Access

Excess Supply
Several Small Studies Have Assessed Leftover Pills, Storage, and Disposal After Surgery

• Asked the patient:
  – How many pills used/remaining
  – Whether they disposed of excess opioid medication
  – How/where they stored excess supply
# Opioid Prescribing: Surgical Procedures

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Mean (range) tablets filled</th>
<th>Mean tablets consumed</th>
<th>Mean tablets remaining</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laparoscopic Inguinal Hernia Repair</td>
<td>33 (15-70)</td>
<td>9</td>
<td>23</td>
</tr>
<tr>
<td>Open Inguinal Hernia Repair</td>
<td>30 (15-120)</td>
<td>9</td>
<td>21</td>
</tr>
<tr>
<td>Laparoscopic Cholecystectomy</td>
<td>30 (0-100)</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>Cesarean Delivery</td>
<td>40 (5-80)*</td>
<td>20*</td>
<td>15*</td>
</tr>
<tr>
<td>Partial Mastectomy</td>
<td>21 (0-50)</td>
<td>3</td>
<td>18</td>
</tr>
<tr>
<td>Partial Mastectomy with Node Biopsy</td>
<td>23 (0-60)</td>
<td>6</td>
<td>17</td>
</tr>
<tr>
<td>Tooth Extraction</td>
<td>28 (n.d.)</td>
<td>13</td>
<td>17</td>
</tr>
<tr>
<td>Dermatologic Surgery</td>
<td>9 (3-20)</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Orthopedic Surgery</td>
<td>80 (n.d.)</td>
<td>n.d.</td>
<td>30</td>
</tr>
<tr>
<td>Upper Extremity Surgery</td>
<td>30 (n.d.)</td>
<td>14 (Bone)</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>9 (Soft Tissue)</td>
</tr>
<tr>
<td>Outpatient Shoulder Surgery</td>
<td>55 (n.d.)</td>
<td>n.d.</td>
<td>20</td>
</tr>
</tbody>
</table>

* Median number of pills

Excess Supply

• Example
  – Patient does not use all of his prescribed medication and leaves the leftover medication in the medicine cabinet. Subsequently, ____________finds the excess supply of XXX.

• Labeling Considerations*
  – *The packaging has characteristics that will destroy XXX after ## days of use, eliminating excess supply of XXX.*

* Any labeling statement examples in this presentation reflect preliminary considerations and are included to generate scientific discussion. They do not represent FDA recommended labeling statements.