RADARS® SYSTEM 10th ANNUAL SCIENTIFIC MEETING

CELEBRATING OUR 10th ANNUAL SCIENTIFIC MEETING
Lessons from the Downward Spiral aka The Bubble Slide

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Professor, University of Colorado School of Medicine
The Anti-ADF Movement: Can ADFs contribute to reducing prescription drug abuse? 

I want everyone in this Chamber to understand this: "Abuse-deterrent opioid is an oxymoron..." 

Senator Markey, MA
FDA’s Throckmorton: Future for AD Opioids. Where are we headed?

• Early: market has a small number of AD products using early AD technology
  – Case by case decision-making

• Intermediate: multiple products approved as abuse deterrent using various technologies
  – Fuller set of regulator issue identified.
  – Guidance outlining FDA’s approach for brand name and generic development is refined
    – Actions potentially shift to class-wide scope

• Late: AD formulations of all major opioids marketed
  – Focus is on supporting iterative improvements in AD technologies.
Current ADFs in the United States

- **OxyContin**, an ER oxycodone tablet formulation, was reformulated in 2010 to deter abuse; the current product is more difficult to crush, break, or dissolve than the original, and when dissolved forms a viscous gel that is difficult to inject through a hypodermic needle.

- **Embeda** is formulated as capsules of ER morphine pellets that contain a sequestered core of the opioid antagonist naltrexone. If the pellets are swallowed, the morphine is gradually released and absorbed, while the naltrexone core passes through the gut intact. If the pellets are crushed, chewed, or dissolved, naltrexone is released, blocking morphine-induced euphoria.

- **Hysingla ER** is an ER hydrocodone tablet formulation; when dissolved it forms a viscous gel that is difficult to inject through a hypodermic needle.

- **Targiniq ER** is an opioid agonist/antagonist combination containing ER oxycodone and naloxone, has been approved by the FDA with claims of abuse deterrence in the labeling, but is not yet commercially available.
The Downward Spiral
Role of Abuse Deterrent Formulations

Person in Pain
Pain Relief from Opioid
Susceptible Pain Patient
Misuse
Abuse
Addiction, Poisoning, Overdose, Death
Substance Abuser
How Can We Prove an ADF Works?

• Draft Guidance Abuse-Deterrent Opioids Evaluation and Labeling, 2013
  – High public health priority
  – Recognizes the value of opioid analgesics in pain treatment

• Premarketing Studies
  – Category 1 - Laboratory-based in vitro manipulation and extraction studies
  – Category 2 - Pharmacokinetic studies
  – Category 3 - Clinical abuse potential studies

• Category 4 - Postmarketing Studies - Postmarketing data to assess the impact of an ADF on actual abuse.
RADARS Examines Prescription Drug Abuse from Multiple Perspectives

- Poison Center Data
- OTP and SKIP Substance Abuse Treatment
- StreetRx.com Illicit Market Price
- Drug Diversion Program
- College Student Survey
- Web Monitoring
Oxycodone ADF – Reduced Use
Number of People Filling Prescriptions

Change from baseline average (%)
Oral and Non-oral Routes of Abuse Decrease after Oxycodone ADF - Poison Center Program
Nonmedical Use and Outcomes Associated with Oxycodone ER have Decreased, 2008 - 2015

Poison Center Deaths Involving per 100,000

NSDUH percentage past month NMU

RADARS Poison Center
Abuse Deterrent Formulation Reduces Street Price, 2013 - 2014

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<tr>
<th></th>
<th>United States</th>
<th>Canada</th>
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<tbody>
<tr>
<td></td>
<td>Number reports</td>
<td>Median Price/mg, US Dollar</td>
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<tr>
<td>Crushable “Old OxyContin”</td>
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<td>Median (range)</td>
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<tr>
<td>Median</td>
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<td>1.00</td>
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<tr>
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Limited Impact Unless Most Opioids Analgesics are Abuse Deterrent
Changes in Abuse Indicators Following Introduction of Abuse Deterrent Formulations

Poison Center Intentional Abuse

<table>
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<th>Events per 100,000 population</th>
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<td>0.104</td>
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<td>Pre ORF</td>
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- Oxycodone ER
- Oxymorphone ER
- Other Opioids

Year/Quarter
Battle of the ADFs

- Niacin
- Prodrug
- Crush Resistance
Summary

• Lots of controversy
  – Cost
  – Fear of increased prescribing
  – Alternatives are plentiful
• Won’t be able to tease out the minor differences until most of the market is ADF
• Then the fun will begin
  – But only if health care payers decide to pay.