Impact of Abuse-Deterrent Formulations
National Rx Drug Abuse Summit
Atlanta, Georgia
April 2014

Richard C. Dart, MD, PhD,
Director, Rocky Mountain Poison and Drug Center
Professor, University of Colorado
Disclosure Statement

• "Richard Dart has financial relationships with proprietary entities that produce health care products and services."

• These financial relationships are research funding from McNeil Consumer Healthcare and Bioclon.

• The RADARS System is financially supported by subscriptions from most pharmaceutical companies that produce prescription opioids or stimulants.

• All relationships are with Denver Health and Hospital Authority, the public hospital for Denver, Colorado.

• Dr. Dart receives no individual compensation.
Total US Pharmaceutical Opioid Consumption
1980 – 2010, Morphine Equivalents (mg per capita)

http://ppsg-production.herokuapp.com/chart
England and Wales Drug Related Deaths 2001 - 2011

*Note: heroin and morphine are reported as one category in the data from England, Wales and Scotland; since the focus of this analysis is on prescription opioids, that category was not included in this analysis.

http://www.whitehouse.gov/blog/2014/02/10/5-things-know-about-opioid-overdoses

FDA Draft Guidance
Abuse-Deterrent Opioids - Evaluation and Labeling

• Prescription opioid analgesics are an important component of modern pain management.
• Abuse and misuse of these products, however, have created a serious and growing public health problem.
• FDA has worked to address this problem while ensuring that patients in pain have appropriate access to opioid analgesics.
Conflicting Views

- FDA advisory committee voted against approval of a hydrocodone product lacking tamper-resistant technology.
  - "I would feel very uncomfortable approving a non-abuse-deterrent product," one of the panelists said at the time.

- Andrew Kolodny, MD, co-founder of PROP, expressed concern that labeling of abuse-resistant products could contribute to false marketing.
  - "If doctors are misled to believe that these formulations are less addictive, and if they develop a false sense of security about these products, that could possibly make the epidemic worse,"

http://www.medpagetoday.com/PublicHealthPolicy/FDAGeneral/36782
Abuse Deterrent Formulations in the United States

OxyContin, Opana ER, Exalgo, Oxecta, Nucynta ER
Abuse Deterrent Formulations
Site of Action

Can ADFs Decrease Progression?

Currently Available

Inject
Snort
Crush
Chew
Swallow
RADARS System
Results through December 31, 2013
What is the RADARS® System?

• History
  – Denver Public Safety Net Hospital for 150 years
    • State sanctioned independent authority
  – Created 2001 by Purdue Pharma
  – 2006, Denver Health and Hospital Authority (DHHA)
    • Independent program
  – Multiple pharmaceutical subscribers
    • Data can only be used for safety reporting

• Conflict of interest statement
  – None, other than running system for DHHA as noted above
RADARS System
Scientific Advisory Board

Principal Investigators
• Theodore J. Cicero, PhD
  Washington University at St. Louis

• Richard C. Dart, MD, PhD
  Denver Health and Hospital Authority

• Hilary Surratt, PhD
  Nova Southeastern University

• Mark W. Parrino, MPA
  American Association for the Treatment of Opioid Dependence

Substance Abuse Experts
• Herbert D. Kleber, MD
  Columbia University

• Sidney Schnoll, MD, PhD
  Pinney Associates

• George E. Woody, MD
  University of Pennsylvania

Law Enforcement
• John Burke
  National Association of Drug Diversion Investigators

Epidemiology/Biostatistics
• Edgar Adams, ScD
  Covance

• Nabarun Dasgupta, MPH
  Founder – EpidemiCo

• Alvaro Muñoz, PhD
  Johns Hopkins University
Show Me The Data

• Do ADFs decrease abuse?
  – OxyContin® (polyethylene oxide), Opana ER® (Intac®), Nucynta ER (Intac®)
  – Exalgo®, Oxecta®, Embeda®
  – Suboxone®, buprenorphine/naloxone combos

• Do they affect outcome?
  – Injection?
  – Mortality?
RADARS System
Schedule II Excluding Oxycodone ER Population
Rates by Program, 2009-2013
Model for Oxycodone Extended Release
RADARS System Poison Centers

![Graph showing intentional exposures per 100,000 population for All Oxycodone ER 95% CI. The graph indicates a peak in 2009 and a decline after the New Formulation was introduced in 2010.]

October 21-22, 2010: Joint Meeting of the Anesthetic and Life Support Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee Meeting Announcement
ADFs–Demand Reduction
People Filling Prescriptions

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**Oxycodone ER**

- **Pre**
- **Post ADF**

**Oxymorphone ER**

- **Pre**
- **Post ADF**

Year/Quarter
Drug Diversion Program
Population Rate, 2009-2013

*Other opioids excluding ER oxycodone and ER oxymorphone.
Poison Center Program
Population Rate, 2009-2013

*Other opioids excluding ER oxycodone and ER oxymorphone
Poison Center Program
Route of Administration, OxyContin

Oral

Non-Oral

Rate per 100,000 Population

Before ADF
After ADF
Transition

Rate per 100,000 Population

Before ADF
After ADF
Transition

Relation of Original OxyContin and Mentions in Poison Center Program
Case Outcome in Poison Center Program - Major Outcome or Death

![Graph showing the rate of major outcome or death for Oxycodone ER and Oxymorphone ER before and after ADF.](image)
Treatment Programs Combined 2009-2013

*Other opioids excluding ER oxycodone and ER oxymorphone.
### Latest prices

<table>
<thead>
<tr>
<th>Drug</th>
<th>Location</th>
<th>Price</th>
<th>Date</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norco hydrocodone, 10/325mg pill</td>
<td>Indianapolis, Indiana</td>
<td>$8</td>
<td>Apr 4</td>
<td>Rate: $$$$$</td>
</tr>
<tr>
<td>oxycodone, 30mg pill</td>
<td>Denver, Colorado</td>
<td>$30</td>
<td>Apr 4</td>
<td>Reasonable $$$$</td>
</tr>
<tr>
<td>Adderall XR, 30mg pill</td>
<td>Lockport, New York</td>
<td>$1.50</td>
<td>Apr 4</td>
<td>Not Bad $$$$</td>
</tr>
<tr>
<td>Adderall XR, 30mg pill</td>
<td>Harrisonburg, Virginia</td>
<td>$12</td>
<td>Apr 4</td>
<td>Rate: $$$$$</td>
</tr>
<tr>
<td>hydrocodone (generic Vicodin), 5mg pill</td>
<td>San Marcos, Texas</td>
<td>$5</td>
<td>Apr 4</td>
<td>Rate: $$$$$</td>
</tr>
</tbody>
</table>
StreetRx, RADARS System Drug Diversion and Silk Road – Price per milligram drug

US StreetRx
Endorsement of Canadian Oxycodone Products in United States

11 States
1 to 4 reports
### Oxycodone ER in US and Canada

#### Crushable “Old OxyContin”

<table>
<thead>
<tr>
<th>Formulation</th>
<th>United States</th>
<th>Canada</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number reports</td>
<td>Reported Median Price per mg, US Dollar (range)</td>
</tr>
<tr>
<td>Apo-Oxycodone CR</td>
<td>24</td>
<td>1.00 (0.15 – 16.80)</td>
</tr>
<tr>
<td>OxyContin*</td>
<td>93</td>
<td>1.00 (0.06 – 10.00)</td>
</tr>
<tr>
<td>Co-Oxycodone CR</td>
<td>11</td>
<td>1.00 (0.30 – 4.00)</td>
</tr>
<tr>
<td>Teva-Oxycodone CR</td>
<td>4</td>
<td>0.88 (0.10 – 3.75)</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td><strong>1.00</strong></td>
<td></td>
</tr>
</tbody>
</table>

#### Abuse Deterrent “New OxyContin”

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</thead>
<tbody>
<tr>
<td></td>
<td>Number reports</td>
<td>Reported Median Price per mg, US Dollar (range)</td>
</tr>
<tr>
<td>Oxycodone ER</td>
<td>277</td>
<td>0.63 (0.03 – 10.00)</td>
</tr>
<tr>
<td>(OxyContin in US, OxyNEO in Canada)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td><strong>0.63</strong></td>
<td></td>
</tr>
</tbody>
</table>

RADARS System Technical Report, 2014-Q2
Other Data Sources
Navippro Treatment Centers

Figure 1. Quarterly prevalence of past-30-day abuse for original ER oxycodone, reformulated ER oxycodone (ORF), or any ER oxycodone (OC or ORF) among individuals assessed for substance abuse treatment.

Other Data Sources
National Survey of Drug Use and Health

Good News – Bad News

“The number of persons aged 12 or older who were current nonmedical users of the pain reliever OxyContin declined from 566,000 in 2010 to 358,000 in 2012.”
Yes, Abuse Deterrent Formulations Can Reduce the Diversion and Abuse of an Opioid Analgesic, but…

Some Important Questions Remain!
Squeezing the Balloon
Heroin - Past Month, Past Year

ADF Oxycodone ER

Numbers in Thousands


Past Month Past Year

NSDUH Report 2012
Can ADFs Bend the Curve?

The RADARS System
Average rate per 100,000 population by formulation
2013

- CS – College Survey
- DD – Drug Diversion
- PC – Poison Center
- TC – Treatment Centers combined
- Methadone, buprenorphine, liquids, injectables excluded
Conclusions

• Formulations that resist crushing and forming injectable solutions can reduce diversion, abuse and the sequelae of abuse of that particular drug.

• The potential impact of ADF technology would be greater if more products used technology.

• However, the “market” will adjust to the new barriers.
Thank You!