Meeting Objectives

• Brief overview of the RADARS System

• Review Colorado Specific Data

• Current area of FDA interest - Abuse Deterrent Formulations (ADFs)
RADARS® System Goals

• Measure rates of abuse, misuse and diversion of prescription drugs

• Identify sentinel events involving the abuse, misuse and diversion of prescription drugs nationwide

• Provide experienced and expert analysis and interpretation of the data
RADARS® System Mosaic Approach

<table>
<thead>
<tr>
<th>College Survey</th>
<th>Early Experimenters</th>
<th>Poison Center</th>
<th>Acute Events</th>
</tr>
</thead>
</table>

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RADARS® System Mosaic Approach

- College Survey
- Early Experimenters
- Poison Center
- Acute Events
- OTP (Opioid Tx Program)
- Patients in Treatment
- SKIP (Survey of Key Informant Pts)
- Patients in Treatment
RADARS® System Mosaic Approach

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- Criminal Justice/Law Enforcement
RADARS® System Mosaic Approach

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- Drug Diversion
- Criminal Justice/Law Enforcement
- Street Price
- Users/Buyers
RADARS® System Process
Tale of Two Denominators

**COUNTS BY SYSTEM**
- UNITED STATES POPULATION

**COUNTS BY SYSTEM**
- UNIQUE RECIPIENTS OF DISPENSED DRUG (URDD) RATE

**= POPULATION RATE**
- Tried and true
- Disease burden on whole population
- Does not account for drug availability

**= UNIQUE RECIPIENTS OF DISPENSED DRUG (URDD) RATE**
- Number of unique people filling prescription for drug
- Accounts for availability of drug in community
- Relates events to corresponding patient benefit
RADARS System Fundamentals

• Independent, third party ownership & operation
  – Denver Health/RMPDC controls scientific rigor & integrity
    • Ensures data quality/integrity, sound methodology and expert analysis and interpretation
    • Protects proprietary data of each company while providing product-specific data to each
    • Provides standardized data collection and reporting, including rich historical data for evaluating trends over time

• Guided by External Scientific Advisory Board
  – Independent panel of key opinion leaders (KOL)
  – Minimize conflict of interest
  – Ensure scientific rigor
  – Provide guidance on program development, interpretation of results, future development of RADARS System
RADARS System Fundamentals

• Qualified Principal Investigator for Each Program
  – Principal investigators provide expertise and credibility
    • Ensures leadership and dedication to success within each program
    • Provides content knowledge, credibility and access to other experts in the field

• Provide Common Ground for Industry, Regulatory Agencies, Academics and Clinicians
  – Host RADARS System Annual Meeting to share current data, trending and new discoveries
  – Meet with each regularly to review data, share ideas, gather feedback about current events, provide guidance
The RADARS® System Poison Center Program
Population Rates per 100,000 by region
1st Quarter 2003 through 3rd Quarter 2012

Population rate per 100,000

United States
Colorado
Denver

Quarterly data from 1st Quarter 2003 to 3rd Quarter 2012 is shown in the graph.
The RADARS® System Poison Center Program
URDD Rates per 1,000 by region
1st Quarter 2003 through 3rd Quarter 2012

URDD Rate per 1,000

- United States
- Colorado
- Denver
The RADARS® System Drug Diversion Program
Population Rates per 100,000 by region
1st Quarter 2002 through 3rd Quarter 2012

Population rate per 100,000


United States
Colorado
Denver
The RADARS® System Drug Diversion Program

URDD Rates per 1,000 by region
1st Quarter 2002 through 3rd Quarter 2012

Chart showing URDD rates per 1,000 for the United States, Colorado, and Denver from 1st Quarter 2002 through 3rd Quarter 2012.
Poison Center Oxycodone Signals
3rd Quarter 2011 – 2nd Quarter 2012

[Map showing regions with signals indicated by red dots, including Denver, Colorado Springs, Pueblo, Alamosa, La Junta, Sterling, Grand Junction, and Craig.]
Drug Diversion Oxycodone Signals
3rd Quarter 2011 – 2nd Quarter 2012

Map showing areas with signals and those without.

- Cities with signals:
  - Denver
  - Colorado Springs
  - Pueblo
  - Alamosa
  - La Junta
- Cities with no signals:
  - Craig
  - Grand Junction
  - Sterling

Legend:
- Grey: No Signal
- Red: Signal
Poison Center Hydrocodone Signals
3rd Quarter 2011 – 2nd Quarter 2012
Drug Diversion Hydrocodone Signals
3rd Quarter 2011 – 2nd Quarter 2012

MAP: Major cities indicated with 'no signal' status.
Colorado Summary

• Poison Center trends indicate Colorado rates have been similar to or lower than national rates

• Drug Diversion trends indicate Colorado rates have been similar to or higher than national rates

• Multiple oxycodone signals detected in both Poison Center and Drug Diversion
  – Signals detected in different 3 Digit Zip Codes depending on program

• Minimal hydrocodone signals detected in Colorado
  – Only signal in southwest corner of state and no diversion signals
Abuse Deterrent Opioids
Abuse Deterrent Formulations

• FDA Draft Guidance on evaluation and labeling for abuse deterrent opioids
  – Specifies that these formulations only address non-oral routes of abuse (i.e. injection, snorting, crushing; oral route of abuse not impacted)
  – Types: physical/chemical barriers, antagonist/agonist combinations, aversion, delivery system, prodrug, combination of >1 type

• Currently several products on the market:

<table>
<thead>
<tr>
<th>OxyContin® (oxycodone)</th>
<th>Opana® (oxymorphone)</th>
<th>Suboxone® (buprenorphine/naloxone)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nucynta® (tapentadol)</td>
<td>Exalgo® (hydromorphone)</td>
<td></td>
</tr>
</tbody>
</table>
OxyContin® Rates per 1,000 URDD

**Poison Center**

- **Exposure/1000 URDD**
  - 2008Q4: 0.1
  - 2009Q2: 0.2
  - 2009Q4: 0.3
  - 2010Q2: 0.2
  - 2010Q4: 0.1
  - 2011Q2: 0.2
  - 2011Q4: 0.3
  - 2012Q2: 0.2

**Drug Diversion**

- **Cases/1000 URDD**
  - 2008Q4: 1.5
  - 2009Q2: 1.0
  - 2009Q4: 0.5
  - 2010Q2: 0.5
  - 2010Q4: 1.0
  - 2011Q2: 2.0
  - 2011Q4: 1.5
  - 2012Q2: 1.0

**Drug**

- **Δ(%)**
  - OxyContin: -52.9%
  - Other Opioids: -16.8%

**Drug**

- **Δ(%)**
  - OxyContin: -31.3%
  - Other Opioids: -10.0%
**OxyContin® URDD Rates per 1,000**

### Opioid Treatment Program

<table>
<thead>
<tr>
<th>Endorsements/1000 URDD</th>
<th>Before Reformulation</th>
<th>After Reformulation</th>
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</thead>
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<td>2009Q3</td>
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<tr>
<td>2012Q1</td>
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### Survey of Key Informant Patients

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</table>

### Drug Endorsements

<table>
<thead>
<tr>
<th>Drug</th>
<th>Δ(%)</th>
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<tbody>
<tr>
<td>Oxycontin</td>
<td>-14.8%</td>
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<tr>
<td>Other Opioids</td>
<td>-11.6%</td>
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</table>

<table>
<thead>
<tr>
<th>Drug</th>
<th>Δ(%)</th>
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<tbody>
<tr>
<td>Oxycontin</td>
<td>-9.4%</td>
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<tr>
<td>Other Opioids</td>
<td>7.6%</td>
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Abuse Deterrent Formulations
Summary

• FDA is engaged in the evaluation and labeling of abuse deterrent opioids
• These activities are impacting the approval of new opioids without abuse deterrent mechanisms
• Data from several sources associate abuse deterrent formulations with reduction of abuse, misuse and diversion
• Not sure yet of the “squeezing of the balloon” phenomenon, do abuse deterrent formulations prevent abuse or just abuse of that product?
Conclusion

- RADARS® System monitors multiple sources using a “mosaic” approach to surveillance of prescription drug abuse, misuse and diversion.
- Colorado data trends for Poison Centers are similar to that of the United States, although the state Drug Diversion activity appears higher than the national average.
- Prescription drug abuse is a complicated issue for which no single intervention will solve. Abuse deterrent formulations appear to be at least part of the solution.