

# The Necessity for REMS

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**Disclosures:** Dr Passik will receive an honorarium from Cephalon

# The Necessity for Opioid REMS

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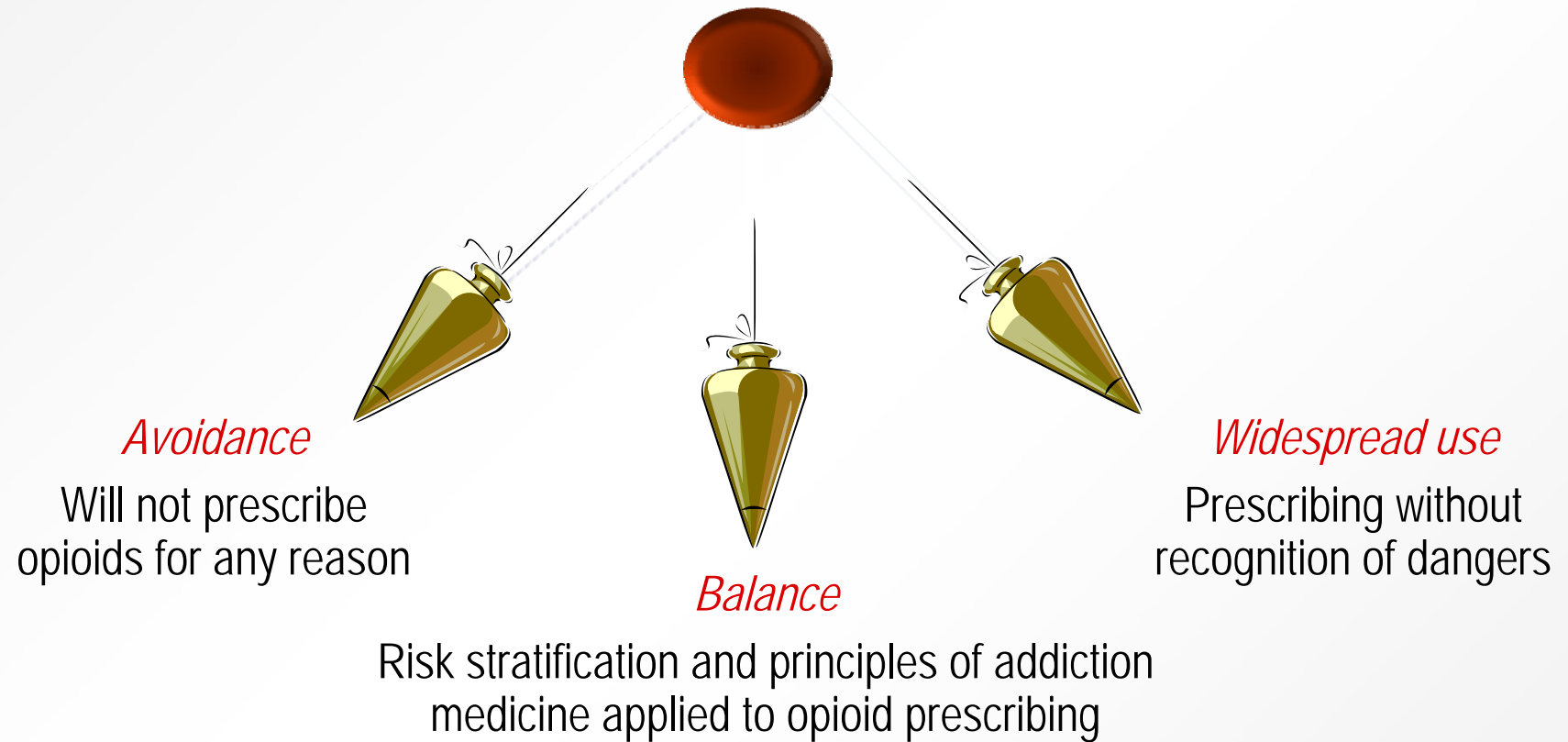
- > Opioids: Benefits and Risks
  - > The Public Health Problem
  - > Time to do the Right Thing: Evolution of REMS
  - > What is REMS?
  - > Components of REMS
  - > Conclusions
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## Opioids: Benefits and Risks

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# The Opioid Prescribing Pendulum

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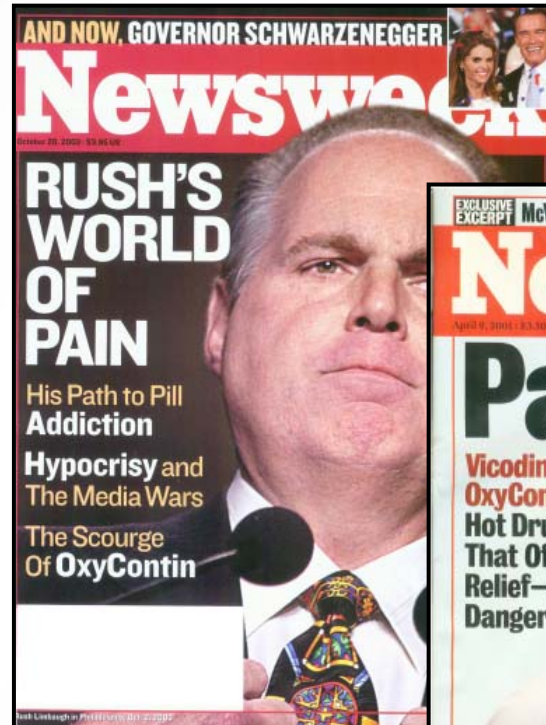
# Opioids: The Benefits

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- > Opioid analgesics represent the cornerstone of treatment for severe chronic pain<sup>1</sup>
- > Opioid prescribing has increased with the recognition that opioids can relieve pain<sup>2</sup>
- > Greater availability has benefited pain patients but has also been associated with increased nonmedical use<sup>3</sup>

# Opioids: The Risks

- > Opioids are linked to increased abuse and nonmedical use<sup>1,2</sup>
- > The potential for opioid overdose, misuse, abuse, diversion, and addiction has generated much public debate with regard to the widespread use of opioids



1. Passik SD, et al. *Clin J Pain* 2006;22:173–81; 2. National Institute on Drug Abuse (NIDA). *NIDA Community Drug Alert Bulletin—Prescription Drugs*. Bethesda, MD: US Dept of Health and Human Services; 2005. NIH Pub. No: 05-5580. <http://www.nida.nih.gov/PrescripAlert/index.html>. Accessed September 2009.

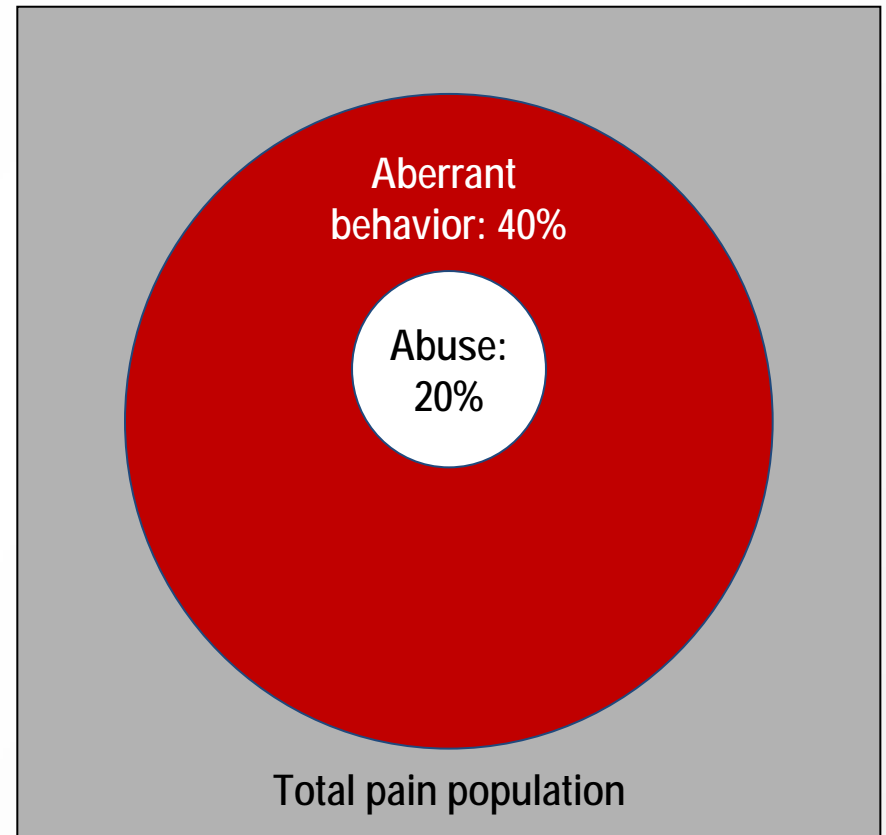
## The Public Health Problem

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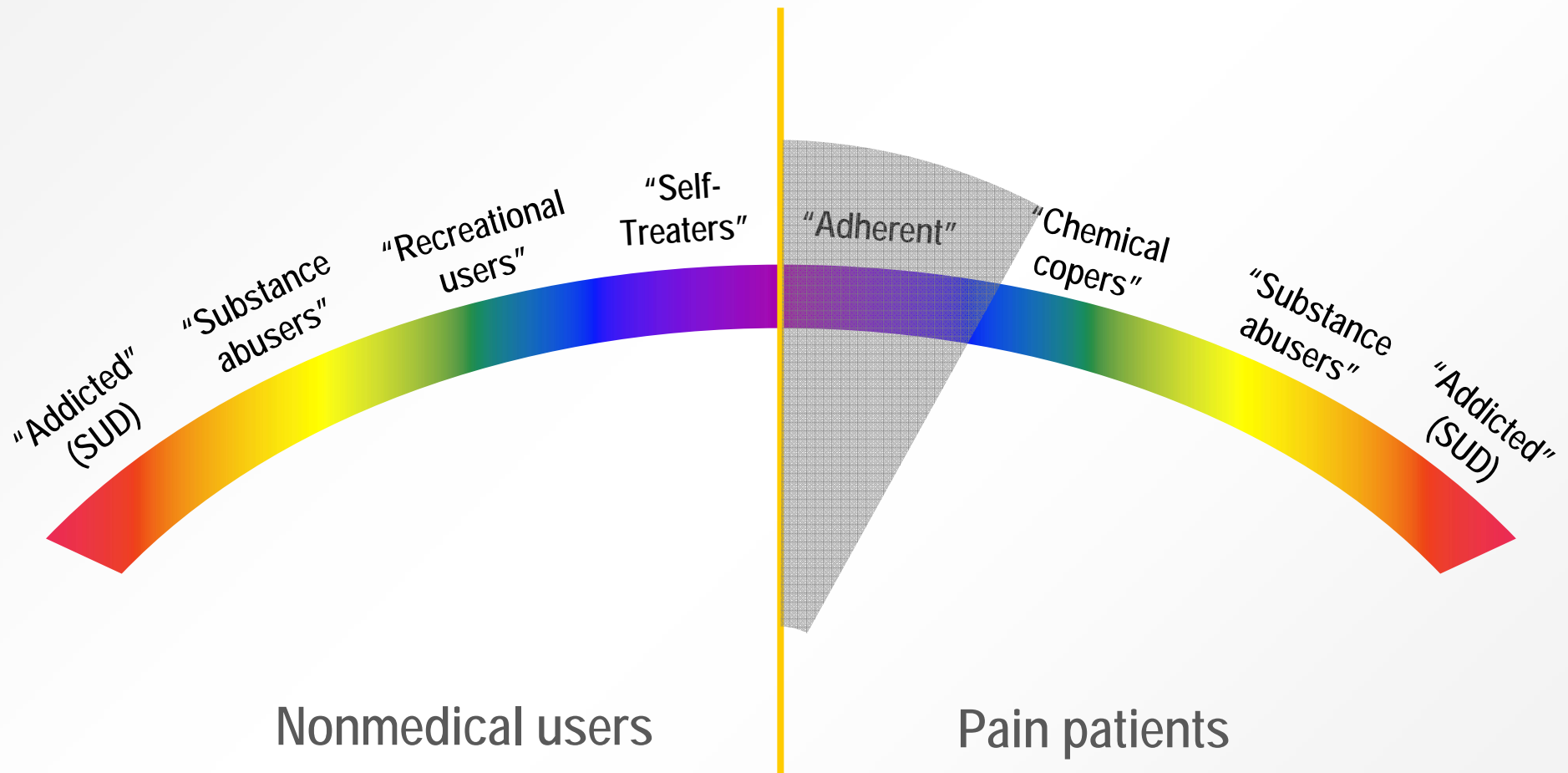
# Prevalence of Opioid Misuse/Abuse in Pain Patients



- > Misuse
  - 40% of opioid-treated chronic pain patients exhibit some form of aberrant behavior
  
- > Abuse
  - 20% of opioid-treated chronic pain patients exhibit behaviors that are consistent with abuse

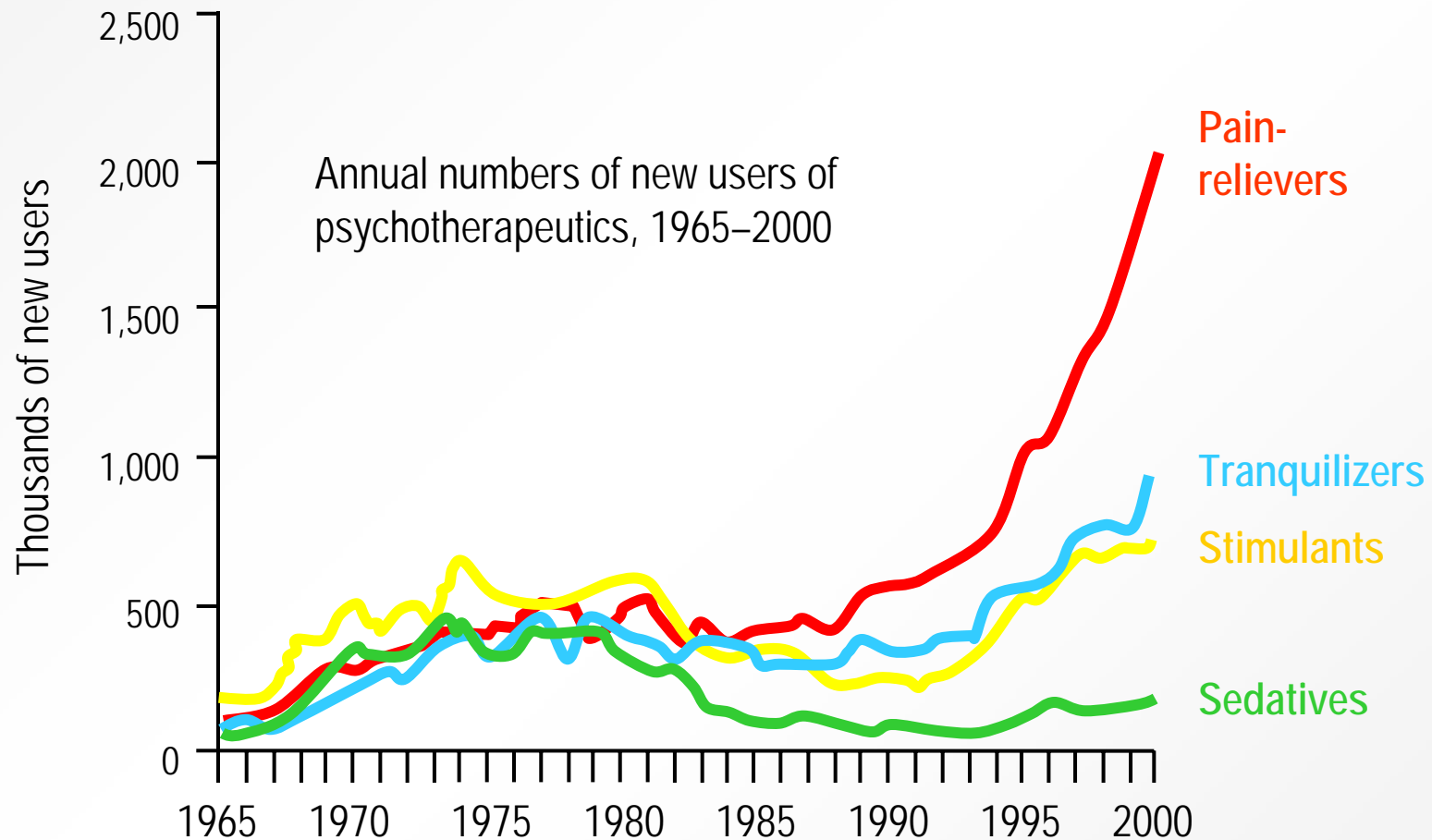


# The Population of Prescription Opioid Users is Heterogeneous



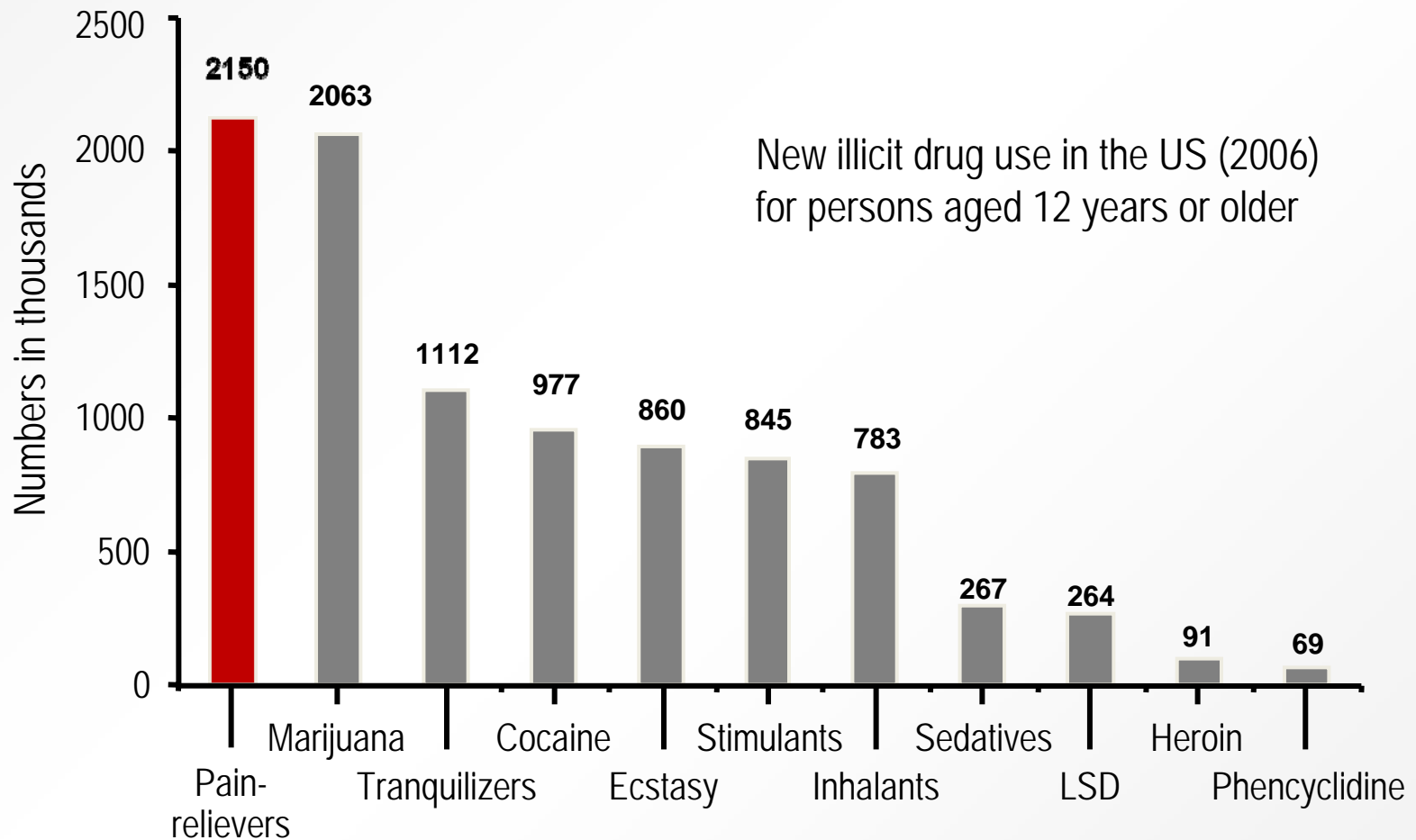
SUD: substance use disorder.  
Passik SD. *Exp Clin Psychopharmacol.* 2008;16:400-4.

# New Nonmedical Users of Psychotherapeutic Agents



Substance Abuse and Mental Health Services Administration (2003). *Results from the 2002 National Survey on Drug Use and Health: National Findings* (Office of Applied Studies, NHSDA Series H-22, DHHS Publication No. SMA 03-3836). Rockville, MD.

# Pain-relievers are the Drug Group Most Abused by the General Public



## Time to Do the Right Thing: Evolution of REMS

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## Time to Do the Right Thing

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- > Steps have been taken to prevent misuse, abuse, and accidental overdose of opioids, but rates have risen over the past decade<sup>1</sup>
- > If misuse and abuse of opioids are allowed to continue unchecked, the government may be forced to discontinue their use
- > It's now time to do the right thing

*"The current strategies for intervening with this problem are inadequate – the risks must be addressed"<sup>2</sup>*

Bob A. Rappaport, MD, Director  
Division of Anesthesia, Analgesia and Rheumatology Products  
Center for Drug Evaluation and Research  
Food & Drug Administration

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1. <http://emedicine.medscape.com/article/287790-overview>. Accessed September 2009; 2. Rappaport BA, March 3, 2009. REMS for Opioid Analgesics: How Did We Get Here? Where are We Going? <http://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM163672.pdf>. Accessed September 2009.

# Evolution of REMS

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Early 1990s

2008

<p><b>Risk Management Plans</b></p> <ul style="list-style-type: none"><li>• Risk assessment</li><li>• Reflected in label</li></ul>	<p><b>Risk Minimization Action Plans (RiskMAPs)</b></p> <ul style="list-style-type: none"><li>• Risk minimization activities eg, education, reminders</li></ul>	<p><b>Risk Evaluation and Mitigation Strategies (REMS)</b></p> <ul style="list-style-type: none"><li>• Elements to assure safe use</li><li>• Assess effectiveness</li></ul>
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# Timeline to REMS

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September 2007

March 2008

2009



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1. <http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCA/SignificantAmendmentsstotheFDCA/FoodandDrugAdministrationAmendmentsActof2007/default.htm>. Accessed September 2009; 2. <http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCA/SignificantAmendmentsstotheFDCA/FoodandDrugAdministrationAmendmentsActof2007/ucm083161.htm>. Accessed September 2009; 3. <http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111350.htm>. Accessed September 2009.

What is REMS?

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## What is a REMS?

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- > REMS = **R**isk **E**valuation and **M**itigation **S**trategy
  - > Designed to manage a known or potential serious risk
  - > Allows appropriate patients continued access to medications
  - > Ensures benefits outweigh any potential safety risks
  
  - > Not driven only by addiction or abuse – there is also a need to ensure that healthcare professionals and patients are fully aware of important safety messages, such as the requirement for patients to be opioid-tolerant before they can take certain medications
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# Components of a REMS: Specifics Will Vary by Product



Medication  
Guide/PPI

Education tools provided to each patient when drug is prescribed/  
dispensed

Communication  
Plan

For example, letters to healthcare providers, communications to  
professional societies, professional education, etc.

Elements to  
Assure Safe Use

Special requirements or restrictions to optimize safe use of  
products

Implementation  
System

Distribution and/or use restrictions that mitigate a serious risk

Timetable for  
Assessment

Minimum FDA requirement 18 months, 3 years, and 7 years after  
REMS approval

*Only mandatory component is 'Timetable for Assessment'  
(but most products with REMS have a medication guide)*

PPI: patient package insert.

Title IX of the FDAAA: REMS Authorities, March 2009. <http://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM163674.pdf>. Accessed September 2009.

# REMS in Other Therapeutic Areas

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- > Risk management programs are not new to medicine
- > Pain medications have not been singled out
- > There are REMS for many other medications

Product	REMS program
Accutane (isotretinoin)	iPLEDGE <sup>1</sup>
Entereg (alvimopan)	EASE Program <sup>2</sup>
Nplate (romiplostim)	NEXUS Program <sup>3</sup>

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1. <https://www.ipledgeprogram.com/>. Accessed September 2009; 2. <http://www.adolor.com/research/index.asp?page=entereg-alvimopan>. Accessed September 2009; 3. <http://www.nplate.com/>. Accessed September 2009.

## Experience with iPLEDGE<sup>1,2</sup>

- > Serious birth defects can occur in pregnant women using isotretinoin
- > iPLEDGE program has improved reporting of pregnancy exposures to isotretinoin
- > There is high compliance in terms of women reading educational materials
  - Nearly all women recall being told by healthcare providers to avoid pregnancy while on isotretinoin
- > Despite initial reactions, patients have accepted it
- > Healthcare providers have a framework for difficult patient conversations
- > Isotretinoin prescriptions dropped after implementation of iPLEDGE but are now back on the rise



"I'm willing to do the extra work because I know it's the right medication for that particular patient"

## Conclusions

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## Conclusions

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- > Opioids are effective analgesics
  - > However, nonmedical use including misuse, abuse, and diversion of opioids is increasing
  - > It is critical to maintain access to these drugs for appropriate patients
  - > As such, it is vital that healthcare providers and patients understand important opioid safety messages
  - > It's time to do the right thing – REMS are necessary to
    - Ensure that the benefits of medications outweigh the risks
    - Minimize harm to patients
  - > REMS exist outside pain medicine, with proven success
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