

Working with Policymakers and Payers to Improve the Incentives for ADFs

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Forum Chair - Abuse Deterrent Coalition



RADARS System Annual Meeting – May 6th, 2016



Disclosures

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- Views reflected herein do not necessarily represent the views of either corporation

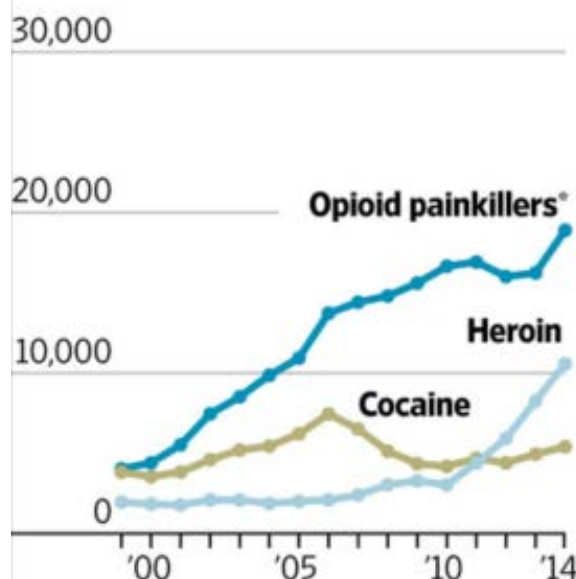
Why We Do What We Do

Every day, 78 people die from an overdose of prescription painkillers in the United States – that's more than 28,000 deaths annually.



Rising Toll

Climbing rates of U.S. overdose deaths from opioid painkillers and heroin have pushed the total number of drug overdose deaths above those from traffic accidents.



*Includes hydrocodone, oxycodone, morphine, codeine and others

Source: Centers for Disease Control and Prevention



THE WALL STREET JOURNAL.

The Washington Post

'We can do more,' FDA says in announcing overhaul of approach to opioid painkillers

The New York Times

Obama Seeks More Than \$1 Billion to Fight Opioid Abuse

By GARDINER HARRIS FEB. 2, 2016



War on Opioid-Abuse

February 5, 2016

New FDA Action Plan and call for more pain management education in medical schools.

By [Nikki Kean](#)



Changing course: A new approach to opioid pain medication at FDA

Posted on [February 5, 2016](#) by [FDA Voice](#)

By: Robert M. Califf, M.D.



Wayne Winegarden and Mia Heck: Addressing West Virginia's drug overdose problem



The Abuse Deterrent Coalition was created to serve as a forum of Abuse Deterrent Formulation Technology Manufacturers, Patient & Issue Associations and Pharmaceutical Manufacturers to educate the public, policy makers and the FDA on the importance of ADF technologies in the fight against prescription drug abuse.

AGENDA

The ability of manufacturers to understand and adhere to federal regulatory requirements and processes has become of increased importance and urgency. This session provides updates to the various changes in the ADF landscape to realistically examine not only what has changed, but where the regulatory process is heading.

- Examine the approach taken by the FDA to approve ADF
 - Compare and analyze ADF and non-ADF opioids given approval and denied
- Investigate the need for ADF development
 - Explore short and long-term benefits of resource allocation
- ADF for stimulants
- Risks associated with ADF investment

Prescription Drug Abuse Deterrence and Incentive Act of 2015

The Changing Debate

2013...

If

2015...

Should & How

201x?...

Must & When

EXAMINING THE APPROACH TAKEN BY THE FDA TO APPROVE ADF

DETECTING ABUSE AND MITIGATING HARM FROM OVERDOSE

In addition to the REMS approach to safety, the FDA has strongly supported the development and assessment of abuse-deterrent formulations of opioids,⁷ five of which the agency has already approved. The pharmaceutical industry has shown significant interest in developing abuse-deterrent opioid formulations and the field is progressing rapidly. The availability of abuse-deterrent formulations raises questions, including how to encourage their use in place of products without abuse-deterrent features and whether to modify criteria for the review and approval of oral opioid formulations that lack abuse-deterrent features or do not offer advantages in abuse deterrence relative to currently marketed products. We will continue to support abuse-deterrent formulations and encourage development of more effective abuse-deterrent features; we are also committed to convening advisory committees to consider new versions of non-abuse-deterrent opioids. In addition, draft FDA guidance on generic abuse-deterrent opioids will review many of the key issues; making this guidance available quickly is a high priority, since the availability of less costly generic products should accelerate prescribers' uptake of abuse-deterrent formulations. However, it is important to recognize that abuse-deterrent formulations by themselves when taken orally do not prevent the development of tolerance or addiction to opioids.



The NEW ENGLAND
JOURNAL of MEDICINE

Role of FDA in the Process

- ❑ Agency has many different responsibilities
 - Ensure the quality and safety during review and approval of new ADF products
 - Develop a roadmap to encourage and guide new ADF developments
 - Evaluate whether ADFs are likely to have meaningful abuse deterrence once launched
 - Make sure that ADF label claims are represented by data
- ❑ Draft Guidance for generic products to contain an ADF issued on March 24th, 2016
- ❑ On April 1, 2015, the FDA issued final guidance on the evaluation and labeling of abuse-deterrent opioids

"It is critical that [...] any characterization of a product's abuse-deterrent properties or potential to reduce abuse be clearly and fairly communicated."

FDA CALLS FOR SWEEPING REVIEW OF OPIOID POLICIES



U.S. Food and Drug Administration
Protecting and Promoting Your Health

FDA News Release

Califf, FDA top officials call for sweeping review of agency opioids policies

Expand access to abuse-deterrent formulations (ADFs) to discourage abuse. The pharmaceutical industry has shown significant interest in developing ADFs and the technology is progressing rapidly. ADFs hold promise as their abuse-deterrent qualities continue to improve and as they become more widely available. The FDA will issue draft guidance with its recommendations for the approval standards for generic abuse-deterrent formulations. Release of this guidance is a high priority, since the availability of less costly generic products should accelerate prescribers' uptake of ADFs. **Outcome:** Spur innovation and generic ADF product development.

SFGATE

New FDA chief cites promise of harder-to-abuse pain drugs

Califf has already pledged to add stronger warning labels to the most-commonly prescribed opioids, and to consult more with outside advisers. **On Tuesday he highlighted the potential of new painkillers designed to discourage abuse.** For instance, the latest version of OxyContin is harder to crush for snorting. When dissolved it turns into a thick jelly that is difficult to inject.

Why is It Important to Consider Multiple Stakeholders in the ADF Space?

- ❑ Misuse, abuse and diversion of prescription drugs has significantly increased over the past 10-15 years
- ❑ It has been recognized as a public health issue of epidemic proportions
- ❑ A variety of initiatives to curb Rx abuse have been implemented

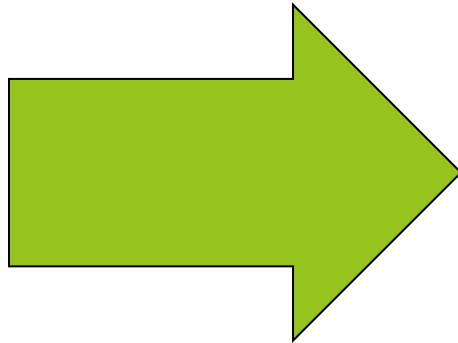
However

- Misuse, abuse and diversion is often considered a societal or just a law enforcement issue only
- No single stakeholder has enough leverage

What are the driving forces around ADFs

Societal concern
about Rx drug
abuse

“A US Public
Health epidemic”



Some care more about this....

FDA

DEA

DAs

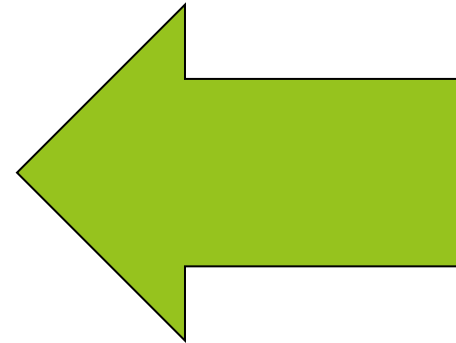
AGs

Lawmakers

**Other
authorities**

Societal concern about
access to affordable
pain medicines

“A US Public
Health epidemic”



... and many care about this as well.

Multimodal Interaction Required

- ❑ Create awareness and understanding about the impact of ADFs (incremental improvement)
 - Educate about ADFs and improvements at payer level
 - Educate policy makers about current barriers for ADFs
- ❑ Clarity about the requirements in the market
 - Policymakers to support FDA in their ability to mandate ADF
 - FDA to develop clear guidelines and a roadmap for mandated ADF requirement
- ❑ Work on improved labeling
 - Enable prescribers and payers to encourage the use of ADFs
 - How can FDA support to encourage the use of ADFs and/or discourage the use of non-ADFs

All aspects are interrelated!

ADF labeling to date

Approved by FDA

(all are extended-release formulations)

Drug Product	Drug Substance(s)	Sponsor	Approval	Marketed
Xtampza™ ER	oxycodone	Collegium	11/06/2015	2H, 2016
MorphaBond	morphine	Inspiron	10/02/2015	--
Hysingla ER	hydrocodone	Purdue Pharma L.P.	11/20/2014	✓
Embeda	morphine + naltrexone (sequestered)	Pfizer	10/17/2014	✓
Targiniq ER	oxycodone + naloxone	Purdue Pharma L.P.	07/23/2014	--
OxyContin	oxycodone	Purdue Pharma L.P.	04/05/2010	✓

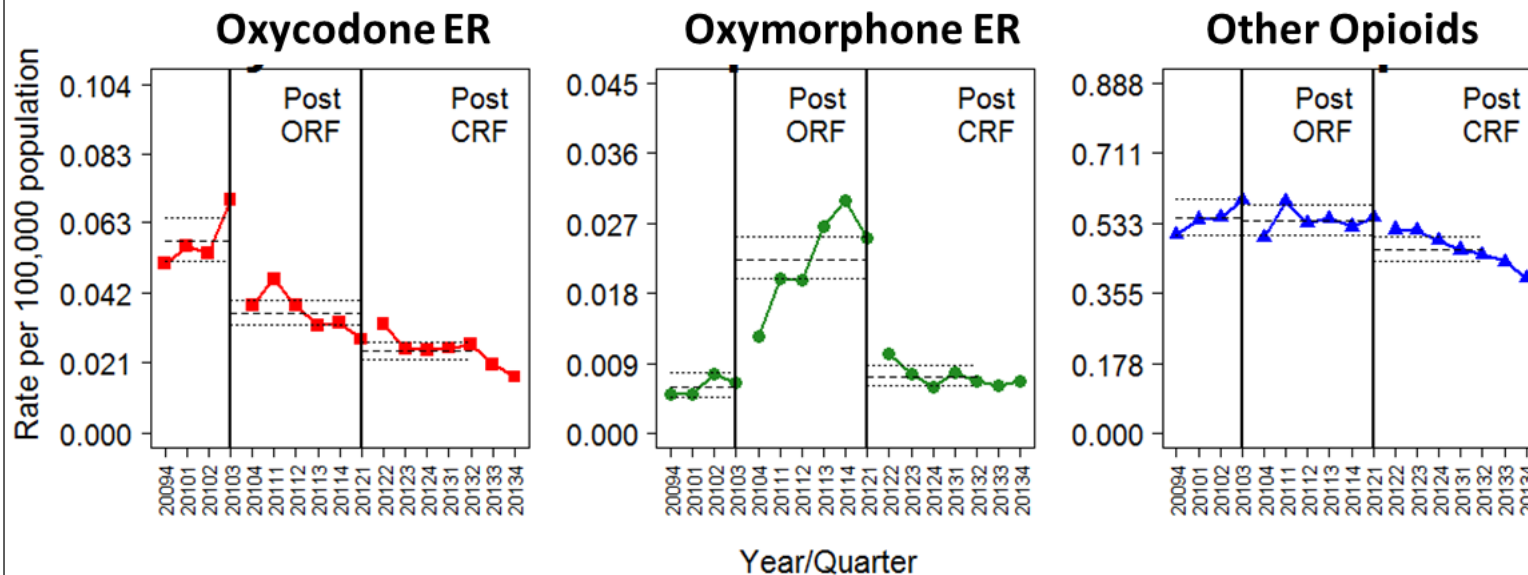
Formulations designed to deter abuse **under review** by FDA

(ER=extended-release; IR=immediate-release formulations)

Drug Product	Drug Substance(s)	Sponsor	Source
KP201	IR benzhydrocodone/acetaminophen	KemPharm	02/10/2016 Press Release ¹
CEP-33237	ER hydrocodone	Teva	02/25/2015 Press Release ²
ALO-02	ER oxycodone + naltrexone (sequestered)	Pfizer	02/13/2015 Press Release ³
MNK-155	ER hydrocodone + acetaminophen	Depomed	05/28/2014 Press Release ⁴

ADFs do in fact have an impact on abuse

Poison Center Program Population Rate, 2009-2013



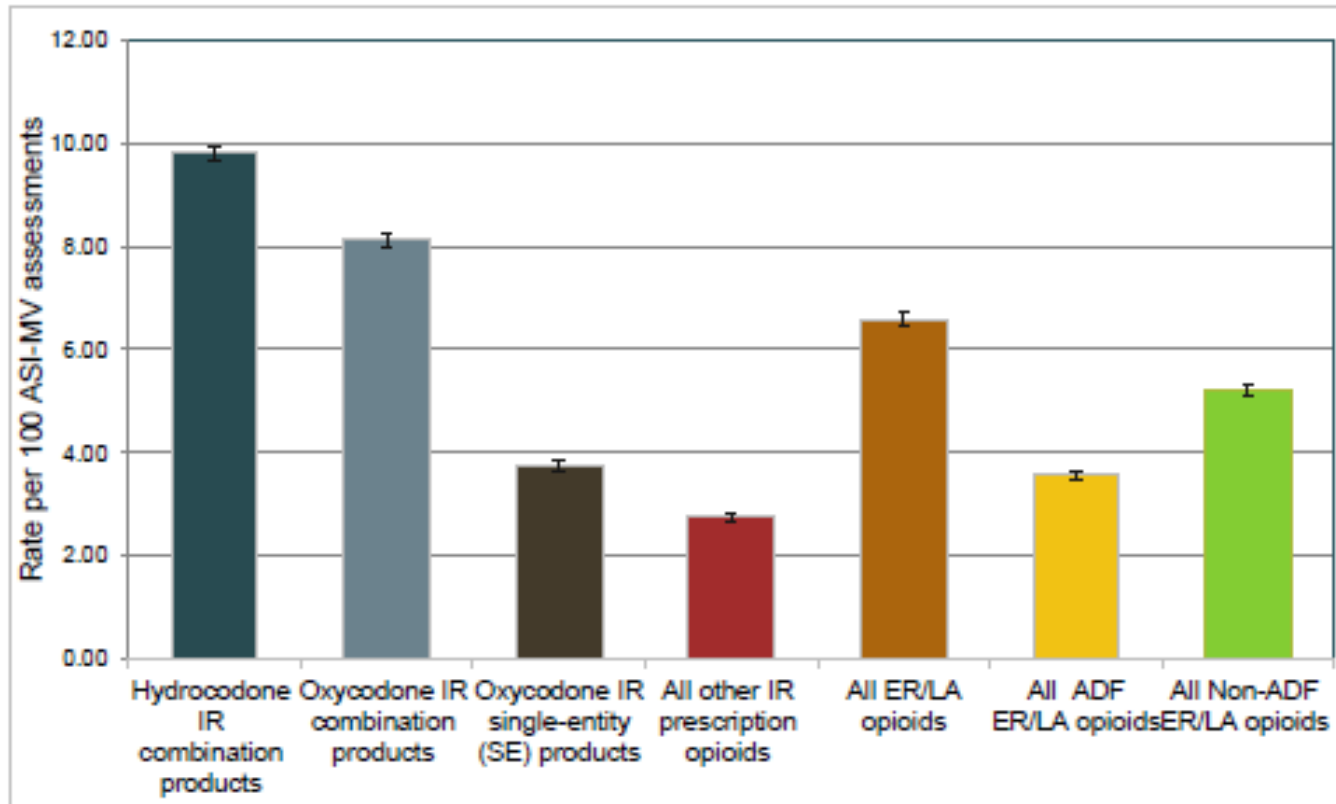
*Other opioids excluding ER oxycodone and ER oxymorphone

Source: RADARS System data. — Presented by Richard C. Dart, MD, PhD - Director, RMPDC; Professor, University of Colorado — Presented at Nat Rx Drug Abuse Summit 2014, Atlanta/GA

IR Opioid abuse patterns

Adult substance abusers assessed for abuse treatment planning (N=151,704)

Figure 1. Past 30-Day Abuse per 100 Assessments



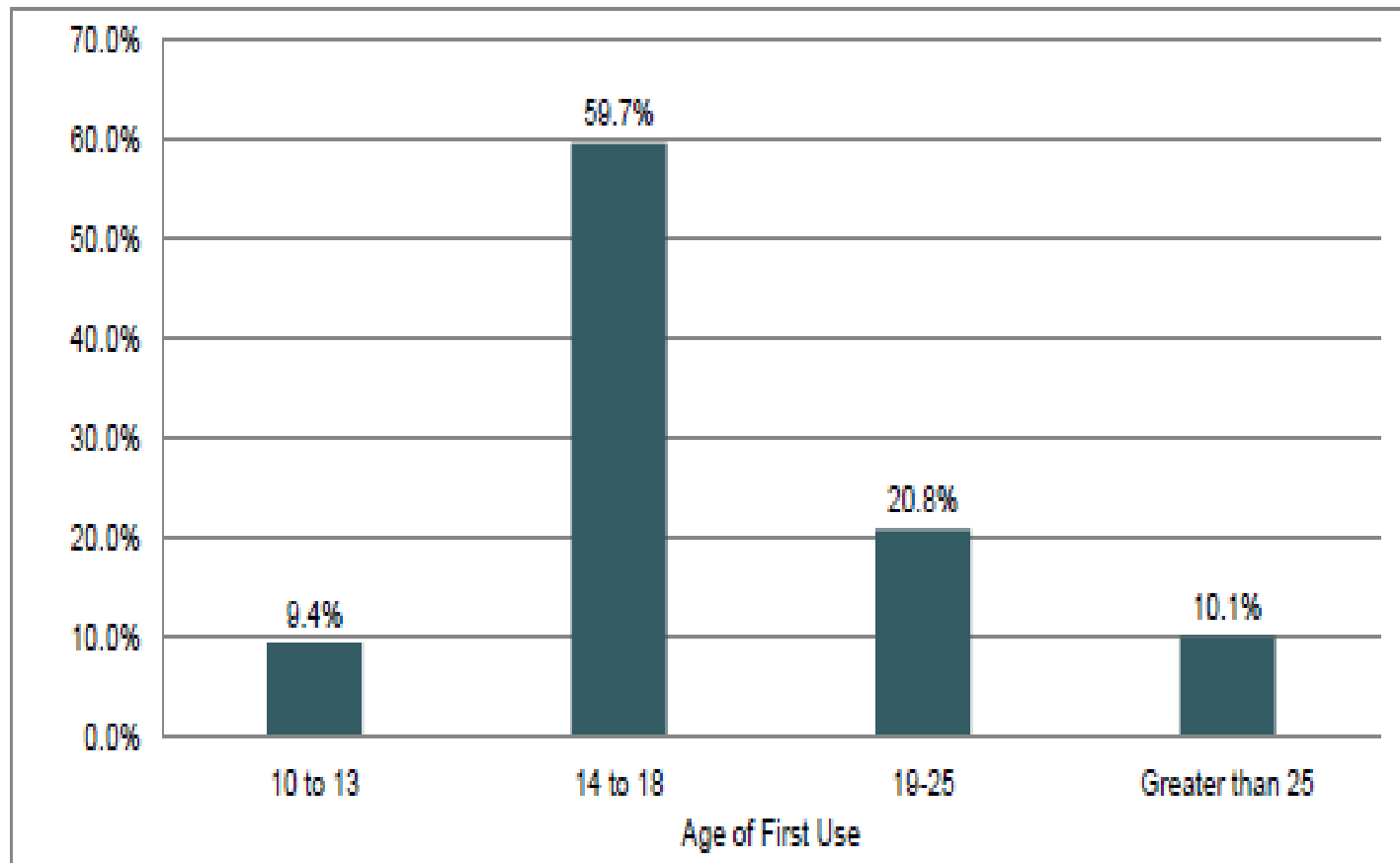
Source:
2015

Cassidy et al.; "Abuse prevalence and patterns for immediate-release hydrocodone combination products"; PAINweek

IR Opioid abuse patterns

Internet survey among adult abusers (N=304)

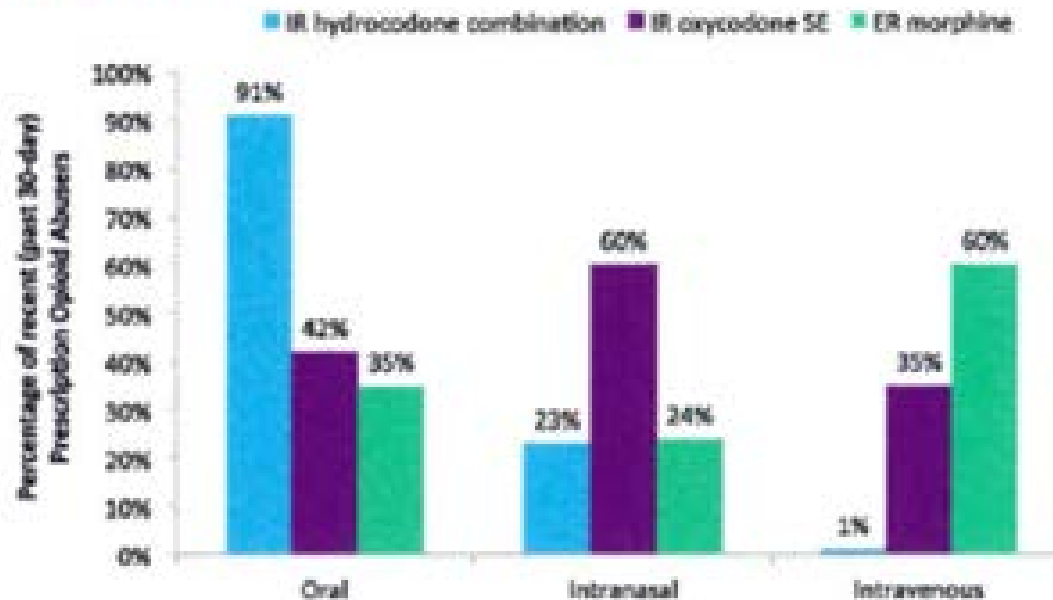
Figure 1. Age at first hydrocodone IR product use among lifetime users



Source: Cassidy et al.; "Patterns of abuse of hydrocodone combination products: Results from an Internet survey of recreational drug users"; PAINweek 2015

Contrary to current FDA belief non-oral (IN) abuse of Hydrocodone/APAP is significant and relevant

Figure 2. Percentage of Recent Prescription Opioid Abusers Reporting Oral, Intranasal, and Intravenous Abuse



Source: NAWPPRO, #Q11-SQ13

Source: Poster presentation at CPDD, June 2015

Stimulant abuse – Signs parallel those of the opioid crisis

- Misuse and abuse of Rx stimulants (DEA schedule II class with high abuse potential) is already prevalent and on the rise ^{1) 2) 3) 4) 5) 6) 7) 8) 9)}
- Abuse of Rx stimulants includes significant non-oral abuse and results in the risk for significant mental and physical health hazards ^{4) 6) 7) 10)}
- Market for Rx stimulants has grown and is expected to continue to grow mainly driven by increased number in ADHD patients/treatments ^{10) 11) 12)}
- Physicians, although aware of the general abuse liability of stimulants, are not adjusting their prescribing behaviors ^{11) 12)}
- Physicians are largely unaware of the need and role of abuse deterrent products in the stimulant space, but favor the development of less abused products incl. ADF reformulations of existing products ^{11) 12)}
- FDA acknowledges the benefit of ADF for stimulants but has not yet taken any action to require reformulations ¹³⁾

1) www.samsha.gov 2) www.deadiversion.usdoj.gov 3) McCabe et al., 2014 4) Monitoring the Future Report (2012)
5) Zosel et al., 2013 6) Sembower et al., 2013 7) Cassidy et al., 2012 8) Bright G.M, 2008 9) RADARS – BU-NA commissioned report, data on file (2015) 10) Express Scripts Lab report (2014) 11) DefinedHealth ADHD market research TRF stimulants for ADHD – BU-NA commissioned report, data on file (2015) 12) Decisions Resources ADHD report (2015) 13) FDA regulations.gov

Nonmedical use of Rx Stimulants – An increasing problem from the Federal Health Agency's view



The screenshot shows the SAMHSA (Substance Abuse and Mental Health Services Administration) website. The header includes the SAMHSA logo, a search bar, and social media links for Facebook, Twitter, YouTube, and a blog. A navigation bar lists various sections: Find Help, Topics, Programs & Campaigns, Grants, Data, Priorities, About Us, and Publications. The main content area features a newsroom section with a sidebar containing links to Newsroom, Media Guidelines for Bullying Prevention, Press Announcements, SAMHSA in the News, and Speeches and Presentations. The featured article is titled "Stimulant-related emergency department visits rise 300 percent among younger adults" and is dated Thursday, August 8, 2013. The article text states: "A new report by the Substance Abuse and Mental Health Services Administration (SAMHSA) shows that some drug-related emergency department visits increased by 300 percent -- from 5,605 visits in 2005 to 22,949 visits in 2011. These visits, made by adults aged 18 to 34, were related to the nonmedical use of central nervous system (CNS) stimulants. On average, about 30 percent of these visits also involved alcohol. In 2011 there were approximately 1.24 million emergency department visits related to the nonmedical use of pharmaceuticals, which include prescription and over-the-counter medications as well as supplements."

Substance Abuse and Mental Health Services Administration
SAMHSA

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Newsroom » Press Announcements » Stimulant-related emergency department visits rise 300 percent among younger adults

Stimulant-related emergency department visits rise 300 percent among younger adults

Thursday, August 8, 2013

A new report by the Substance Abuse and Mental Health Services Administration (SAMHSA) shows that some drug-related emergency department visits increased by 300 percent -- from 5,605 visits in 2005 to 22,949 visits in 2011. These visits, made by adults aged 18 to 34, were related to the nonmedical use of central nervous system (CNS) stimulants. On average, about 30 percent of these visits also involved alcohol.

In 2011 there were approximately 1.24 million emergency department visits related to the nonmedical use of pharmaceuticals, which include prescription and over-the-counter medications as well as supplements.

<http://www.samhsa.gov/newsroom/press-announcements/201308080100> (accessed August 28, 2015)

rate rises to 850 initiates a day.

Non-medical use of stimulant medication is also at its peak in November, December, and April. Each year about 137,000 full-time college students start using prescription stimulants non-medically (400 on an average day). During November, December, and April the average daily initiation rate climbs to above 500 (peaking at 585 in November).

Although the report is not designed to determine the cause behind the trends in initiation, the rise in the initiation of

<http://www.samhsa.gov/newsroom/press-announcements/201508271215> (accessed August 28, 2015)

Nonmedical use of Rx Stimulants – An increasing problem also from DEA perspective

U.S. DEPARTMENT OF JUSTICE • DRUG ENFORCEMENT ADMINISTRATION
OFFICE OF DIVERSION CONTROL

NFLIS NATIONAL FORENSIC
LABORATORY
INFORMATION SYSTEM

**Special Report: ADD/ADHD Stimulants in NFLIS,
2007-2011**

Highlights
An estimated total of 13,697 reports of attention deficit disorder (ADD) and attention deficit hyperactivity disorder (ADHD) stimulants were submitted to State and local forensic laboratories in the United States from January 1 through December 31, 2011, and analyzed by March 31, 2012.

Introduction
The National Forensic Laboratory Information System (NFLIS) is a program of the Drug Enforcement Administration (DEA), Office of Diversion Control, which systematically collects


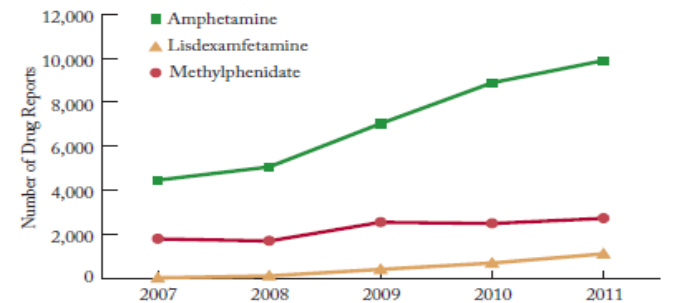


Table 1 *ADD/ADHD STIMULANT REPORTS TO NFLIS, 2007 AND 2011*

Drug	2007		2011	
	No.	% of Total	No.	% of Total
Amphetamine	4,451	71.4	9,890	72.2
Lisdexamfetamine	4	0.1	1,097	8.0
Methylphenidate	1,776	28.5	2,710	19.8
Total ADD/ADHD Stimulants	6,231	100.0	13,697	100.0

Figure 1 National trends of ADD/ADHD stimulants in NFLIS, 2007-2011



Toxic Exposures

The Substance Abuse and Mental Health Services Administration's Drug Abuse Warning Network (DAWN) tracks emergency department (ED) visits involving CNS stimulants (including amphetamine, dextroamphetamine, methylphenidate, and miscellaneous drugs). These ED visits increased 37% over the period from 2007 to 2010 (from 48,732 to 66,888 visits). ED visits specifically for the ADD/ADHD stimulants amphetamine,

dextroamphetamine, and methylphenidate increased 21% (from 24,856 to 30,175 visits). Controlling for population size, in 2010 there were 17.5 visits involving any CNS stimulant per 100,000 general population, but 63.9 visits for persons aged 18 to 20. The rate of visits specifically involving the ADD/ADHD stimulants amphetamine, dextroamphetamine, and methylphenidate was 30.0 visits per 100,000 persons aged 18 to 20, whereas rates for other age groups ranged from 9.4 to 16.2 visits.

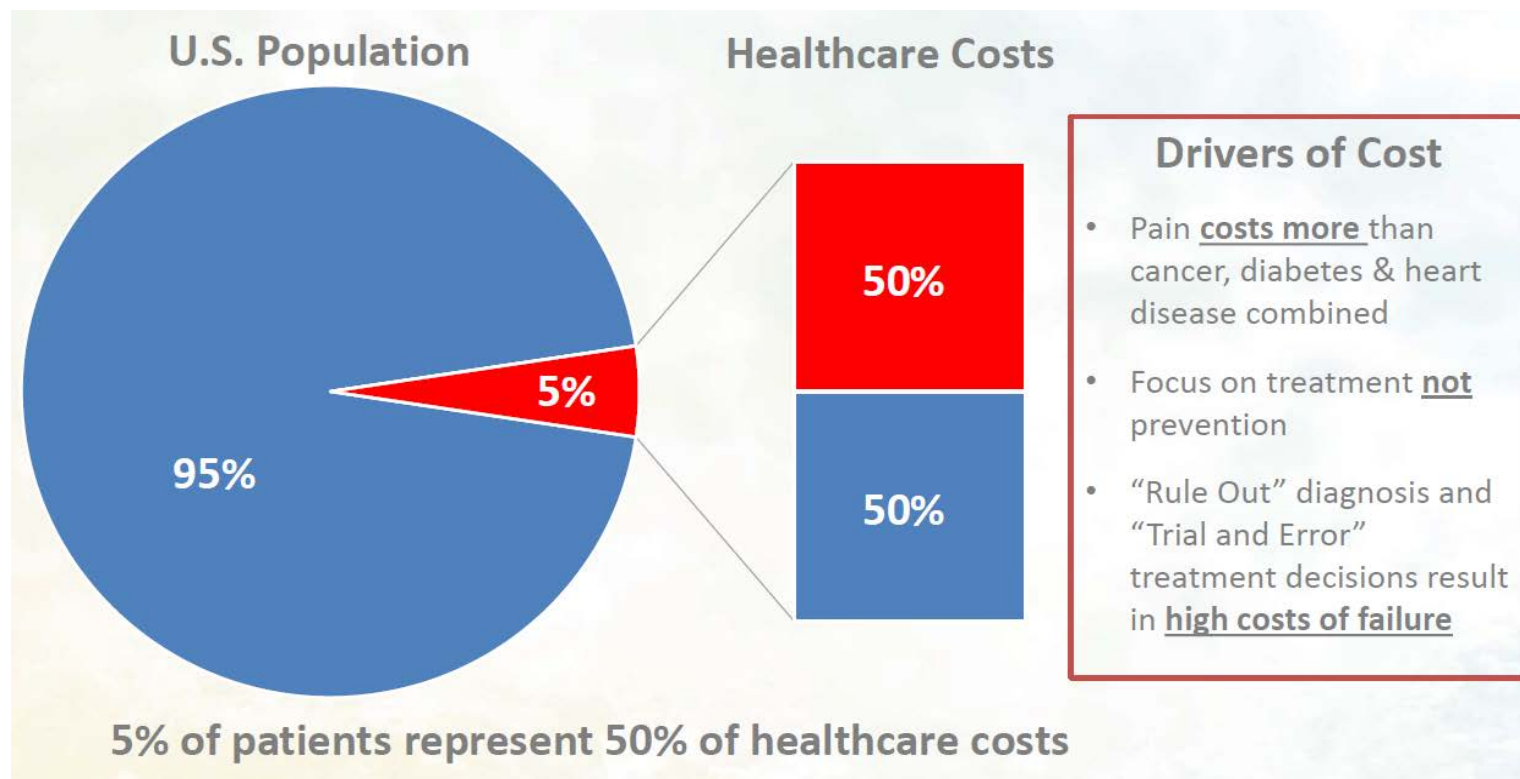
INVESTIGATING THE NEED FOR ADF DEVELOPMENT

Increasing the number of generic opioids with ADF properties is critical for preventing opioid abuse.

2015	Generic Opioids	Branded Opioids
Number of pills prescribed	240,120,330	8,853,402
Number of pills with ADF properties	5,329,632	5,068,398

Nearly **60% of branded opioids** contain ADF properties, compared to only **2% of generic products**

U.S. Healthcare System Remains Highly Inefficient



Approximately \$800 billion spent on chronic pain

Source: Proove Biosciences Inc. 2016 Pain Forum Presentation.

INVESTIGATING THE NEED FOR ADF DEVELOPMENT

“Prescribing abuse-deterrent opioids implies that many patients will be switching from lower-priced generic drugs to higher-priced patented drugs – at least until generic versions of abuse-deterrent formulations become available. **The question naturally arises: are the current higher prices for abuse-deterrent opioids worth the expense?**”

Forbes

- Wayne Winegarden,

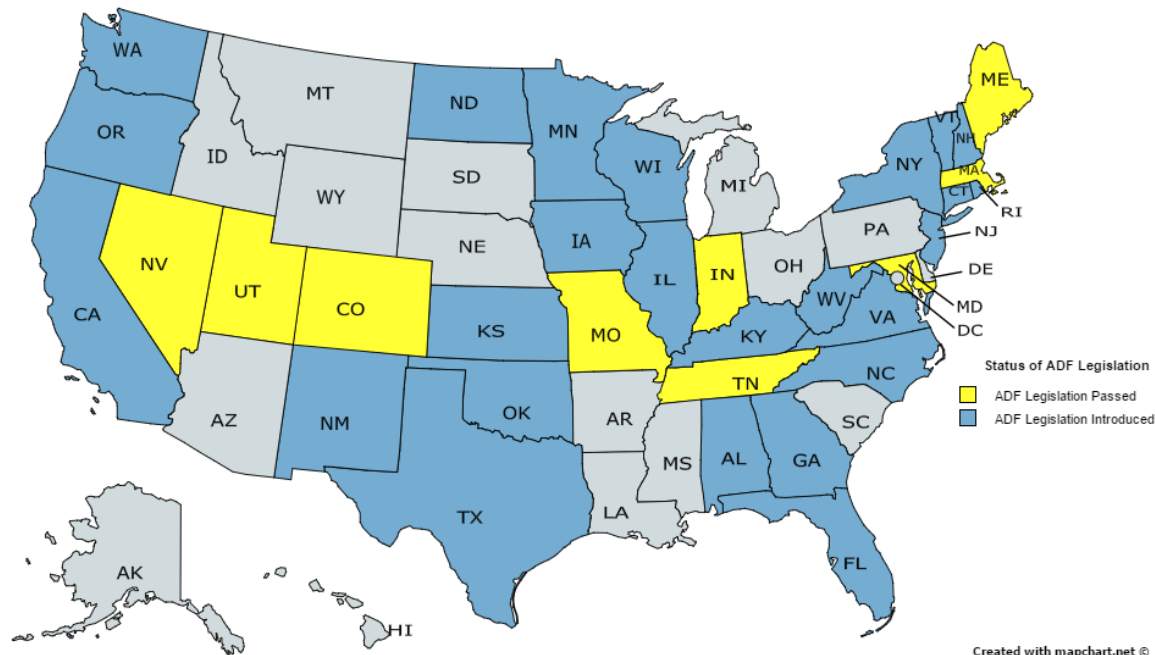
Total Annual Benefits per Patient from Abuse-deterrent Opioids			
	Benefit per Patient	Additional Per-patient Annual Cost Premium of Abusers	Percentage Reduction
Health expenses commercially-insured	\$2,146.51	\$9,456	22.70%
Health expenses Medicaid/Uninsured	\$2,070.18	\$11,501	18.00%
Non-health related expenses	\$2,498.26	\$12,414	20.1%

A study that examined the impact from an abuse-deterrent formulation found that it reduced abuse of opioids by 18 percent among Medicaid patients and 23 percent for commercially insured patients.

In total, such a reduction in opioid abuse creates \$1 billion in benefits.

Concern for opioid abuse remains high but there is need for support of ADF policy

- The DEA **rescheduled hydrocodone** from Class III to Class II, effective as of October 2014¹
- More and more states introduce **abuse-deterrent properties (ADP) legislation**
- In general, plans must provide equal or preferred coverage for ADF as for non-ADF products



¹DEA. Rescheduling of Hydrocodone Combination Products From Schedule III to Schedule II. August 22, 2014. http://www.deadiversion.usdoj.gov/fed_regs/rules/2014/fr0822.htm.

National omnibus research confirms strong support for federal standards to mandate ADFs

- **Almost 2/3** of adults believe The Food & Drug Administration should require that pharmaceutical manufacturers include an Abuse Deterrent Formulation in all of their most abusable drugs currently available, both name-brand and generic.
- **55%** of adults think pharmaceutical companies should be allowed up to three years to make their products safer to ensure there are no drug shortages.
- **71%** believe The Food & Drug Administration should be responsible for developing a uniform federal standard for Abuse Deterrent Formulation in drugs.
- **65%** would support legislation introduced in the US Congress to require all pharmaceutical manufacturers to add the latest and most effective Abuse Deterrent Formulation to their most highly abusable drugs (as determined by the Drug Enforcement Agency) within the next four years. It would include strict safeguards to ensure patients in pain received appropriate treatment as determined by their physician.

Survey by Repass Partners. Sample: 1,500 adults 18+; Geography: US/Weighted to Census Demographics; Data Collection: Online, double opt-in panel; Data Collection Dates: February 9-18, 2016



National omnibus research confirms strong support for federal standards to mandate ADFs

- Some people believe the best use of governmental resources to combat drug abuse is to wean abusers off of the prescription medications, while others believe the best solution is to deter teens and others who have not yet abused prescription drugs by making them more difficult to abuse. **However, the vast majority (65%) favor both approaches as equally important.**
- It is estimated that the cost to apply the latest Abuse Deterrent Formulation technology designed to deter injection or inhalation of prescription pain medications or stimulants would be less than the cost of treating people who would subsequently begin to abuse those drugs. **64% support this type of legislation.**

Survey by Repass Partners. Sample: 1,500 adults 18+; Geography: US/Weighted to Census Demographics; Data Collection: Online, double opt-in panel; Data Collection Dates: February 9-18, 2016



Summary on results of US Government Relations

- ADC has become the driver in the strategy for a mandated FDA requirement for ADF.
- ADC is being positioned as a solution provider and a stakeholder network is being built.
- A tactical process to promote awareness for ADF legislation (“Son of STOPP”) has been laid out and is being initiated.
- A detailed communication plan has been compiled for 2016.
- Timeline for the legislative process cannot be guaranteed.
- Legislative goal is to introduce the bill, both as a “free standing” initiative and as part of correctional legislation to ACA, expected in the next Congress.
 - Legislative strategy is designed to drive regulatory action
- In response to CARA, the Energy and Commerce Committee passed an amendment exempting ADF’s from the definition of line extension.



Senator Tim Kaine



Senator Shelly
Moore Capito



Senator Kelly Ayotte



Senator Richard
Blumenthal



Senator Pat
Toomey

114TH CONGRESS S. _____
1ST SESSION

IN THE SENATE OF THE UNITED STATES

February xx, 2016

MRS. XX (for herself, and ...) introduced the following bill;
which was referred to the Committee on _____

A BILL

To reduce prescription drug diversion and abuse and to
implement requirements for the adoption of abuse-
deterrent medications.

1 *Be it enacted by the Senate and House of*
2 *Representatives of the United States of America in Congress*

DRAFT BILL

Abuse Deterrence Coalition Members

www.abusedeterrent.org

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Nursing®

CLAAD Center for Lawful Access
and Abuse Deterrence

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intellipharma

Summary

- ❑ ADFs are being recognized as a valuable component in the combat against Rx drug abuse – Opioids & Stimulants
- ❑ FDA increasingly acknowledges its responsibility to provide guidance to industry for ADF development and to bring more ADF products (incl. IR opioids) to market
- ❑ Real-life incentives are still missing and adequate labeling and support from payers are key hurdles
- ❑ Working with all relevant stakeholders to create awareness, acceptance and incentives is still to be improved and intensified

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