ADF Replacement (oxycodone hydrochloride) Abuse-Deterrent Immediate-Release Tablets

November 14, 2018

Mallinckrodt Pharmaceuticals

Joint Meeting of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee

Introduction

Martha Schlicher, PhD

Vice President

Research and Development, Generic Business Unit

Mallinckrodt Pharmaceuticals

Reducing Opioid Abuse:
An Important Public Health Priority for FDA

"Transitioning from the current market, dominated by conventional opioids, to one in which most opioids have abuse-deterrent properties, holds significant promise for a meaningful public health benefit."

- FDA Statement, 2017

Mallinckrodt Requesting Approval for ADF Replacement

- Mallinckrodt immediate-release (IR) single-entity (SE) oxycodone tablets currently 15% of market
  - Roxicodone®
  - Generic oxycodone
- Requesting NDA approval for abuse-deterrent formulation (ADF) with label claims
  - Intranasal (IN)
  - Intravenous (IV)
- Mallinckrodt intends to replace all currently marketed IR SE oxycodone tablets with ADF Replacement (MNK-812)

ADF Replacement Characteristics

- Conventional solid dosage manufacturing process
  - Five strengths: 5, 10, 15, 20, 30 mg

Attribute	Purpose
Hard, non-brittle tablet	Provide resistance to physical manipulation
Gelling agents	Produce viscous solution in small volumes of aqueous solvents to deter IV abuse
Aversive agents	Create nasal irritation to discourage IN abuse

Components of ADF Replacement Tablets

Proposed Function	Component
Active pharmaceutical ingredient (API)	Oxycodone HCl
Abuse deterrence	Tartaric acid* Citric acid Effersoda* Polyethylene glycol Polyethylene oxide Glucomannan Sodium carboxymethyl cellulose Hydroxypropylmethyl cellulose Xanthan gum
Other	Butylated hydroxytoluene Magnesium stearate Opadry® coating materials

- **Does not contain high molecular weight (HMW) PEO as used in Opana® ER**
- **HMW PEO in ADF Replacement similar to that in OxyContin® at > 20x lower amounts**

- All excipients generally regarded as safe (GRAS) or in FDA-approved oral drug products

*** Also functions as disintegrant**

ADF Replacement is Bioequivalent to Roxicodone

- Submitted for FDA approval under the 505(b)(2) pathway
- Bioequivalence studies demonstrate ADF Replacement is therapeutically equivalent to Roxicodone
- Meets regulatory requirements for approval and would receive same indication as Roxicodone

…an opioid agonist indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate

Key Findings from Abuse Deterrence Studies Support Label Claims

Intranasal (IN)

- Resisted physical manipulation
- Reduced early positive effects
- Difficult to snort; aversive agents caused pain and burning
- Subjects did not express willingness to snort again

Intravenous (IV)

- Multiple gelling agents
- Resisted all common IV methods
- Multi-step procedure with advanced techniques required
- No evidence of overt toxicity from injection of extracts

ADF Replacement can be expected to reduce abuse compared to products it would replace

Mallinckrodt Committed to Opioid REMS Requirements

- Medication Guide
- Elements to Assure Safe Use
  - Healthcare provider training
  - Independent continuing education activities
  - Tools on safe use, storage, and disposal of opioids
  - Encourage training on safe use and appropriate prescribing
- REMS assessments to FDA

Additional Post-Market Activities to Provide Important, Meaningful Information

- Additional safety measures
  - Enhanced pharmacovigilance, tailored AE questionnaire
  - Web monitoring for safety signals
- Additional intended vs. unintended use information
  - Prescription rates / transition
  - Street price data
  - Drug user chat rooms
  - Poison control center monitoring and product-specific inquiries
- Physician focus groups to understand education needs on limitations of ADFs
- Category 4 studies to evaluate effectiveness in reducing abuse

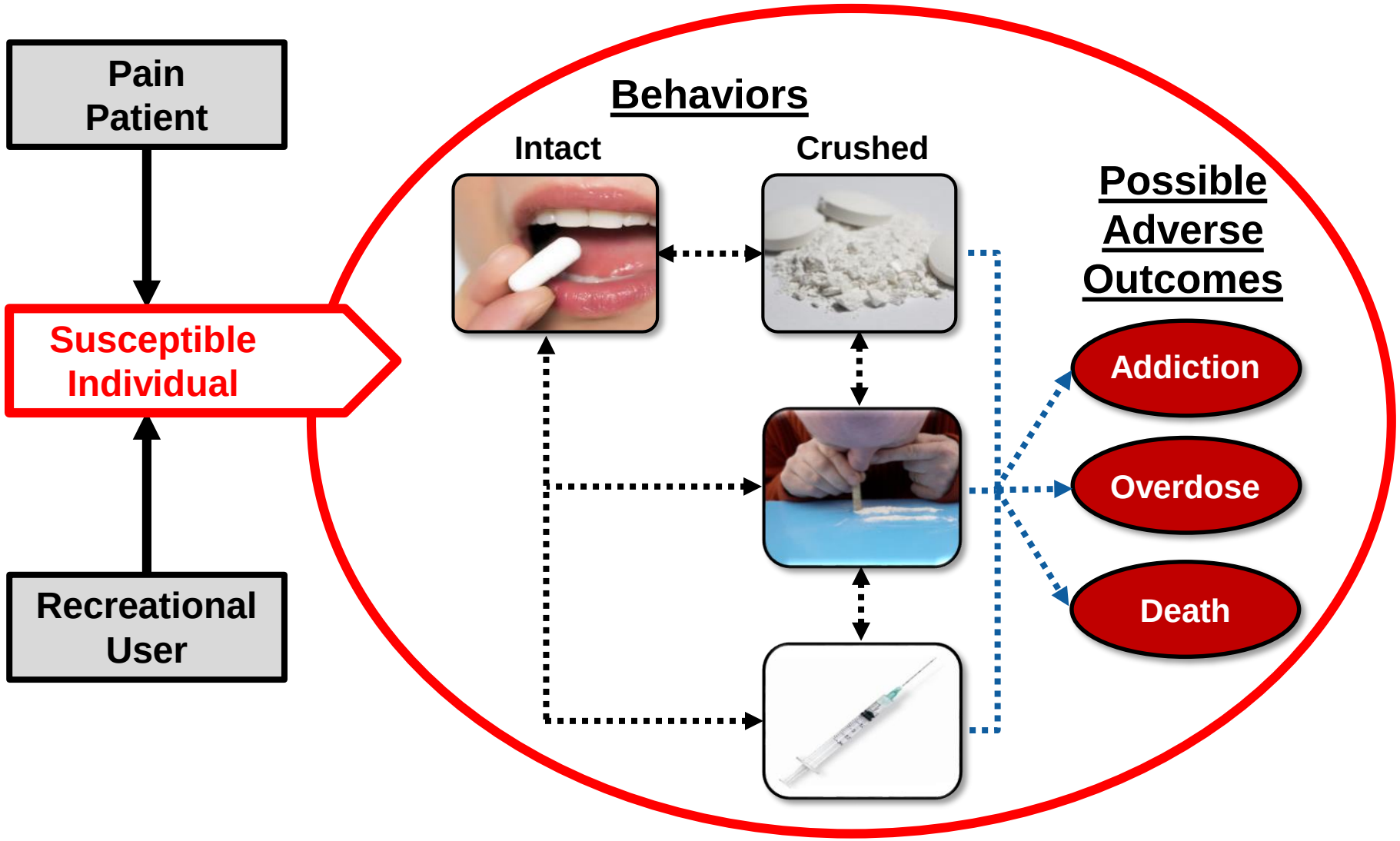
Agenda

Public Health Need for Abuse-Deterrent IR Opioid Analgesics	**Richard Dart, MD, PhD** Director, Rocky Mountain Poison & Drug Center Executive Director, RADARS® System
Category 1 *In Vitro* Studies	**Edward Cone, PhD** Principal Scientist, Drug Delivery & Abuse-Deterrent Drug Products Pinney Associates
Nonclinical Excipient Safety Studies	**Mike Orr, PhD, DABT** President/CEO Orr Nonclinical Consulting, LLC
IN Human Abuse Potential Study	**Sandra Comer, PhD** Professor of Neurobiology (in Psychiatry) Division on Substance Use Disorders Columbia University
Clinical Perspective	**Jeff Gudin, MD** Director, Pain Management & Palliative Care Englewood Hospital and Medical Center

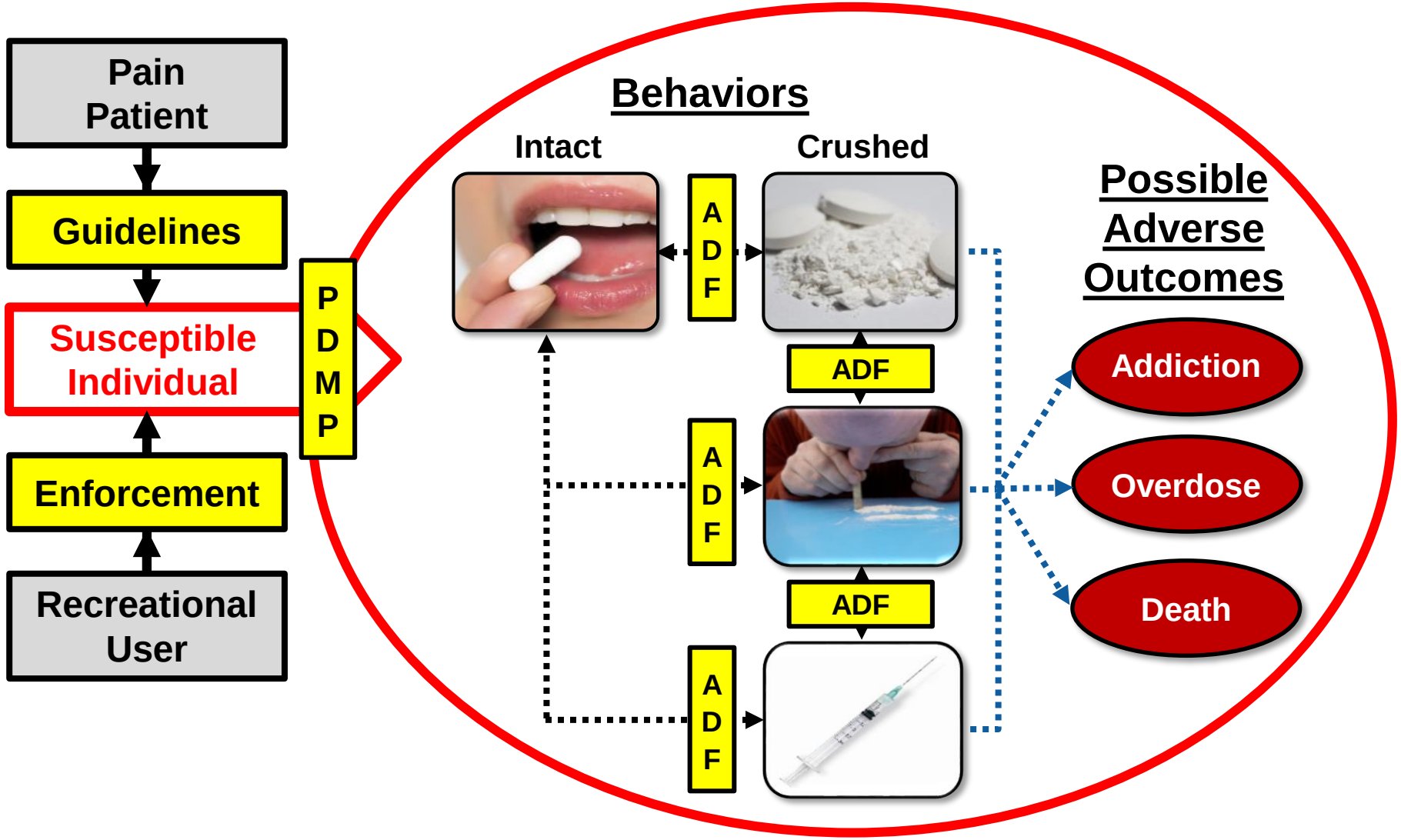
Public Health Need for Abuse-Deterrent IR Opioid Analgesics

Richard C. Dart, MD, PhD
Director, Rocky Mountain Poison & Drug Center
Professor of Emergency Medicine,
University of Colorado School of Medicine
Executive Director, RADARS® System

Pathways to Opioid Abuse



ADFs Offer Potential to Deter Initiation to Non-Oral Routes of Abuse



Expectations and Limitations of ADFs

What ADFs CAN Do

- Reduce IN and IV abuse of specific product
- Make diversion less attractive
- Deter initiation to non-oral routes of abuse

What ADFs CANNOT Do

- Reduce IN and IV abuse of other opioids
- Reduce oral overconsumption

ADFs Can Impact Different Types of Individuals

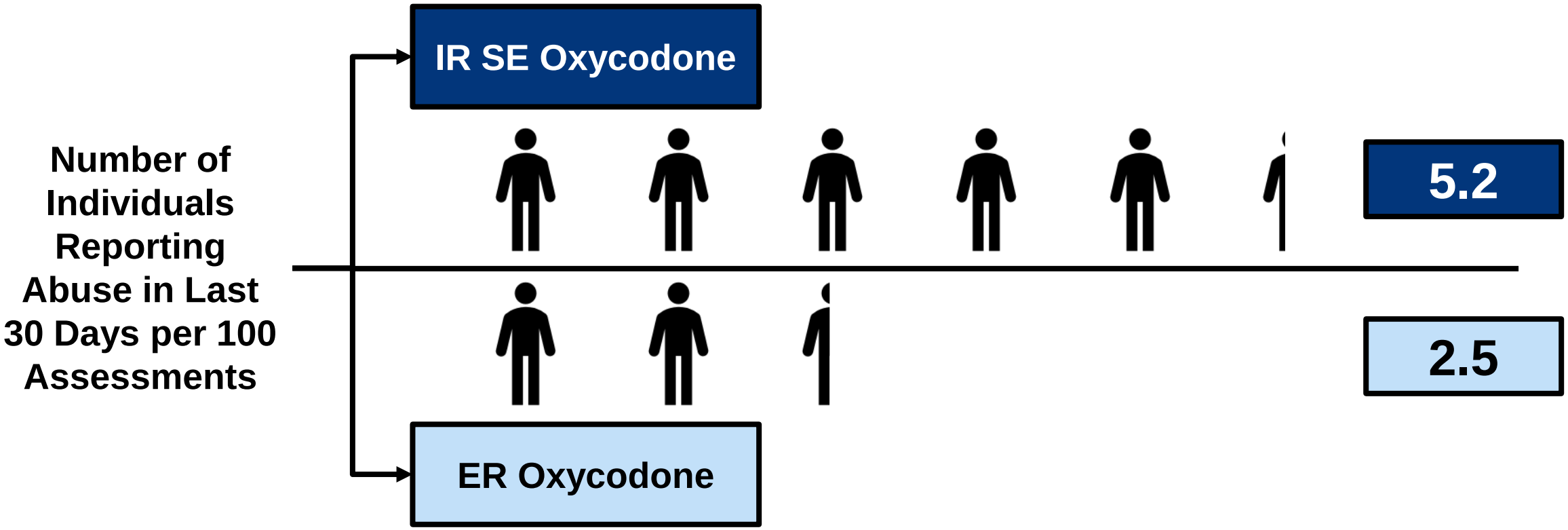
Patient with Pain	▪ **Makes their medication less attractive for misuse and diversion**
Novice / Recreational User	▪ **Deter initiation and progression of IN and IV abuse**
Persons with Severe Opioid Use Disorder	▪ **Make dangerous routes of abuse more difficult**

IR Opioids Preferred Over ER Opioids for Abuse

- IR opioids abused and diverted more frequently than ER[1,2]
  - 4.6-fold higher abuse
  - 6.1-fold higher diversion
- IR SE opioids preferred over ER opioids[2]
  - Immediacy of high
  - Ease of snorting or injection
    - No abuse-deterrent properties
    - No acetaminophen or ibuprofen

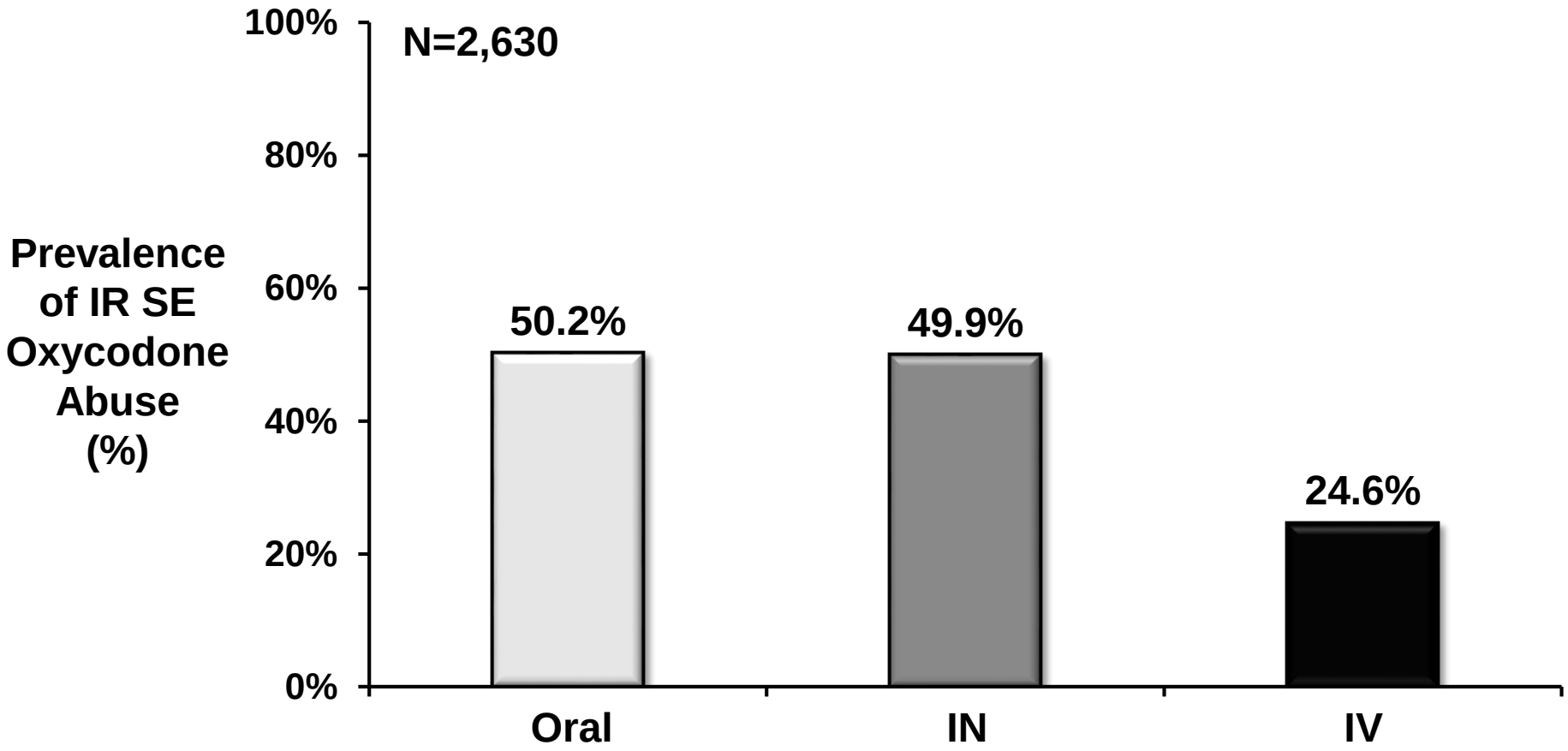
1. Iwanicki et al. *PLoS One* 2016;11:e0167499.
2. Cicero et al. *Pharmacoepidemiol Drug Saf* 2017;26:56-62.

Rate of Abuse of IR SE Oxycodone Greater than ER Oxycodone



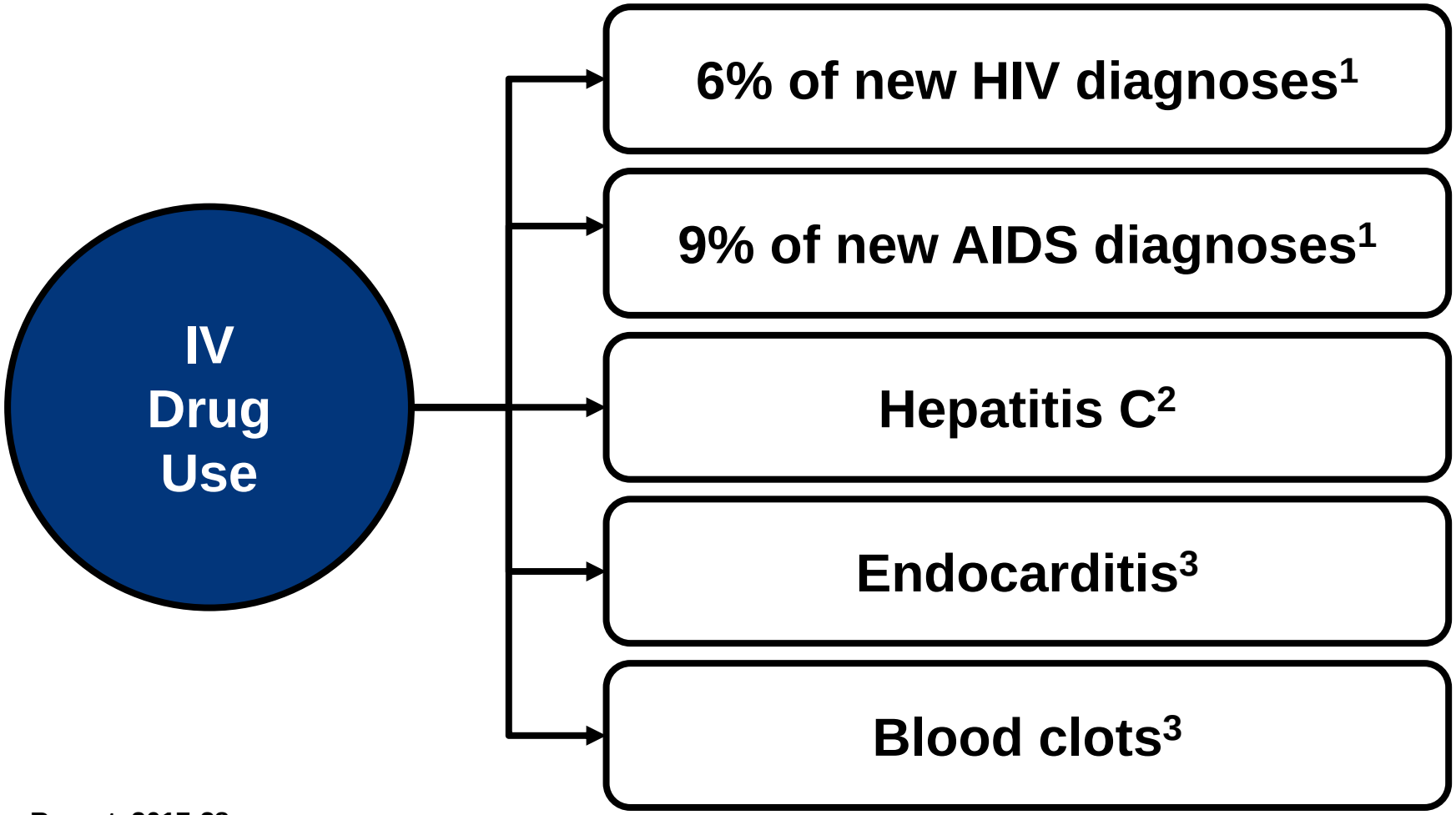
NAVIPPRO Addiction Severity Index-Multimedia Version (ASI-MV) 2017.

IR SE Oxycodone Widely Abused via IN and IV Routes



NAVIPPRO Addiction Severity Index-Multimedia Version (ASI-MV) 2017.

IV Route Poses Additional Risks for Serious Health Consequences



1. CDC. HIV Surveillance Report, 2017;28.
2. Liang & Ward. *NEJM* 2018;378:1169-71.
3. Larney et al. *Drug Alcohol Depend* 2017;171:39-49.

ADFs Important, Yet Underutilized Component to Address Opioid Abuse in US

- Goal: produce safest product possible for each type of opioid
- ADFs offer mechanism to deter abuse by non-oral routes
- ADFs currently comprise very small portion of market
- FDA has advocated for transitioning market to ADF
  - Development and approval pathway clearly established
- All products should be in abuse-deterrent form

Category 1 Studies

Edward Cone, PhD
Principal Scientist, Drug Delivery & Abuse-Deterrent Drug Products
Pinney Associates

Category 1 Studies for ADF Replacement

- Evaluated physicochemical properties of ADF Replacement to make IN and IV abuse more difficult
- Designed in accordance with the FDA Guidance on ADFs[1]
  - Incorporated feedback from FDA
- Roxicodone used as non-ADF comparator

1. FDA. *Abuse-Deterrent Opioids – Evaluation and Labeling: Guidance for Industry*. 2015.

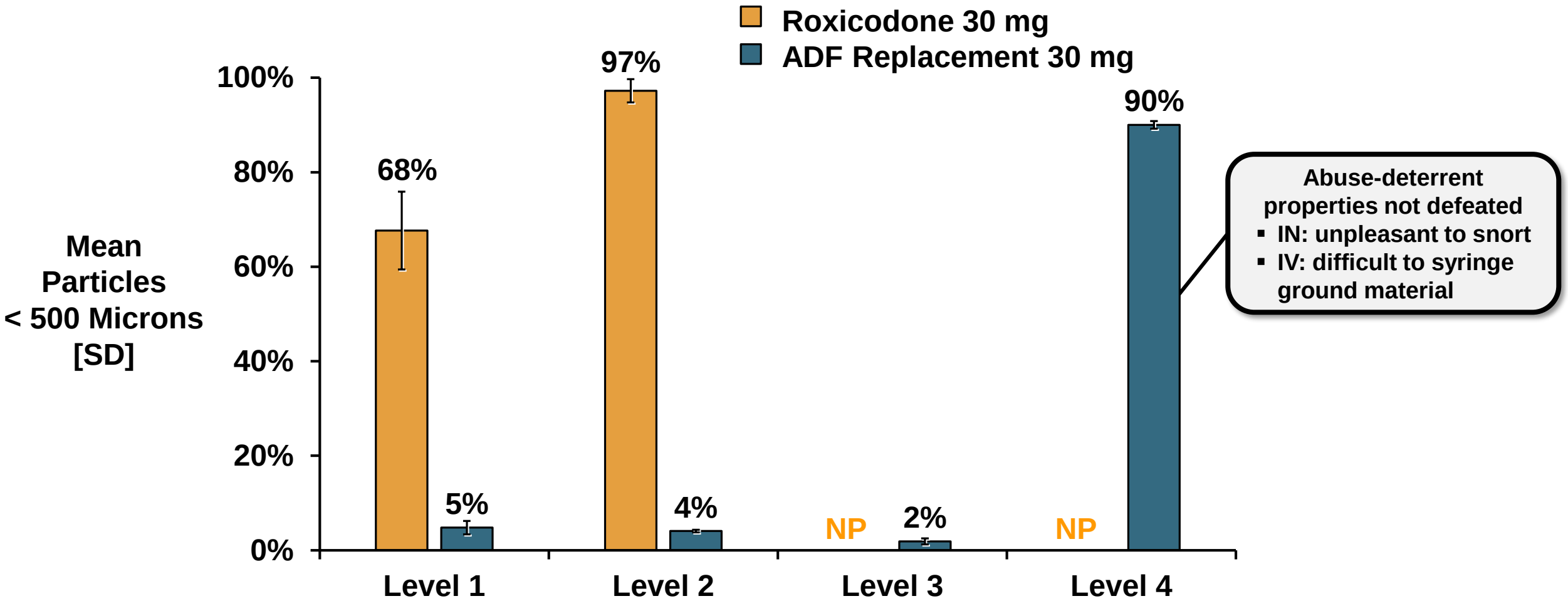
Particle Size Reduction Studies

- IR products designed to release drug rapidly
- Particle size reduction does not change oral release profile
- Rationale: prepare usable form of drug for IN or IV use

Particle Size Reduction Studies Identified Methods to Achieve Smallest Particles

- Evaluated ability to crush, cut, grate, grind, and mill Roxicodone and ADF Replacement tablets
- 4 levels of manipulation formally evaluated
  - Tested until no further particle size reduction occurred
  - Most effective manipulation for each product used in human abuse potential study

ADF Replacement Difficult to Physically Manipulate



NP = not performed

Small Volume Extraction and Syringeability

Rationale: determine conditions necessary to achieve high yield of syringeable oxycodone

Background on Selection of Methods and Interpretation of Small Volume Extraction Results

- ADFs are pain medications that must be bioavailable
- Can be overcome with sufficient time, effort, materials, and knowledge
  - Abuse-*deterrent*, not abuse-*proof*
- Goal of testing: determine whether extent of work required to overcome barriers can be expected to deter abuse
- Pretreatment conditions and advanced techniques selected to challenge abuse-deterrent properties

Small Volume Extraction Experiments to Understand IV Abuse Potential

- 1,836 combinations of conditions tested (> 5,000 samples)
- Iterative testing approach to challenge ADF Replacement

Common Methods
(288 combinations of conditions)

- Intact and ground Roxicodone and ADF Replacement
- Most frequently used solvent for IV abuse
- Various temperatures, needles, agitation, volumes, extraction times

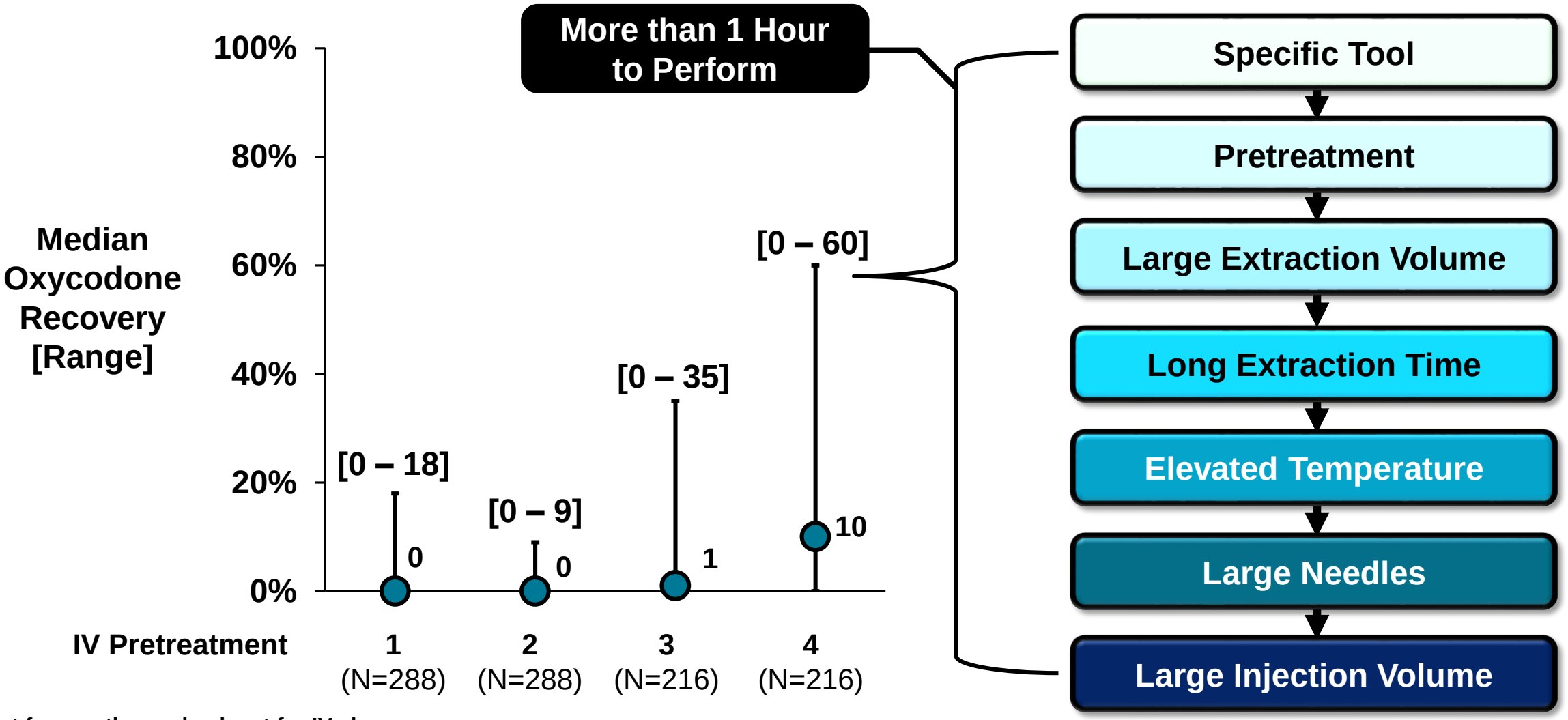
Advanced Methods
(1,548 combinations of conditions)

- Intact and ground ADF Replacement
- Further evaluated with various pretreatments and other directly injectable solvents

Common Methods Could Not Be Used to Prepare IV Solutions of ADF Replacement

Yield of Syringeable Oxycodone	n (%) of Conditions	
	Roxicodone (N=144 Conditions)	ADF Replacement (N=144 Conditions)
< 5%	0	141 (98%)
5% to 10%	0	2 (2%)
> 10% to 20%	0	1 (< 1%)
> 20% to 40%	15 (10%)	0
> 40% to 60%	73 (51%)	0
> 60% to 100%	56 (39%)	0

Pre-Treatment Conditions Required to Challenge ADF Replacement Abuse-Deterrent Properties



Most frequently used solvent for IV abuse

ADF Replacement Demonstrated Physical And Chemical Barriers to IN and IV Abuse

Study	Relevant Route of Abuse	Key Findings for ADF Replacement
Physical manipulation (particle size reduction)	**IN, IV**	▪ Difficult to crush ▪ Particle size reduction does not defeat IN or IV abuse-deterrent properties
Small volume extraction and syringeability	**IV**	▪ ADF Replacement difficult to syringe ▪ Creates substantial barrier to injection

Nonclinical Excipient Safety Studies

Mike Orr, PhD, DABT
Orr Nonclinical Consulting, LLC

Rationale for Performing Excipient Safety Studies

- All ADF Replacement excipients safe for oral use
- Concerns about repeated IV injection of HMW PEO in Opana ER[1]
  - ADF Replacement does not contain this type of PEO
- General toxicology studies conducted to understand safety profile of all excipients via IV route

1. Hunt et al. *Blood* 2017;129:896-905.

Design Elements of Nonclinical Excipient Safety Studies

- Sponsor designed studies in consultation with FDA
  - *In vitro* hemolytic potential, plasma compatibility, and platelet aggregation studies
  - *In vivo* multiple-dose IV toxicity study
- Test Article 1 and Test Article 2
  - Selected based on conditions achieving highest yields of syringeable oxycodone from two IV pretreatments

In Vitro Blood Compatibility Studies

- Hemolytic potential
- Plasma compatibility
- Platelet aggregation

No Evidence of *In Vitro* Hemolysis

Condition in Human Blood	Hemoglobin (mg/dL)	Hemolysis
Negative Control	**5**	**-**
Test Article 1	**9**	**Negative**
Test Article 2	**1**	**Negative**
Positive Control	**5895**	**Positive**

- Positive result defined as 500 mg/dL increase relative to negative control

No Evidence of Human Plasma Incompatibility or Increased Platelet Aggregation

- Human plasma incompatibility not observed with Test Articles
  - Test Article 1: no macro or micro observations
  - Test Article 2: cloudy appearance likely due to presence of finely suspended particles observed prior to mixing
  - Test Articles 1 and 2 both negative for protein flocculation
- Increased platelet aggregation not observed with Test Articles
  - Results similar to negative control and within normal reference range for healthy blood donors

In Vivo Multiple-Dose IV Toxicity Study

- Evaluated local and systemic effects of ADF Replacement extracts

Test Articles in Multiple-Dose *In Vivo* IV Toxicity Study in Rabbits

- 12 female rabbits randomized equally to receive once daily bolus injections (1 mL/kg) for 3 days
  - Test Article 1, N=4
  - Test Article 2, N=4
  - Control Article (0.9% sodium chloride), N=4
- Dose volume selected based on tolerability profile of oxycodone
- Dose volume in rabbit relative to human
  - ~10-fold higher based on body surface area
  - ~58-fold higher based on mL/kg

Multiple-Dose *In Vivo* IV Toxicity Study Methods

- Animals monitored ≥ 2x/day for abnormal findings
- Full panel of clinical pathology tests performed
  - Hematology, coagulation, clinical chemistry, urinalysis
  - Standard panel of tissues collected
  - Select organs evaluated microscopically

Summary of *In Vivo* Excipient Safety Study

- No evidence of overt toxicity or tissue damage
- Test Articles not associated with signs or symptoms of thrombotic microangiopathy
- Test Article 2: statistically significant increases in fibrinogen (1.5-fold) and increases in spleen weights (50%)
  - Not considered adverse by independent pathologist
- Minimal to slight microscopic pathology observations
  - Not considered adverse by independent pathologist

Intranasal Human Abuse Potential Study

Sandra D Comer, PhD

Professor of Neurobiology (in Psychiatry)

Division on Substance Use Disorders

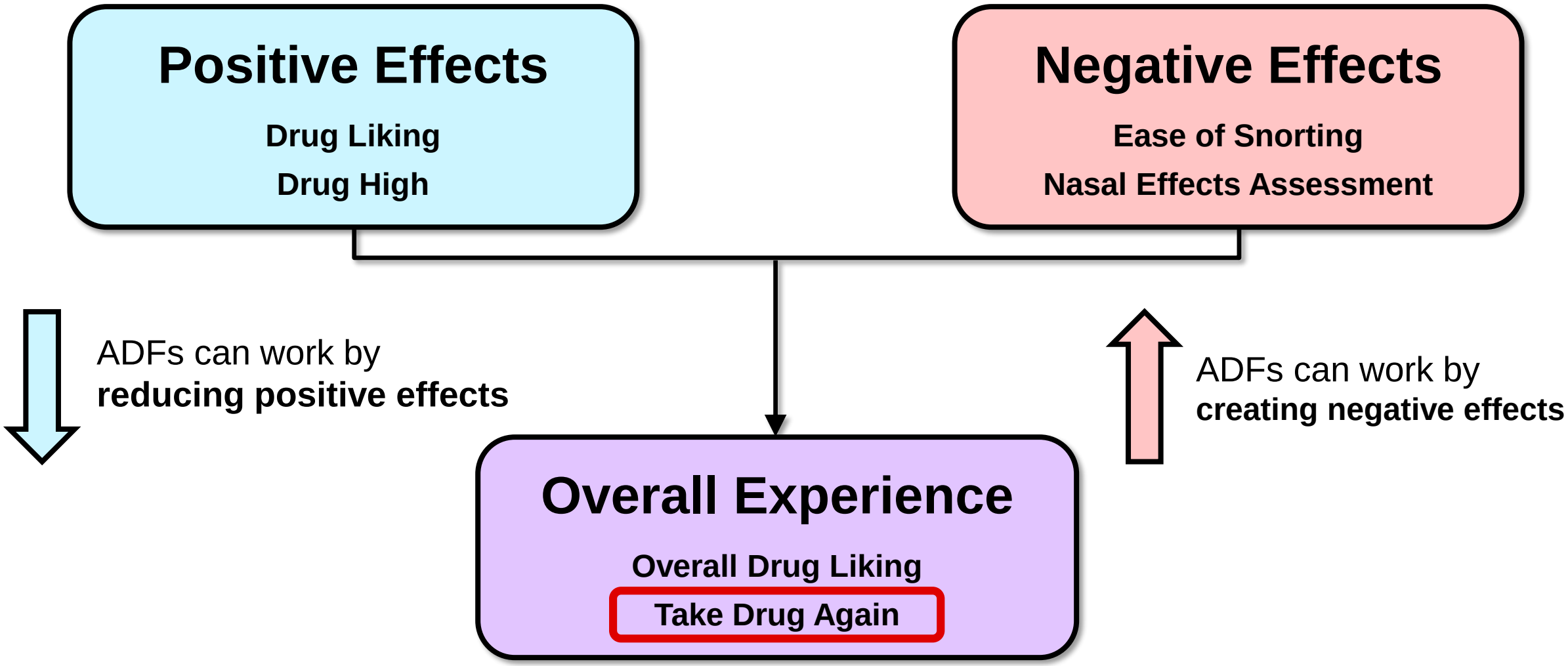
Columbia University

Rationale for Snorting IR Opioids is Faster Onset of Effects

- IN administration bypasses first-pass metabolism
  - Faster drug entry into bloodstream and brain
  - Faster onset of “positive effects” such as liking and high
- IN and oral administration of IR opioid have similar maximum positive effects[1-3]
- **Motivation for snorting: faster onset of positive effects**
  - Early timepoints are important

1. Webster et al. *Pain Med* 2018 Mar 28.
2. Mickle et al. *Pain Med* 2017 Oct 28.
3. FDA Briefing Document for Avridi™.

Different Mechanisms of IN Abuse Deterrence



Design: IN Human Abuse Potential (HAP) Study

- Randomized, double-blind, double-dummy, placebo-controlled, 4-period crossover study
  - Non-dependent, recreational opioid users
  - Recent IN experience with opioids
- Qualification Phase
  - Naloxone challenge test: not physically dependent on opioids
  - Drug discrimination test: able to discriminate IN 15 mg Roxicodone from placebo
- 38 subjects completed study

IN HAP Study Treatments

- 72-hour washout period between treatments

Treatment	Double-Dummy Treatment
Oral ADF Replacement (30 mg)	IN Roxicodone placebo
IN ADF Replacement (30 mg)	Oral ADF Replacement placebo
IN Roxicodone (30 mg)	Oral ADF Replacement placebo
Oral ADF Replacement placebo	IN Roxicodone placebo

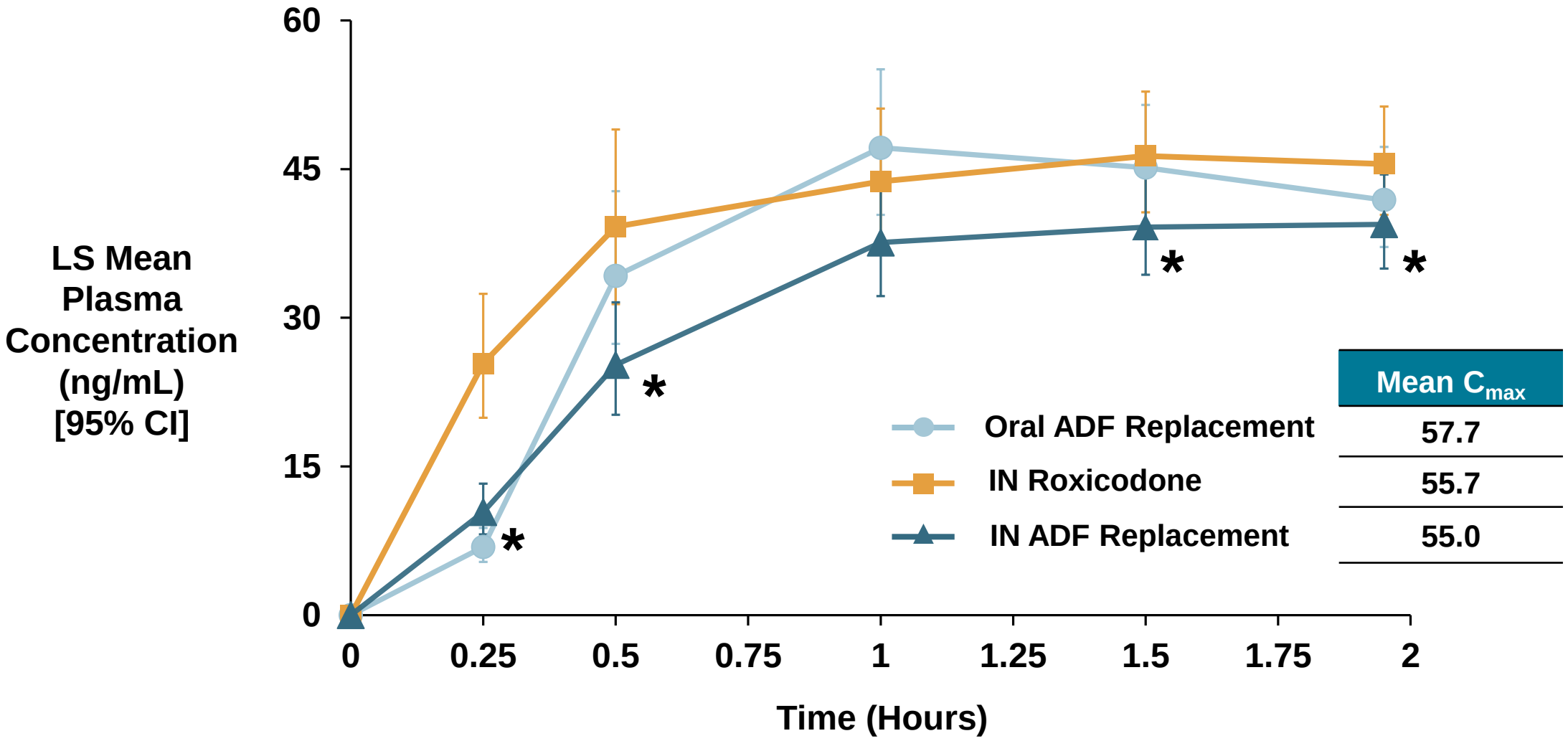
IN HAP Study Key Assessments

Assessments	Timing of Assessment
Primary	
Drug Liking E_{max}	▪ Max score 15 min to 12 hrs post dose
Secondary*	
Drug Liking	▪ 15 min to 12 hrs post dose
Drug High	▪ 15 min to 12 hrs post dose
Ease of Snorting Assessment	▪ Within 5 min post dose
Nasal Effects Questionnaire	▪ 15 min to 12 hrs post dose
Overall Drug Liking	▪ 12 and 24 hrs post dose
Take Drug Again	▪ 12 and 24 hrs post dose

*All secondary assessments evaluated independently without any ranking assignment

Pharmacokinetics

Lower Oxycodone Concentrations at Early Time Points for IN ADF Replacement



* p < 0.05 for IN ADF Replacement vs. IN Roxicodone

Pharmacodynamics: Positive Effects

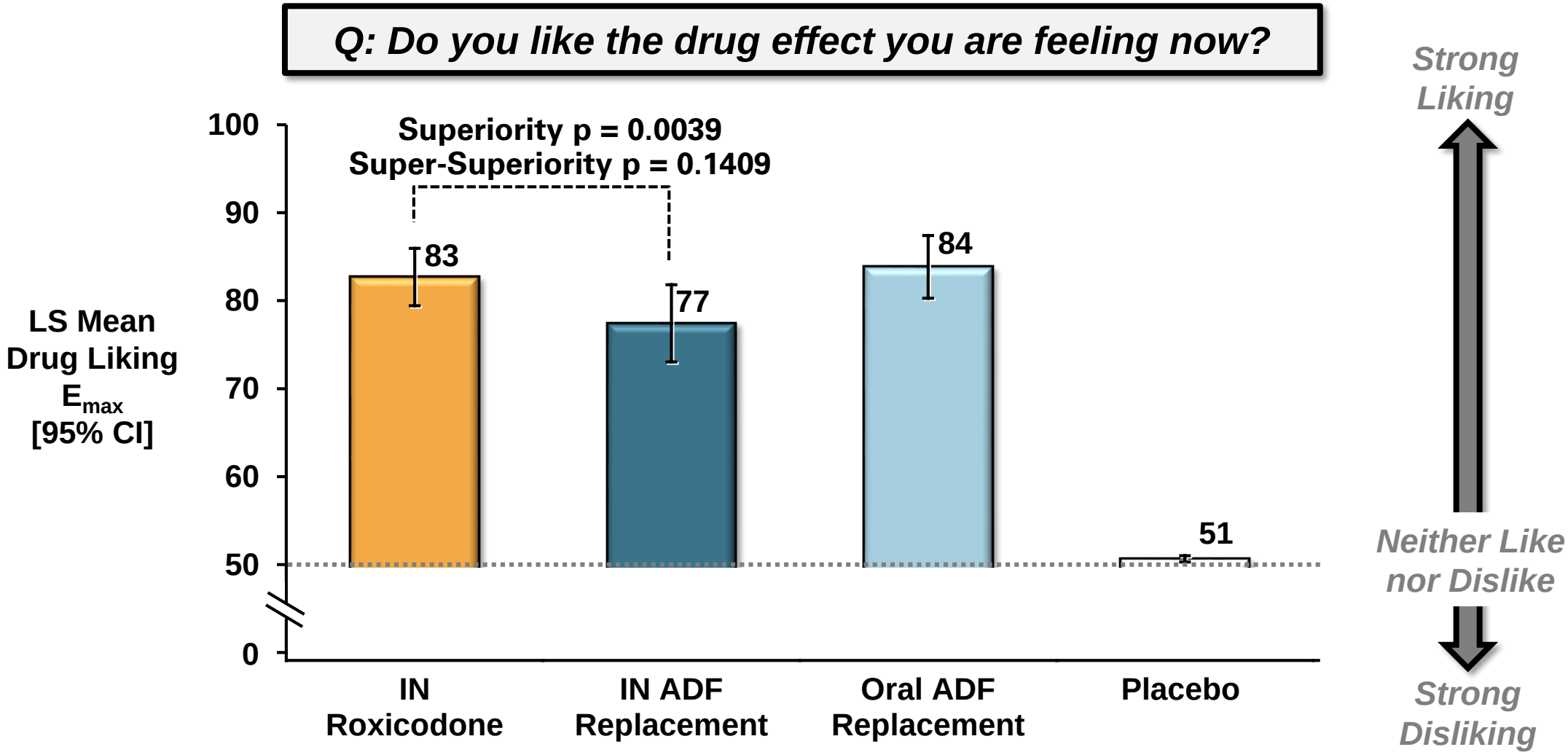
- Drug Liking
- Drug High

Primary Endpoint Evaluated with Superiority Margin Per FDA Guidance

- Primary endpoint: maximum Drug Liking (E_{max})
- Approved ADFs have needed to show statistically significant effect
  - Often referred to as “superiority”
- FDA Guidance requires use of superiority margin (δ*)
  - Requires that ADF show statistically significant effect by specific margin
  - Often referred to as “super-superiority”
- ADF Replacement study used 10% superiority margin

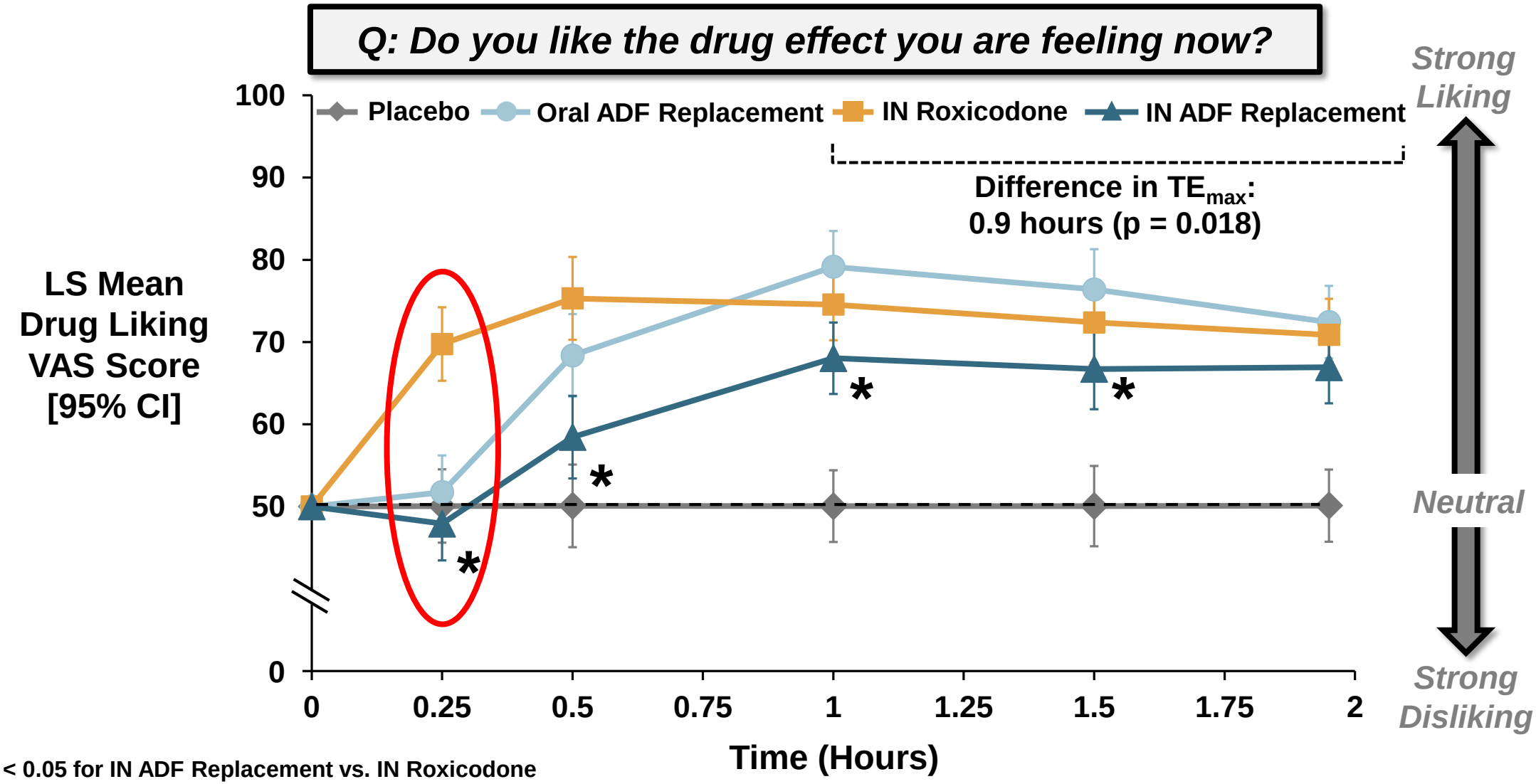
Primary Endpoint: Drug Liking E_{max}

Q: Do you like the drug effect you are feeling now?



Based on FDA Analysis

Lower and Delayed Drug Liking for IN ADF Replacement at Early Time Points

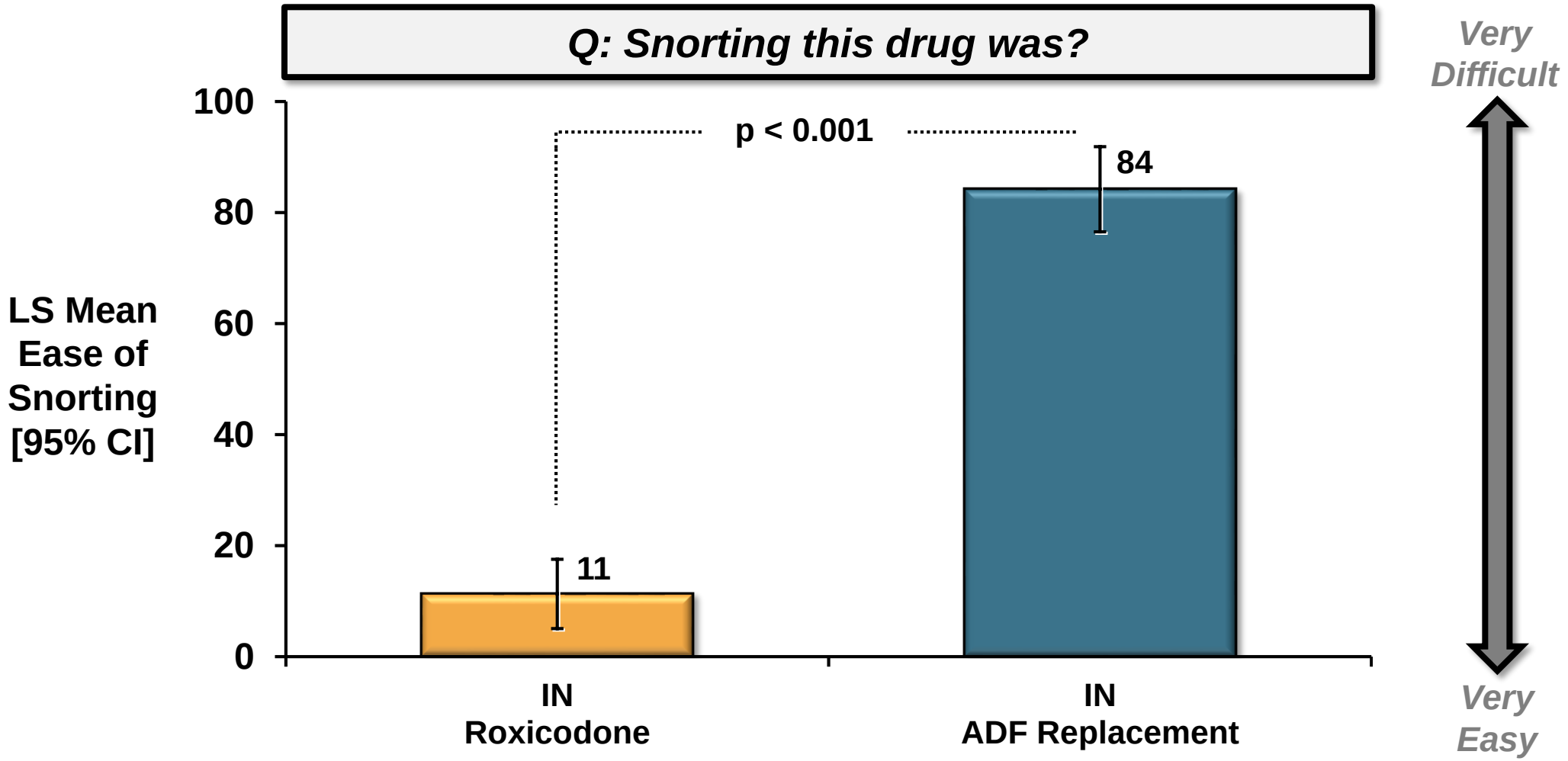


* p < 0.05 for IN ADF Replacement vs. IN Roxicodone

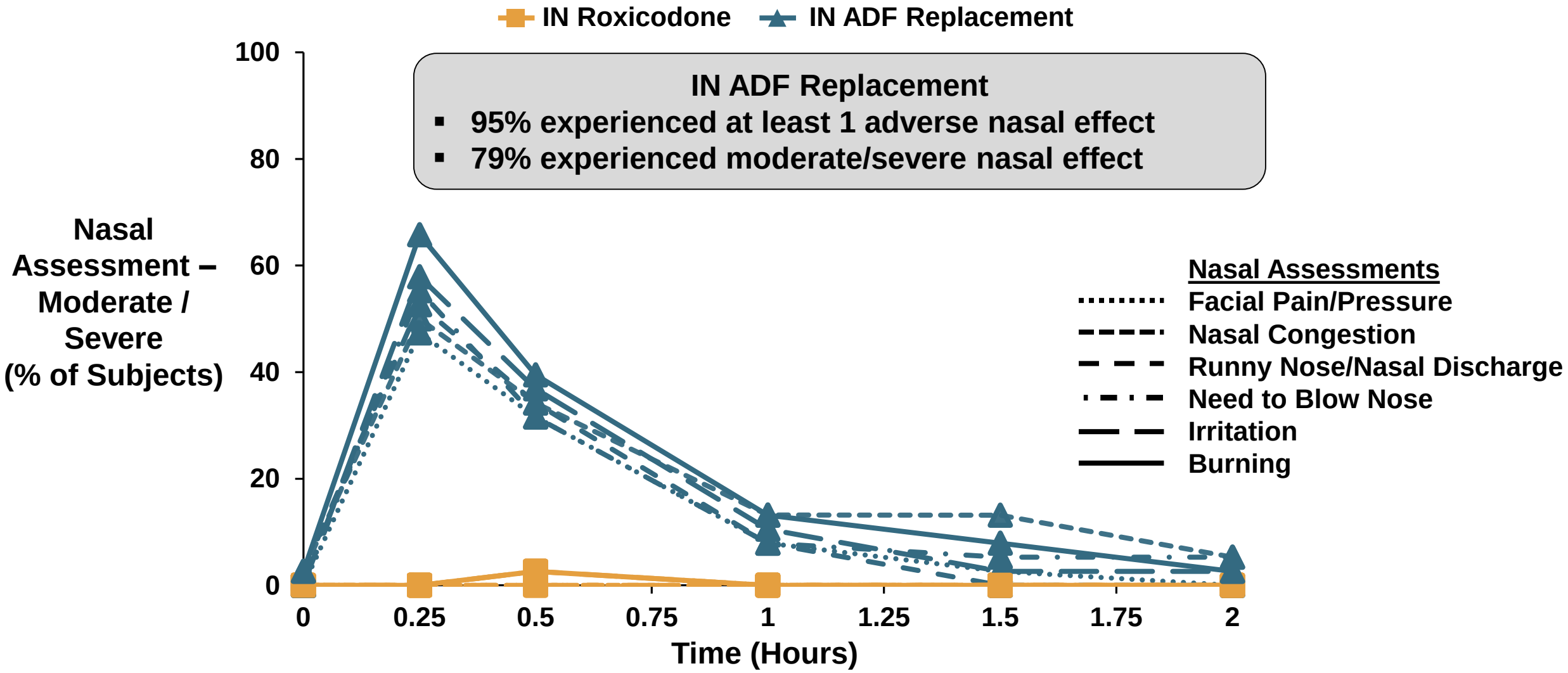
Pharmacodynamics: Negative Effects

- Ease of Snorting
- Nasal Effects Questionnaire

ADF Replacement Significantly More Difficult to Snort Than Roxicodone



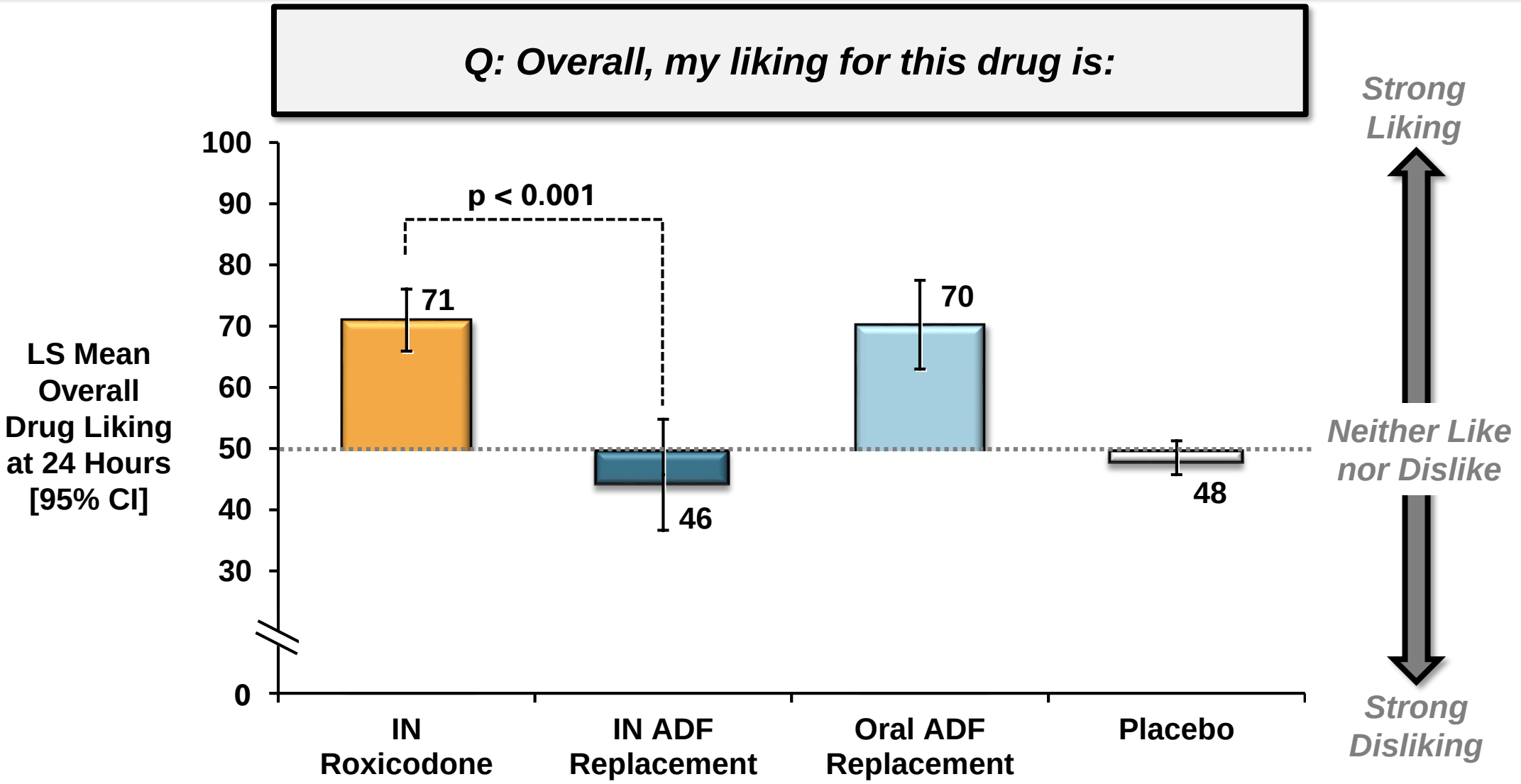
ADF Replacement Causes Adverse Nasal Effects



Pharmacodynamics: Overall Drug Taking Experience

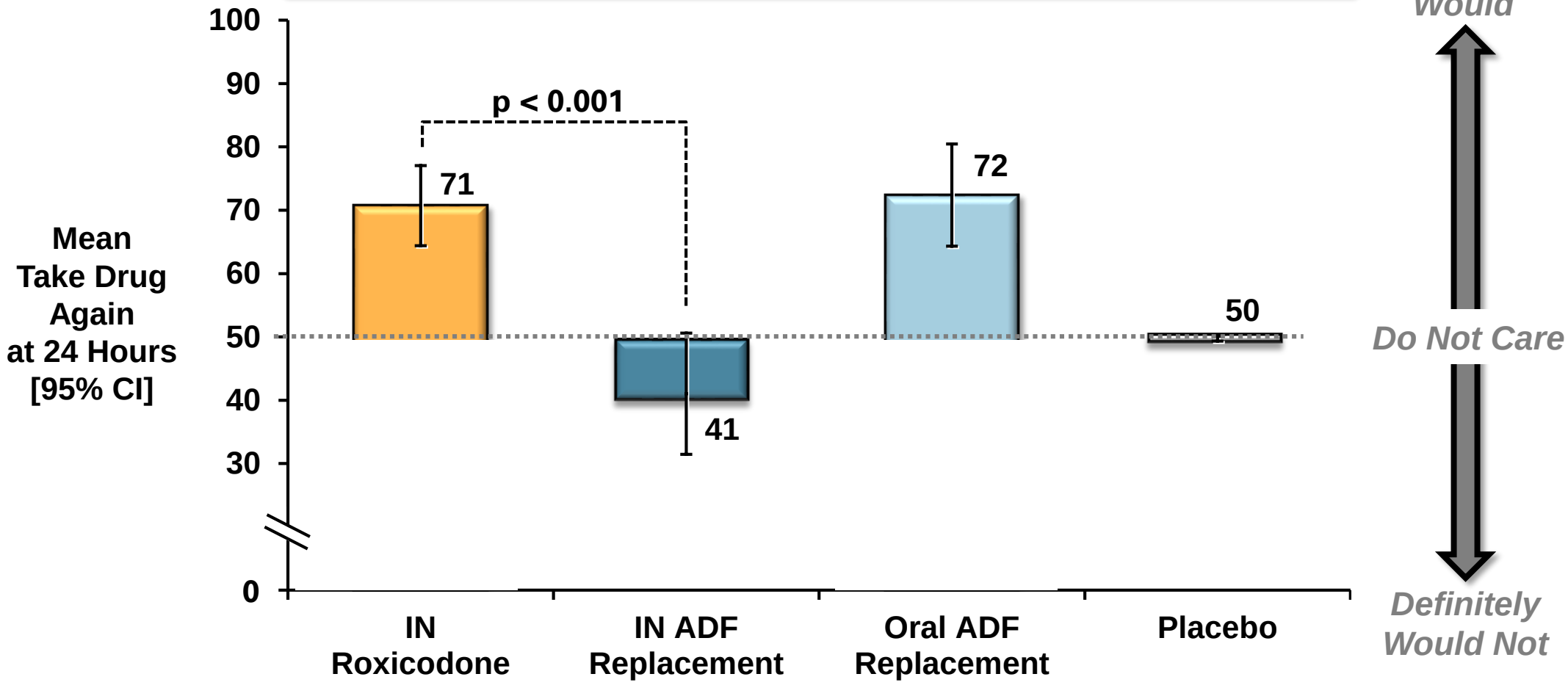
- Overall Drug Liking
- Take Drug Again

Significantly Lower Overall Drug Liking for IN ADF Replacement at 24 Hours



Significantly Lower Take Drug Again for IN ADF Replacement at 24 Hours

Q: Would you want to take the drug you just received again, if given the opportunity?



ADF Replacement Can Be Expected to Reduce IN Abuse

Positive Effects

- Drug Liking E_{max} significantly lower, but not super-superior to Roxicodone
- ✓ Significant decrease in Drug Liking and High at early timepoints

Negative Effects

- ✓ More difficult to snort than Roxicodone
- ✓ Aversive agents cause burning, irritation, and pain

Overall Experience

- ✓ Overall Drug Liking similar to placebo
- ✓ Subjects did not want to snort ADF again

Clinical Perspective

Jeffrey Gudin, MD

Director, Pain Management and Palliative Care

Englewood Hospital and Medical Center

Balancing Patient Need with Public Health Challenge

- Opioids remain needed treatment option for pain
- Clinicians typically feel comfortable evaluating patient's potential risk of abuse
  - But cannot control diversion
- ADF safeguards against abuse intended for patients and anyone with access to medicine cabinet

FDA Questions for Joint Committee

- Can ADF Replacement be expected to deter abuse?
  - Nasal route
  - IV route
- Concerns regarding public health impact of ADF Replacement on misuse and abuse of opioids?
- Should ADF Replacement be approved?

Questions should be considered in light of <u>replacing</u> Mallinckrodt's marketed non-ADF tablets

Can ADF Replacement Be Expected to Deter Abuse by Nasal Route of Administration?

- Physical and chemical properties
- IN HAP study
- Precedent set by FDA-approved IR ADF (RoxyBond™)

ADF Replacement Has Physical and Chemical Properties to Deter IN Abuse

Properties	ADF Replacement	Current Roxicodone and Generic
Physical	▪ Difficult to manipulate ▪ Required most advanced level of manipulation	▪ Easily manipulated with simple tools
Chemical	▪ Difficult to snort ▪ Aversive agents cause pain and burning	▪ Easy to snort ▪ No agents to discourage IN abuse

IN HAP Study Demonstrates ADF Replacement Can Be Expected to Deter IN Abuse

Endpoint	Mean for IN Administration		Difference (p-value)
	Roxicodone	ADF	
Drug Liking E_{max}			
ADF Replacement	83	77	6 (0.0039)
RoxyBond	83	71	12 (< 0.001)
Take Drug Again E_{max}			
ADF Replacement	77	46	31 (< 0.001)
RoxyBond	82	62	20 (< 0.001)

Lack of willingness to snort again consistent with aversive effects

Statistics based on FDA Briefing Documents for ADF Replacement and RoxyBond.

Can ADF Replacement Be Expected to Deter Abuse by IV Route of Administration?

- Physical and chemical properties
- Category 1 studies
- Precedent with FDA-approved IR ADF (RoxyBond)

ADF Replacement Has Physical and Chemical Properties to Deter IV Abuse

Properties	ADF Replacement	Current Roxicodone and Generic
Physical	▪ Difficult to manipulate ▪ Required most advanced level of manipulation	▪ Easily manipulated with simple tools
Chemical	▪ Multiple gelling agents make injection difficult	▪ No barriers to injection

Category 1 Studies Demonstrate ADF Replacement Can Be Expected to Deter IV Abuse

IV Abuse Assessment	Roxicodone	ADF Replacement	RoxyBond[1]
Difficult to syringe?	No	Yes	Yes
Low yields in vast majority of conditions?	No	Yes	Yes
Required advanced conditions for IV abuse?	No	Yes	Yes
Worst-case yield with pretreatment	n/a	60%	66%

- Complex, multi-step processes (> 1 hr)
- Abuse-deterrent, not abuse-proof

1. Inspirion Delivery Sciences, LLC Slides for April 5, 2017 Advisory Committee.

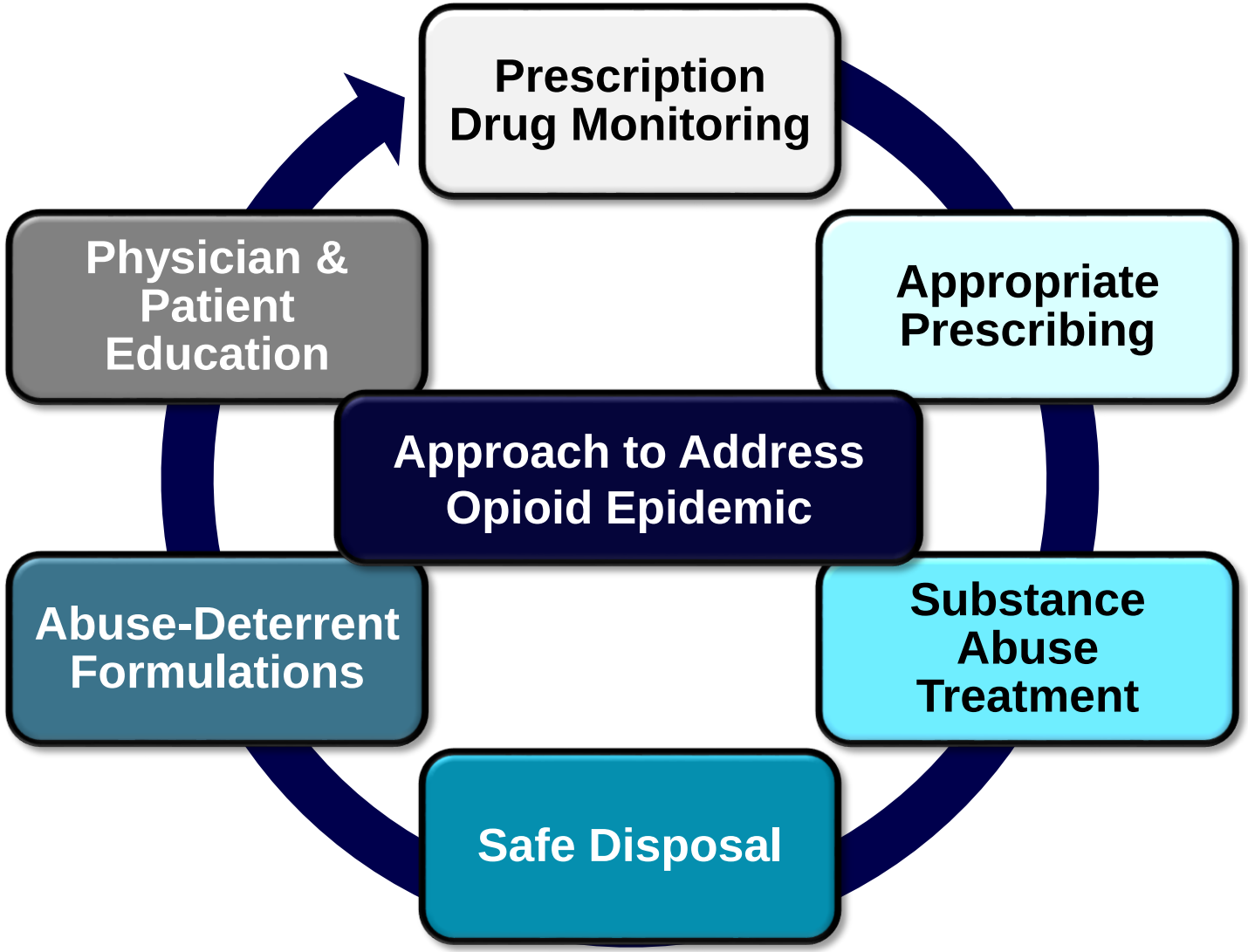
Concerns Regarding Public Health Impact of ADF Replacement on Misuse And Abuse of Opioids?

Benefit-Risk Analysis for Public Health Concerns

ADF Public Health Concern	Benefit-Risk Analysis
Low uptake or limited public health impact	▪ Replacing currently marketed branded and generic tablets
Can send false sense of security to prescribers	▪ Approval of ADFs have not increased prescribing ▪ ADF Replacement will not be promoted
Cannot deter initiation to dangerous routes	▪ Contains aversive agents to discourage IN abuse
Should not push individuals to IV abuse	▪ Extensive multi-step process required
Injected excipients may cause serious health consequences	▪ No evidence of overt toxicity from excipient safety studies ▪ Most dangerous ingredient for injection is oxycodone

Should ADF Replacement be Approved?

ADFs Part of More Comprehensive Plan to Address Prescription Opioid Epidemic



ADF Replacement in Interest of Patients and Public Health

- FDA has advocated for transitioning market to ADFs
  - Meaningful public health benefit expected from providing safeguards against abuse
- Approval of ADF Replacement would allow for transition

Mallinckrodt's IR SE oxycodone products <u>without</u> safeguards against abuse would no longer be available

Millions of prescriptions replaced by ADF that

- Is therapeutically equivalent
- Discourages snorting
- Makes IV injection difficult

ADF Replacement (oxycodone hydrochloride) Abuse-Deterrent Immediate-Release Tablets

November 14, 2018

Mallinckrodt Pharmaceuticals

Joint Meeting of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee

BACK-UP SLIDES

Figure 7: Oxycodone Plasma Concentrations for 3 Subjects with T_{max} Values of 6-8 Hours in Fed Bioequivalence Study Following Administration of ADF Replacement 15 mg Tablets

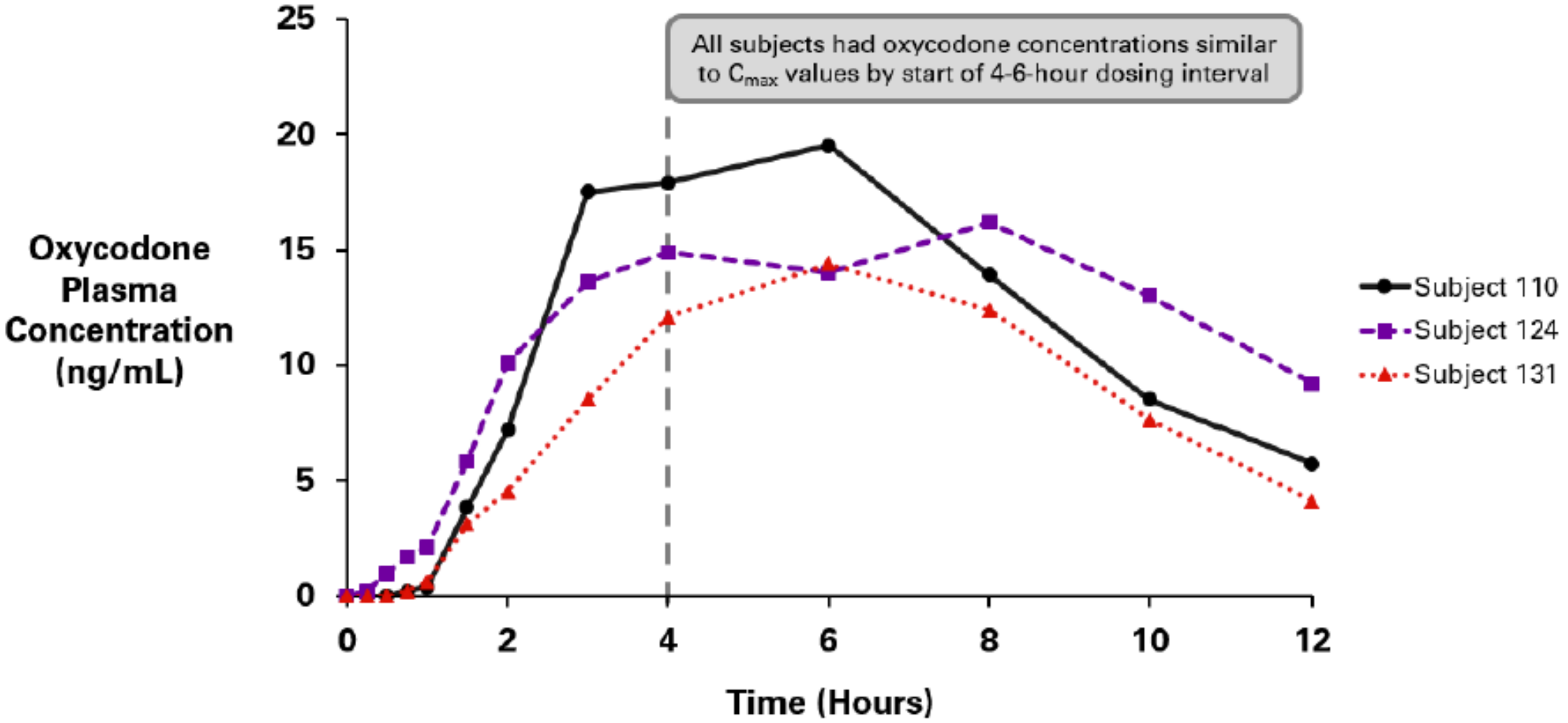
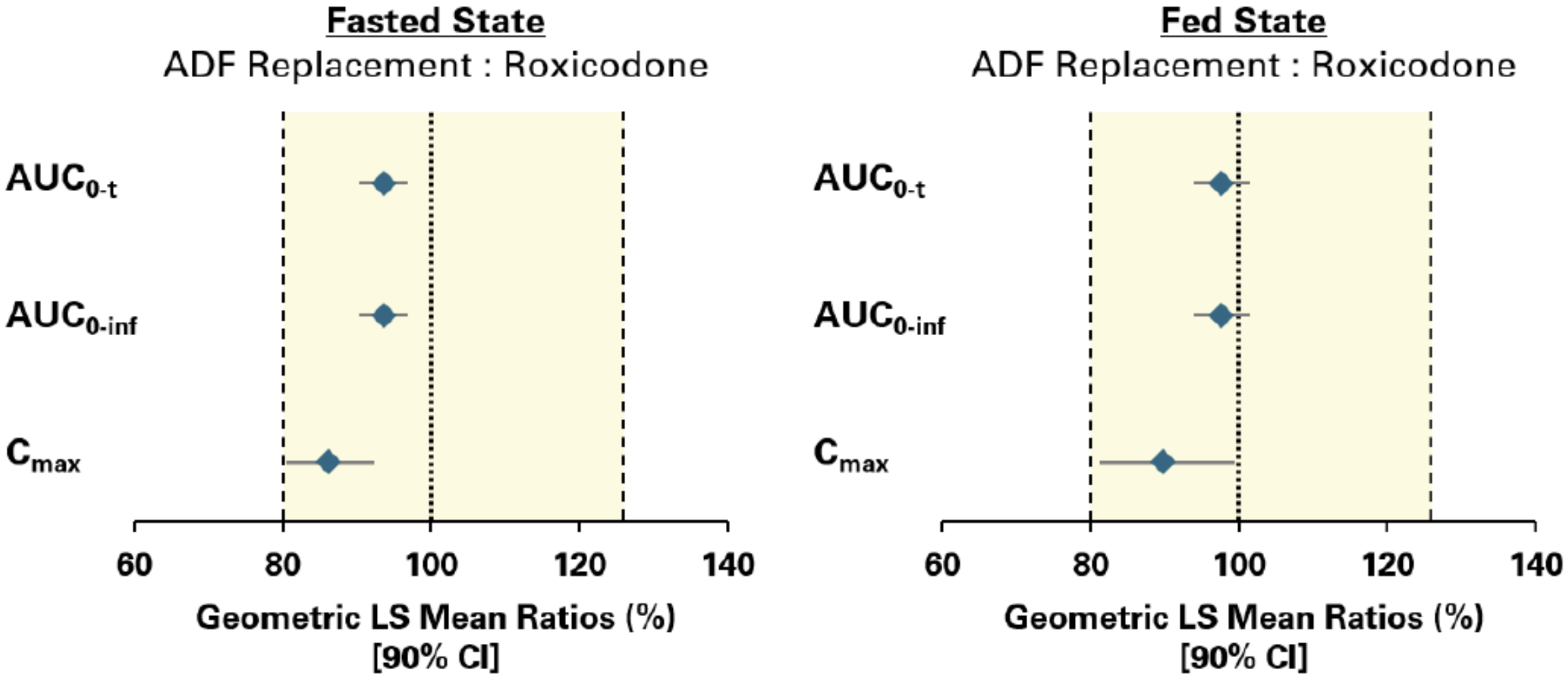


Figure 1: Bioequivalence of ADF Replacement to Roxicodone 15 mg Tablets in Fasted and Fed States



Note: Yellow shaded area indicates pre-specified bioequivalence bounds of 80% to 125%.

Respiratory AEs Driven by Aversive Agents

System Organ Class Preferred Term, N (%)	**Intact Oral MNK-812 N=41**	**Intranasal MNK-812 N=40**	**Intranasal Oxycodone (IR) N=42**	**Placebo N=42**
Subjects at least 1 AE	32 (78)	29 (72.5)	24 (57.1)	12 (28.6)
Respiratory, Thoracic, Mediastinal Disorders	6 (14.6)	21 (52.5)	4 (9.5)	6 (14.3)
Cough	3 (7.3)	11 (27.5)	1 (2.4)	3 (7.1)
Nasal Discomfort	0	10 (25.0)	0	1 (2.4)
Nasal Congestion	1 (2.4)	2 (5.0)	1 (2.4)	0
Hiccups	2 (4.9)	1 (2.5)	1 (2.4)	0
Oropharyngeal Pain	1 (2.4)	1 (2.5)	0	1 (2.4)
Paranasal Sinus Discomfort	0	1 (2.5)	1 (2.4)	0
Epistaxis	0	0	0	1 (2.4)
Hypoxia	0	0	0	1 (2.4)
Nasal Pruritus	0	1 (2.5)	0	0
Pulmonary Congestion	0	0	0	1 (2.4)

HMW PEO in Opana ER Not Present in ADF Replacement

	ADF Replacement	OxyContin	Opana ER (Reformulated)
Type of HMW PEO	Similar to OxyContin	4 million	7 million
% HMW PEO in Tablet	< 2%	≥ 65%	> 60%

No Rationale for Needle / Dose Sharing with ADF Replacement

	ADF Replacement	OxyContin	Opana ER (Reformulated)
Type of HMW PEO	Similar to OxyContin	4 million	7 million
% HMW PEO in Tablet	< 2%	≥ 65%	> 60%
API	oxycodone	oxycodone	oxymorphone
Oral Bioavailability	85%	85%	10-15%
IV Dose Potency Relative to Oxycodone	1x	1x	10-20x more potent
Single Tablet Suitable for Sharing IV	No	No	Yes
Prescriptions in 2017	-	3.4 million	306,000