



Alcohol Clinical Trials Initiative: ACTIVE workgroup

History and Progress

Raymond F. Anton, MD
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ACTIVE workgroup

Pharmaceutical Companies:

Abbott Labs

Alkermes

Glaxo Smith Kline

Johnson and

Johnson

Lilly

Lundbeck

Schering Plough

NIAAA :

Raye Litten

Dan Falk

NIDA :

David McCann

FDA:

Celia Winchell

Tom Permutt

ACNP Academic experts:

Ray Anton - Chair

Ray Bartus – co-Chair

Bankole Johnson

Tom Kosten

Hank Kranzler

Chuck O'Brien

Stephanie O'Malley

Karl Mann (Europe)

Roger Meyer

Steering Committee: Anton, Bartus, Falk, Litten, Kranzler, Palumbo (J&J), Silverman (Alkermes), Winchell, Timm (ACNP)

In May 2007 a meeting sponsored by ACNP was held to:

“Define The Opportunities and Impediments for Drug Discovery in Alcohol and Substance Abuse”

Representative Attendees:

Director of NIAAA (T.K. Li) and other staff

Director of NIDA (Nora Volkow) and other staff

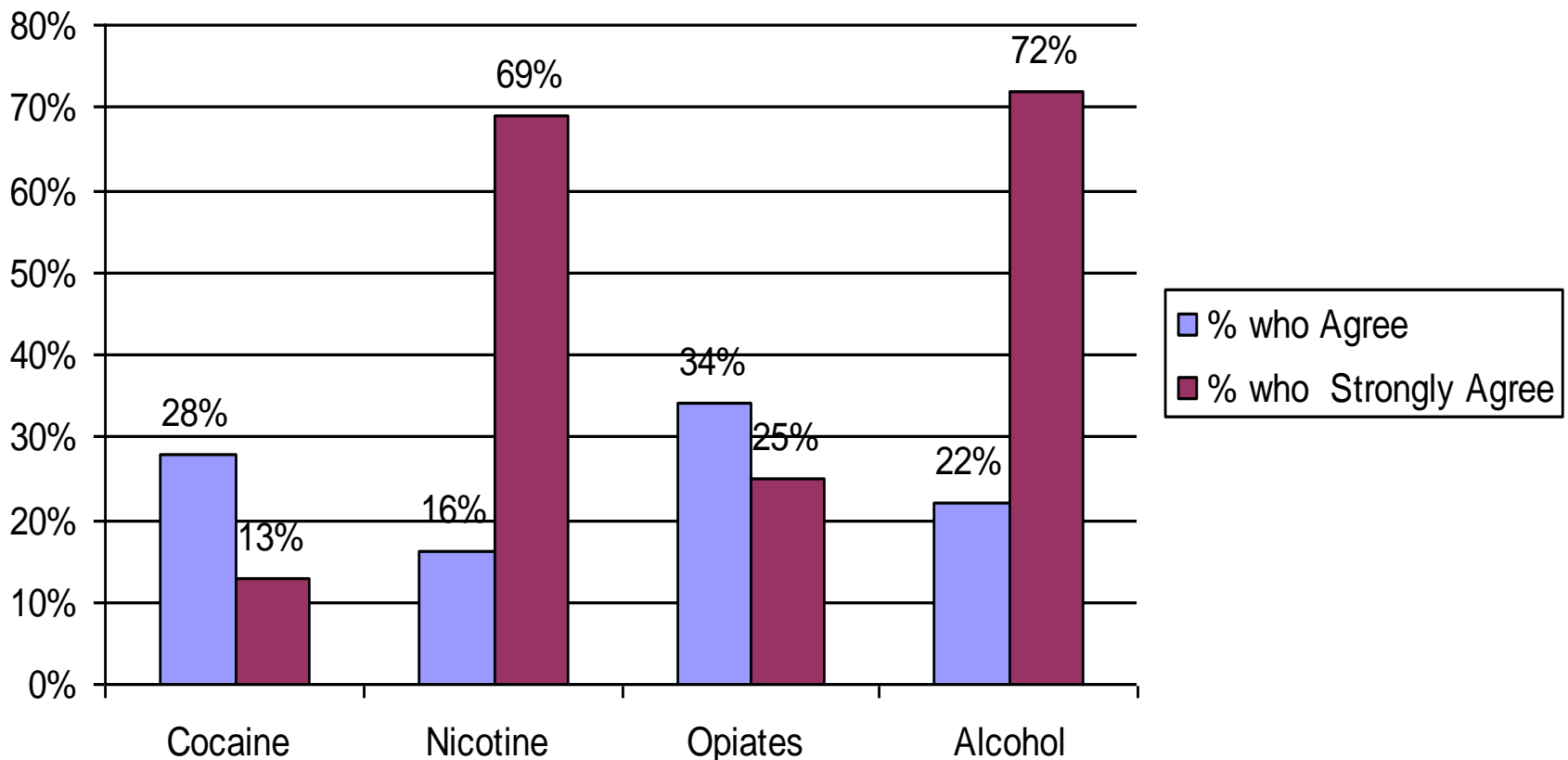
FDA (Bob Rappaport, Celia Winchell)

37 reps of 29 pharmaceutical companies

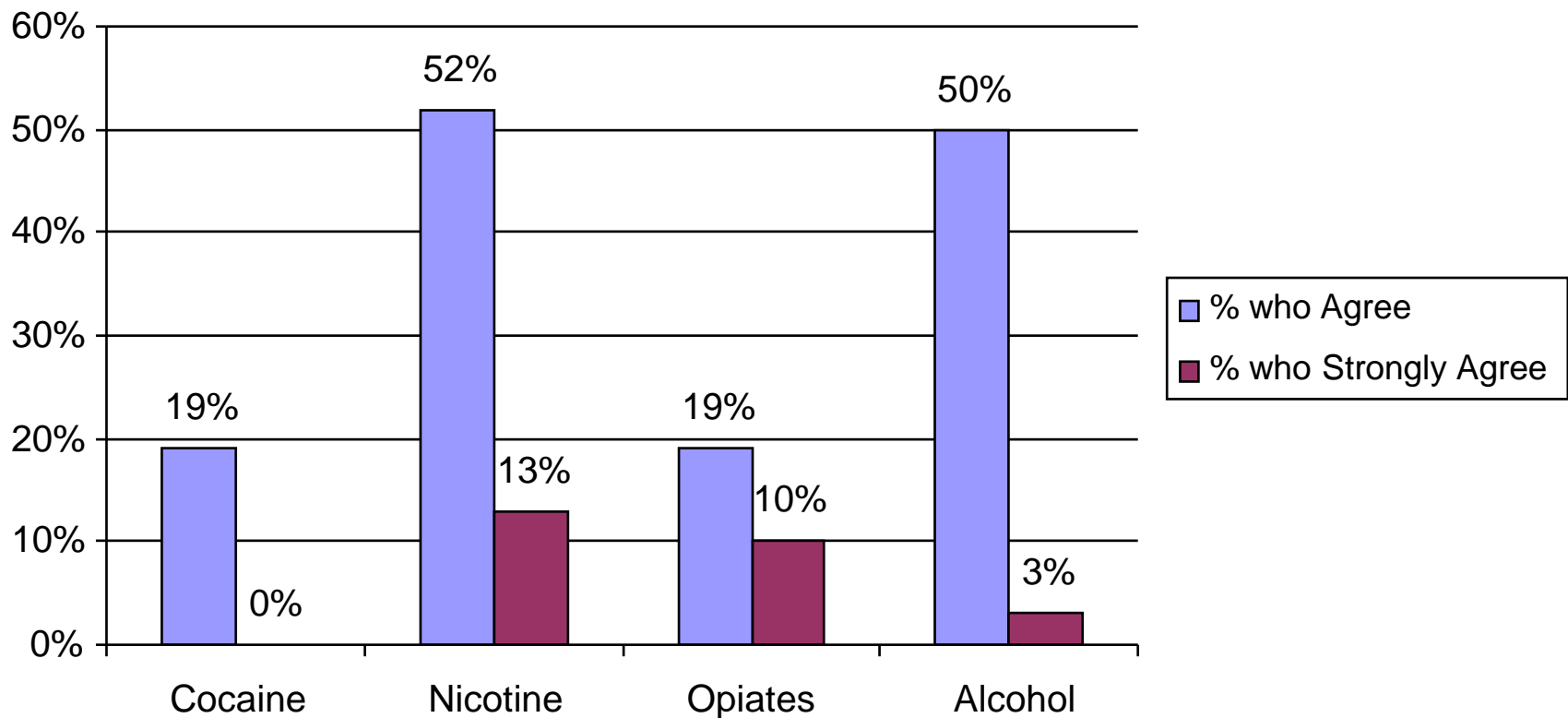
9 ACNP member academic “experts”

Health Care Economist – (Eric Goplerud)

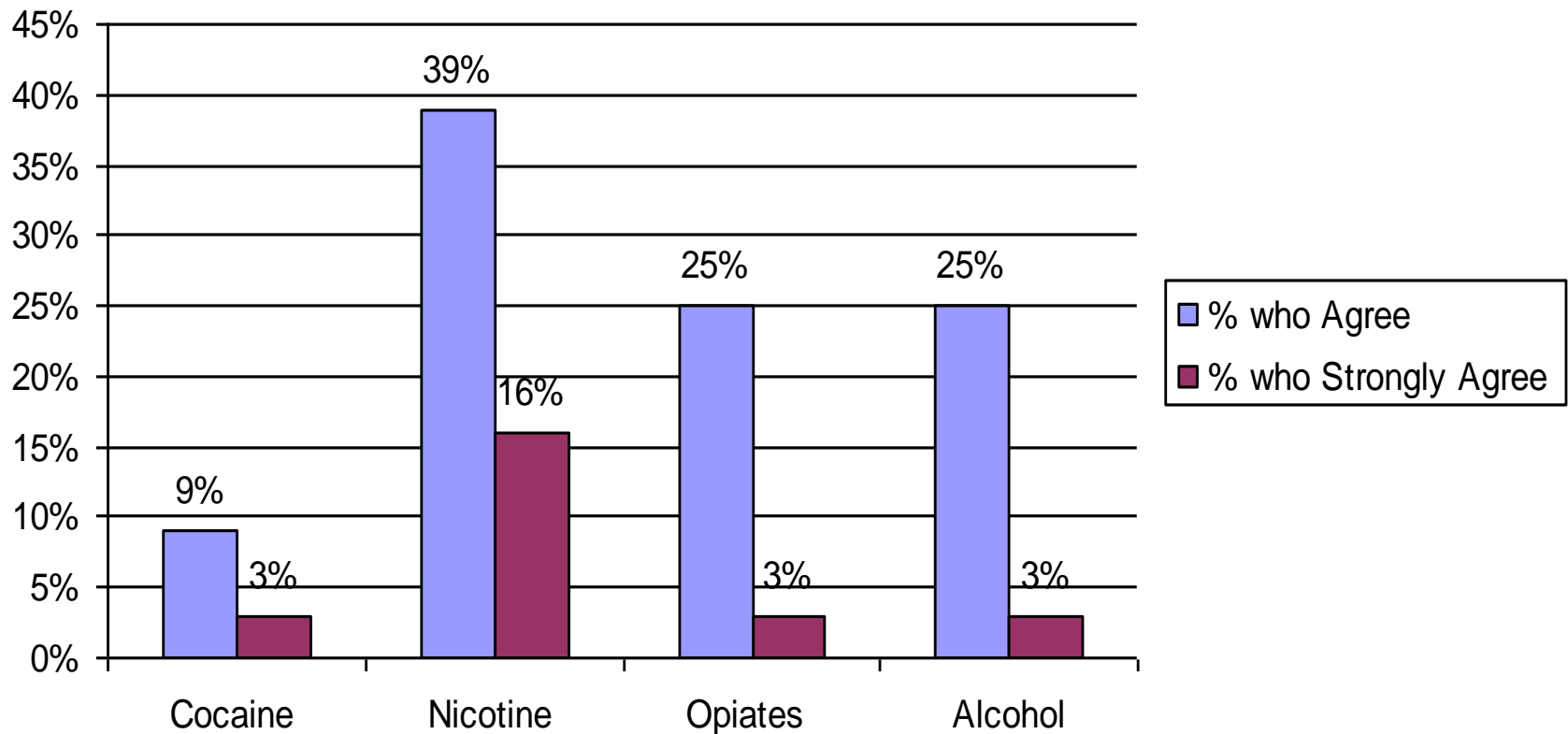
Industry Attendees Who Agree or Strongly Agree the Market is Substantial Enough to Develop Medications for Various Addiction Treatments



Industry Attendees Who Agree or Strongly Agree that Methods for Clinical Trials Are Well-Developed for Testing New Medications for Various Addiction Treatments



Industry Attendees Who Agree or Strongly Agree that Regulatory Issues are Clear for Medication Development for Various Addiction Treatments



Triangle of Opportunities?

Pharmaceutical Companies

Provide drugs
to test

Submit protocols
and data

Provide
guidance

Can provide clinical
trial methods

NIAAA/NIDA

FDA

Can assistance each other on best
clinical trial methods/endpoints

The ACTIVE Process

- May 2007 meeting consensus led to a recommendation that a process (workgroups) move forward to better define issues and opportunities for medication development for alcohol and other substance abuse
- All companies approached to contribute – 5 responded positively BUT only for alcohol medication develop
- subsequently 2 more companies joined
- Since Jan. 2009 there have been 7 data based meetings
- Overview paper currently published online, first data paper under review

Consensus Issues being Addressed for Alcohol Dependence Clinical Trials

- **Handling missing data**
- **Placebo response rates and predictors**
- **Clinical trial length**
- **Primary drinking outcome/endpoint measures**
- **Randomization abstinence requirement**
- **Inclusion of psychiatric co-morbidities?**
- **Need for patient reported outcome (PRO) scales**
- **PRO and/or biomarkers of drinking as endpoints**

The Alcohol Clinical Trials Initiative (ACTIVE): Purpose and Goals for Assessing Important and Salient Issues for Medications Development in Alcohol Use Disorders

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Although progress has been made in the treatment of alcohol use disorders, more effective treatments are needed. In the last 15 years, several medications have been approved for use in alcohol dependence but have only limited effectiveness and clinical acceptance. While academics have developed some 'standards' for the performance of clinical trials for alcohol dependence, they vary considerably, in the type of populations to be studied, the length of trials, salient outcome measures, and data analyses to be used (especially in the treatment of missing data). This variability impedes the commercial development of medications to treat alcohol dependence. Using a model similar to that used to develop an expert consensus for medications to improve cognitive aspects of schizophrenia (MATRICS) and in the treatment of pain (IMPACT), a workgroup has been formed under the auspices of ACNP, known as the ACTIVE (Alcohol Clinical Trials Initiative) group, to evaluate data from completed clinical trials to develop a consensus on key issues in the conduct of clinical trials in alcohol dependence. ACTIVE consists of academic experts, industry representatives, and staff from the Food and Drug Administration, the National Institute on Alcohol Abuse and Alcoholism, and the National Institute on Drug Abuse. This paper describes the rationale behind the effort, its history and organization, and initial key questions that have been identified as the primary focus of the workgroup. Future papers will focus on knowledge gained from the re-analysis of completed trials and provide consensus opinions regarding the performance of clinical trials that might be undertaken in the future.

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