7th Dialogue Session - September 27-28, 2023

Cross Company Abuse Liability Council

FDA Controlled Substance Staff

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Cross Company Abuse Liability Council

Opening Remarks

Beatriz Rocha, MD, PhD
Head Regulatory / Product Development &
Market Access Consulting
Fortrea

Creation of the Cross Company Abuse Liability Consortium

38 representatives from **18 pharmaceutical companies**
convened to discuss their experiences and challenges in the assessment of abuse potential

June 2006

RESULTS

Companies experiencing similar issues
Diverging opinions on scientific methodology (study design and data interpretation) / interactions with regulators

Agreement to work together for sharing of non-proprietary information and explore ways to advance the field

Four workgroups working independently/ quarterly meetings

- Regulatory
- Nonclinical
- Clinical
- Risk Management

2006 – Regulatory Context

EMA CHMP
Published Guideline for the nonclinical investigation of dependence potential

Controlled Substance Staff within the FDA to oversee the evaluation of abuse potential of drugs under development

Since 1990, FDA through the Drug Abuse Advisory Committee issued several draft guidances but none was publically available

Companies Unite to Advance Regulatory Landscape of Abuse Potential Assessment

Bringing together private and public stakeholders in an effort to address critical public health needs and to bridge scientific gaps.

Three key groups of stakeholders:

- Controlled Substance Staff (CSS) of FDA
- Pharmaceutical Research and Manufacturers of America (PhRMA)
- Cross Company Abuse Liability Consortium (CCALC)

2008 – First Major Initiative – FDA Dialogue Session

Collaboration Milestone – PhRMA sponsored Dialogue Session with FDA/CSS

- Hypothetical drug development case studies
  - scientific results /differing opinions in interpretation
- FDA staff/ representatives from 25 companies
- Both CCALC and CSS slide decks made publically available

2010 – 2nd FDA Dialogue Session

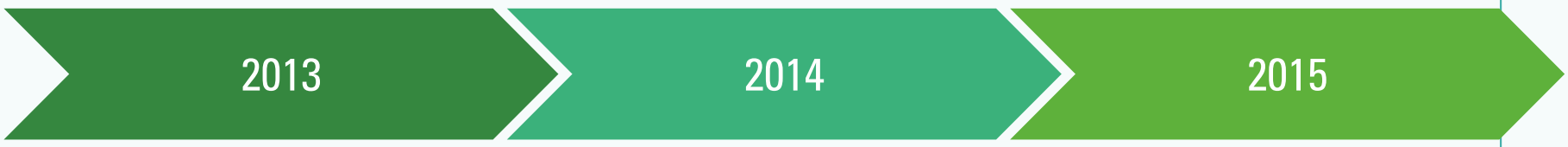
- CCALC Presentations of relevant issues and proposed improvement, followed by FDA's comments
- Very helpful exchange of information
- FDA indicated willingness to accept additional written comments and minutes of the session were submitted to the docket

Companies Unite to Advance Regulatory Landscape of Abuse Potential Assessment (*Rocha et al – Reg Focus 2011;16:8-13*)

Since 2010…

- 3rd FDA Dialogue Session – Abuse Deterrent Formulations (ADF)
- Draft Guidance ADF for Opioids Analgesics

- Final ADF Guidance published
- 4th FDA Dialogue Session – New challenges - Real-world data needed to assess whether the approval of an AD opioid product actually reduces opioid-related abuse, misuse, addiction, overdose, or death
- Post-marketing Requirements for additional studies for all drugs with approved abuse-deterrent language



2017

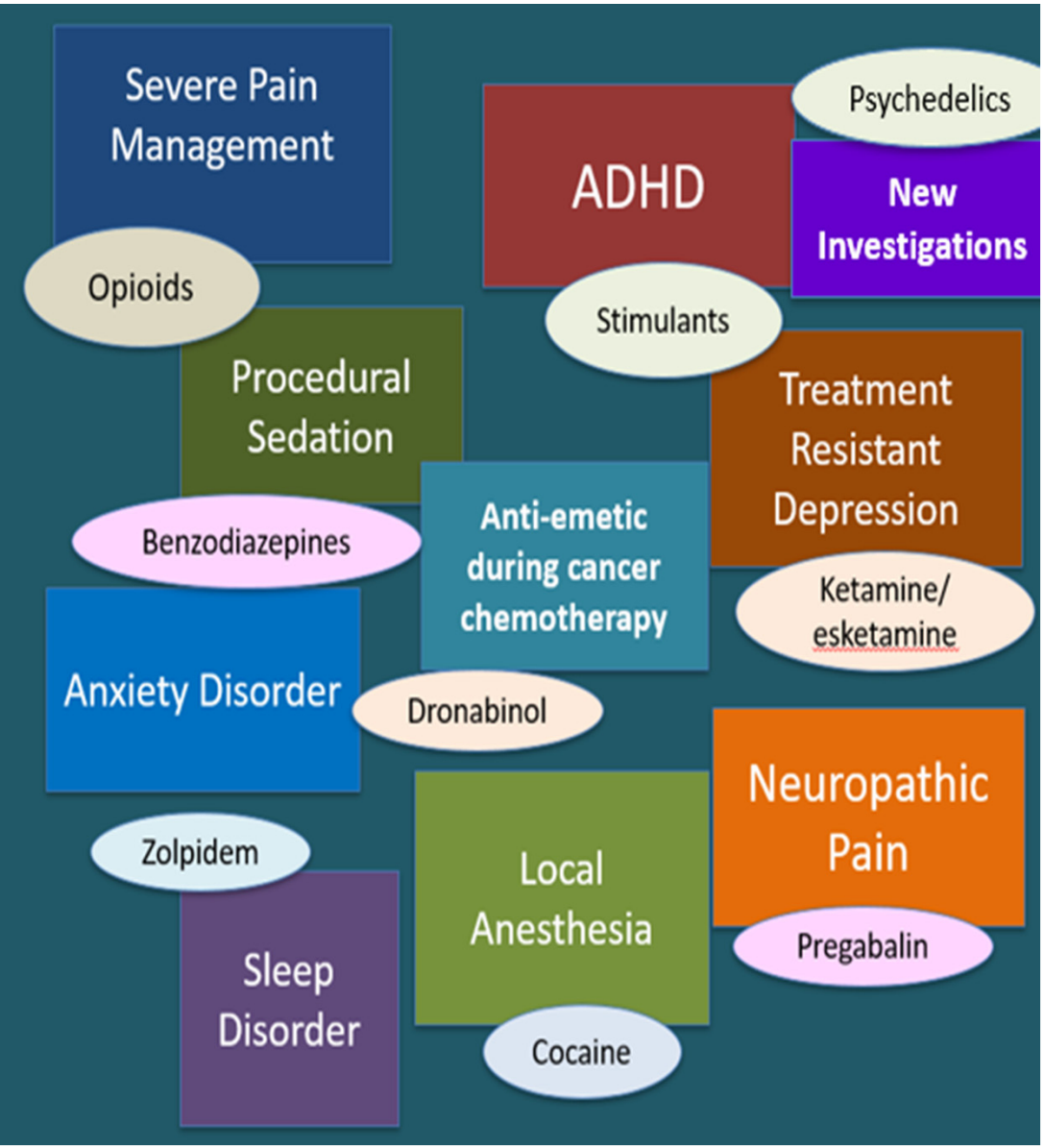
Final Assessment of Abuse Potential Guidance published

CCALC
From Consortium to Council

2015 – CCALC incorporated in the state of DE as Cross Company Abuse Liability Council

abuse

- Membership maintained average ~80
- Fall 2023 - 7th FDA Dialogue Session



U.S. FOOD & DRUG ADMINISTRATION

FDA Opening Remarks

Dominic Chiapperino, PhD

Director, Controlled Substance Staff
FDA's Center for Drug Evaluation and Research

Context for CCALC-FDA in 2023

Changes within FDA's Center for Drug Evaluation and Research to address drug abuse liability

- Controlled Substances Program, with Controlled Substances Initiatives staff

We are now more than six years out from the issuance of the 2017 "final" guidance for industry, Assessment of Abuse Potential of Drugs

- There has been a maturing of regulatory requirements, processes within FDA, and interactions with industry for their assessment of abuse risks as part of drug development
- There are still shifting patterns in nonmedical use of Rx drugs, abuse of illicit drugs, and new hot areas in drug development
- We have mutual interests with industry and academia for optimization of regulatory science for purposes of assessing abuse potential and dependence liability

Some Benefits of Matured Regulatory Interactions

- Earlier discussions between CSS and industry during drug development
  - Early review of industry proposals for assessing drug abuse and dependence risks of an investigational drug
- Adequate NDA submissions; less frequent incidents of incomplete data packages to assess abuse and dependence
- Appropriate consultation between CDER/Office of New Drugs' review divisions and CSS
- Timely communications between FDA and the Drug Enforcement Administration (DEA) for efficient drug scheduling actions
  - Enhanced by the Memorandum of Understanding between the agencies
  - Implementation of provisions from 2015 legislation, the Improving Regulatory Transparency and New Medical Therapies Act for efficient drug control actions by DEA

Responsiveness to Shifting Patterns in Nonmedical Substance Use

- The science and methodologies to assess the abuse potential of new molecular entities in drug development can also answer questions about real-world nonmedical use of drugs
  - New or changing postmarket signals of drug abuse and misuse
  - Polydrug use and drug combinations in illicit drug trafficking
  - Designer drugs in illicit channels
- We need better understanding of marketed unapproved drugs representing nonmedical substance use of unknown or unclear intent
- FDA is striving to better communicate drug risks and to conduct research to answer questions about drug safety, abuse liability, and reasons for nonmedical use
- The agenda for today and tomorrow will stimulate discussion both for assessing new molecular entities and for understanding real-world substance use patterns

Agenda Highlights…

- Topic #1: Exploring the Sensitivity of Pharmacodynamic Endpoints in the Human Abuse Potential (HAP) Study
  - ***Discussion to hypothesize reasons for occasional discordant findings between nonclinical and clinical studies, and between HAP studies versus epidemiological data***
- Topic #2: Evolving Statistical Methodology to Assess HAP Studies
  - ***Discussion of issues relating to HAP study qualification procedures and margin (δ); treatment of outlier responses; recommendations for a modified completer population as the primary population for analysis***
- Topic #3: Identifying and Reporting Relevant Adverse Events (AEs) Related to Abuse Potential Across Clinical Trials
  - ***Discussion of recommended AE terms on which to focus for abuse potential signal detection; ideal ways to present and analyze data; utility of AE analysis in assessment goals***
- Topic #4: Incorporating Behavioral Economic Assessments (Preclinical and Clinical Discussion)
  - ***Discussion of pros and cons of BE models for abuse potential assessment for regulatory purposes***

Agenda Highlights (continued)…

- Topic #5: Methodological Considerations for the Abuse Potential Evaluation of Psychedelics (Preclinical and Clinical Discussion)
  - ***Discussion of recommended studies and data for an abuse potential assessment; necessity of a HAP study; design considerations for a HAP study for psychedelic drug***
- Topic #6: Evaluating Physical Dependence and Withdrawal (Preclinical and Clinical Discussion)
  - ***Discussion of recommendations on protocol design; utility and necessity of preclinical versus clinical assessments; regulatory fulfillment for abuse potential assessment versus clinical safety of drug discontinuation***
- Topic #7: Discussion of Preclinical Assessments and Best Practices
  - ***Discussion of protocol design issues and utility of preclinical methods in abuse potential assessment***

On to the first presentation and panel discussion, Topic #1….