



FDA Activities in Analgesic Drug Development, Research and Safety

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NIH



Public Meetings Held in Last Year

- Hydrocodone up-scheduling advisory committee meeting
 - Vote: 19 Y, 10 N, 0 Ab
- Zohydro (single-entity) hydrocodone extended-release product advisory committee meeting
 - Vote: 2 Y, 11 N, 1 Ab
- Part 15 Hearing on use of opioids in CNCP
 - Reviewing docket and transcripts and considering possible regulatory actions

ER/LA Opioid REMS Goes Live

- Approved July, 2012
- Educational CME modules based on FDA Blueprint became available March, 2013
- Companies must assure opioid prescribers undertake the training
- Ongoing series of assessments

Abuse-deterrent Formulations

- *Guidance for Industry: Abuse-Deterrent Opioids – Evaluation and Labeling*
- Draft published January, 2013
- Four tiers of possible labeling claims based upon abuse-deterrent properties:
 - Tier 1: The Product is Formulated with Physicochemical Barriers to Abuse (in vitro data)
 - Tier 2: The Product is Expected to Reduce or Block Effect of the Opioid When the Product is Manipulated (pharmacokinetic data)
 - Tier 3: The Product is Expected to Result in a Meaningful Reduction in Abuse (abuse-liability data)
 - Tier 4: The Product has Demonstrated Reduced Abuse in the Community (long-term epidemiology data)

Abuse-deterrent Formulations

- OxyContin
 - Citizen’s Petition and Labeling Supplement
 - Agency responded to CP on X-X-13 and approved supplement on X-X-13
 - Data from in vitro and abuse liability studies demonstrated some degree of abuse-deterrence for nasal and IV routes of abuse
 - Oral abuse still possible
- Opana ER
 - Citizen’s Petition
 - Agency responded on 5-10-13
 - Did not find the data from in vitro, abuse-liability or epidemiological studies adequate to support claim of abuse-deterrence
- Note: Abuse-deterrent generics guidance under development

Studies of Long-term Efficacy and Safety of Opioids in CNCP

- Efficacy
- RESOLVE ACTION Working Group
- To be discussed further at a think tank of stakeholders to be convened by CTTI/Duke
- Safety
- Will also discuss development of long-term observational epidemiological study of safety, focusing on addiction, overdose, hyperalgesia, etc.

Safe Use Initiative

Mission:

Creating non-regulatory solutions and interventions to preventable drug harm through collaborations within healthcare communities

Goal:

To reduce preventable harm from FDA regulated drugs

FDA Regulatory

- Risk Evaluation and Mitigation Strategy (REMS)
 - Measure impact
- Labeling changes
- Advisory committee
- Require new studies to assess observed safety signals
- Drug safety communications
- Develop guidance documents

FDA Safe Use

- Convene stakeholders:
 - Identify drug safety issue (s)
 - Discuss barriers
 - Propose interventions
- Create voluntary collaborative efforts
 - Implement interventions
 - Measure impact
- Federal, non-federal partners (private)
- Join ongoing drug safety activities
- Support literacy, adherence, HIT activities

Safe Use Initiative

Choosing a Program for Collaboration and Development of Intervention(s)

Criteria List

CDER Regulated Drug

Preventable Harm

Appropriate Timing

Impact on Public Health

Stakeholder Collaboration

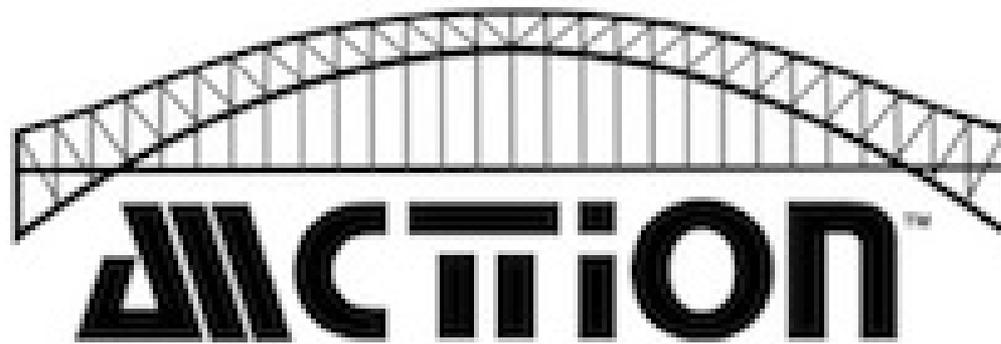
Strategies and Interventions

Outcome Measurements

Safe Use Initiative

Safe Use Programs and Supported Research

- **Developing a model Patient Prescriber Agreement for Opioid Treatment**
- **Safe Disposal of Fentanyl Patches**
- **Centers for Excellence in Regulatory Science and Innovation (CERSI)** – U. MD examining patient prescriber agreements for opioids
- **Prescription Behavior Surveillance System (PBSS)**
- **Opioid Research Cooperative Agreements**
 - South Carolina – Academic Detailing of Opioid Prescribers
 - Oregon – Urine drug screening in the VA
 - Wisconsin – Tools and toolkit to enhance safe opioid prescribing
 - Maimonides – Utilize NY PDMP data to identify and educate prescribers



ACTION: Objectives & Structure

- Public-private partnership 1) to bring together thought leaders, all stakeholders, to advance research, and 2) to have the private partner raise funds for the needed research
- Initially one-year contract intended to advance the field of analgesic clinical trial design and the development of safer, effective analgesic drug products (2009)
- Contract competed and awarded to University of Rochester – Dr. Robert Dworkin, leading pain researcher and clinical trialist
- Next iteration: a five-year Cooperative Agreement (grant), again competed and awarded to U of R – Dr. Dworkin (2010)

ACTTION: Meeting Its Goals and Providing Public Health Benefits

- Initiated because of the paucity of safe analgesics and the unreliability of analgesic trials in demonstrating efficacy, even in well-established analgesic drugs
- ACTTION enormously successful in first two years: 1) number/extent of working groups, sub-consortia and other projects (17), 2) inclusion of key stakeholders, e.g., academics, industry and patient advocates, 3) actual work product, i.e., publication of 12 articles in peer-reviewed journals, and 4) funds raised (\$3.2 M)
- Expanded to include anesthetic, addiction and painful peripheral neuropathies, because the problems are the same
- Frequent conferences, scientific workshops, consortia meetings, are also interim deliverables

ACTION: Current Sub-Consortia

- Sedation Consortium on Endpoints and Procedures for Treatment, Education, and Research
- Consortium for Addiction Research on Efficacy and Safety
- Pediatric Pain Research Consortium
- Preclinical Pain Research Consortium for Investigating Safety and Efficacy
- Clinical Endpoints and Procedures for Peripheral Neuropathy Trials
- Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials
- Abuse Liability Evaluation for Research, Treatment, and Training
- Randomized Enrollment Study of Opioid Long-term use to evaluate Efficacy
- Pain-Related Outcomes Training and Evaluation for Conducting Clinical Trials

ACTION: Current Projects

www.action.org

- Development of a comprehensive, evidence-based acute and chronic pain taxonomy (modeled on DSM-III)
- Community Patient Awareness About Clinical Trials
- Resource for Evaluating Procedures and Outcomes of Randomized Trials
- Repository of Registered Analgesic Clinical Trials
- Safety and Benefit-Risk Reporting and Evaluation
- Retrospective Evaluation of Patient-Level Information from Controlled Analgesic Trials of Efficacy
- Analgesic Comparative Effectiveness and Pragmatic Trials
- Standardized Analgesic Database for Research, Discovery, and Submissions