2nd Human Abuse Liability & Abuse-Deterrent Formulations

Avoid Regulatory Penalties and Improve Market Success by Clearly Demonstrating Reduction of the Abuse Potential in New and Existing Drugs

November 2-3, 2015 | Hyatt Regency Bethesda | Bethesda, Maryland

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EGALET

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JANSSEN

Travis Mickle
CEO
KEMPHARM

Audra Stinchcomb
CSO
F6 PHARMA

David Horton
Principal Scientist, Safety Pharmacology
PFIZER

Joseph Stauffer
CMO
CARA THERAPEUTICS

Preclinical and Clinical Techniques to Minimize Drug Abuse Potential

Regulatory and Methodological Updates for Demonstrating Abuse Potential!

♦ EGALET Optimizes Abuse-Deterrent Product Label Claims
♦ PFIZER Improves the Clinical Predictive Value of Preclinical Abuse Potential Models
♦ ATLANTIC PHARMA Pursues Generic Candidates After Changes to Regulatory Tiered Safety Claims

Technical Breakthroughs in Abuse-Deterrent Formulations!

♦ CARA THERAPEUTICS Refines Non-Addictive Kappa Opioids
♦ RECKITT BENCKISER Designs Subcutaneous Time-Release Opioids to Eliminate Oral Supply
♦ ACURA PHARMA Prepares for Anti-ADF Countermeasures from Drug Abusers

Improvements in Abuse Liability Trial Design!

♦ MITSUBISHI TANABE PHARMA Ranks the Best Pain Scales for Trial Questionnaires
♦ TEVA Designs Test Protocols for ADF Categories 1-3
♦ UPSHER-SMITH Accounts for Missing Data in Statistical Analysis

“Helpful, thought-provoking, and very interesting presentations. I appreciated the rich source of data and information.”
—Manager, Regulatory Affairs, SUNOVION

“Excellent presentations and good dialogue.”
—Senior Director, Clinical Research, EGALET CORPORATION

For More Information Call 866-207-6528 or Visit www.exlevents.com/hal
Dear Colleague,

Popular concern over the addiction potential of opioid analgesics, as well as stimulants, benzos and other drugs, is putting tremendous pressure on the drug industry. Amidst fears from patients, physicians and payers, the past year has seen the FDA release several different versions of regulatory guidelines clarifying their expectations for both the technical development of less addictive drugs as well as for best practices in designing preclinical and clinical studies that give the most accurate assessment of a drug’s abuse potential.

Now in its second year, ExL Events’ Human Abuse Liability & Abuse-Deterrent Formulations conference is the only event available that gives you in-depth industry knowledge on the approach required for demonstrating the improved safety of your opioids and other potentially addictive therapeutics in order to improve market potential. Join us this year to learn how to:

✧ Adapt to new and pending regulatory guidelines for both branded and generic drugs
✧ Design analgesics that have a non-addictive pharmacology
✧ Select the most appropriate comparator drugs and adverse event terminology during clinical research
✧ Minimize the abuse risk of drugs through multiple delivery mechanisms, including oral, topical and subcutaneous
✧ Employ the ideal data tracking techniques to illustrate changes in the real abuse levels of specific drugs and formulations
✧ Engage with more than 100 industry experts on the latest regulatory and technical approaches for lowering the abuse potential of prescription drugs

We look forward to welcoming you to Bethesda this fall!

Sincerely,

Matt Greenbaum

Matt Greenbaum
Production Team Leader, ExL Events
mgreenbaum@exlevents.com

If you require overnight accommodations, please contact the hotel at 1 888-421-1442 or 402-592-6464 and request the group rate for ExL’s HAL and CNS Meetings. The group rate is available until October 12, 2015. Please book your room early as rooms available at this rate are limited.

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Obtaining abuse-deterrent claims in a product label requires an understanding of the technical aspects of the April 2015 FDA Guidance on Abuse-Deterrent Opioids - Evaluation and Labeling. In addition, it requires familiarity with how the Agency views this evolving field in the context of wanting to see “incremental improvement” in new product candidates being submitted for review. An appreciation of both of these factors will be helpful in the design and execution of an abuse-deterrent development program with the goal of achieving strong label claims.

- Review the final FDA Guidance on Abuse-Deterrent Opioids and highlight the key changes compared to the draft Guidance.
3:30 **Evaluate Abuse Deterrence in Clinical Trials: Adverse Events and Other Outcomes of Interest**
Currently abuse deterrence is evaluated with in vitro laboratory, pharmacokinetic and human abuse potential studies. However, other relevant data obtained during clinical development may be integral to evaluating the effectiveness of an abuse deterrence product and its safety profile. Examination of various safety data, patient reported outcomes and other measures can generate relevant data for assessing the robustness and characteristics of an ADF.

- Understand the relevant adverse events evaluated for abuse and dependence potential
- Identify other outcome measures that can measure the effectiveness of an ADF
- Examine strategies for evaluating the safety profiles of ADFs

Beatrice Setnik, Vice President, Clinical Pharmacology, INC RESEARCH

5:45 **Networking Reception Sponsored by**

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4:15 **Manipulations of Abuse-Deterrent Formulations at the Clinical Pharmacology Unit**
Scott Smiley, Director, Pharmacy Operations, VINCE & ASSOCIATES CLINICAL RESEARCH

5:00 **Exciting Challenges in the Preclinical Abuse Liability Testing of Novel CNS-Active Drug Candidates**
Discovery phase information can help you pre-emptively eliminate compounds with poor developability and reduce unnecessary drug discrimination studies. The high early failure rate of many compounds means an over-reliance on drug discrimination screening puts you at risk for wasting resources before the critical decisions have been made to proceed with a candidate — so well-designed preclinical models are vital for displaying statistical significance at lower drug levels. By properly designing your studies, you can build a framework for convincing comparisons of different abuse-deterrent products and methods.

- Discuss the performance of preclinical animal models within the context of the latest regulatory guidelines
- Properly actualize drug abuse models that can test for active metabolites that would otherwise be overlooked
- Rigorously compare the performance of different ADF varieties such as aversion agents and antagonists

Greet Teuns, Scientific Director, Toxicology, Safety Pharmacology, CNS and Drug Abuse, JANSSEN

5:45 **Networking Reception Sponsored by**

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8:00 Continental Breakfast

**Tuesday, November 3, 2015**

8:45 Track Chairperson’s Opening Remarks
Lorraine Rusch, Ph.D., Vice President, Business Development, VINCE & ASSOCIATES CLINICAL RESEARCH

9:00 **Modify Abuse Liability Trial Designs with Greater Versatility for Generic Drugs**
As long as the FDA isn’t asking for behavioral data, your abuse liability trial setup may be straightforward. Blood test results will reveal the presence of antagonists from ADFs and help clarify whether the product is still abuse-prone.

- Craft the best study design to clarify patient responses on product preferability
- Validate in-vitro data to predict the results of human trials
- Extrapolate the protocol changes necessary to get abuse-deterrent label claims on generics, and how best to proceed without access to innovator NDA

Lynn Webster, Vice President, Scientific Affairs, PRA HEALTH SCIENCES

**Track A: Abuse Liability Test Design**

**Track B: Technical Breakthroughs in Abuse Deterrence**

**Defining the Next Generation of Abuse Deterrence Techniques**
Drug manufacturers are heeding market and regulatory pressure with the development of abuse-deterrent oral opioids. As research validates that these medicines remain effective while reducing rates of abuse, more must be done to foster a broader market transition to ADFs. Other commonly abused medications – not just for pain, not just pills, and not just branded drugs – should be made abuse-deterrent, and payers should cover them.

- Discuss the spectrum of abuse-deterrent technologies currently recognized by FDA
- Highlight novel delivery systems, low-residual-dose technologies, and other next-generation concepts of abuse deterrence
- Call for a forward-thinking expansion of the definition of abuse-deterrent medications as part of efforts to encourage widespread adoption

Michael Barnes, Executive Director, CENTER FOR LAWFUL ACCESS AND ABUSE DETERRENCE
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<tr>
<th>Time</th>
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<td>Risk Management and Monitoring Plans to Predict Abuse Potential</td>
<td>Lisa Benaise, Head, Office of Medical Safety Evaluation, MITSUBISHI TANABE PHARMA</td>
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<tr>
<td>9:45</td>
<td>Advance Transdermal Patch Delivery Systems into Abuse Deterrence</td>
<td>Audra Stinchcomb, CSO, F6 PHARMA</td>
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<td>10:30</td>
<td>Networking Break</td>
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<td>11:00</td>
<td>Understand Regulatory Expectations and Optimize Submission and Post-Submission Discussions with FDA</td>
<td>Penny Levin, Director, Global Regulatory Intelligence and Policy, TEVA</td>
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<td>11:45</td>
<td>Proper Statistical Foundations for Human Abuse Clinical Trials</td>
<td>Vincent Yu, Director, Biometrics, UPSHER-SMITH</td>
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<td>Analyze the Scientific and Market Potential for Kappa Opioids</td>
<td>Joseph Stauffer, CMO, CARA THERAPEUTICS</td>
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<td>12:30</td>
<td>Luncheon</td>
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<td>1:30</td>
<td>Select Databases and Define Terms to Track Abuse</td>
<td>Soledad Cepeda, Director, Epidemiology, JANSSEN</td>
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<td>Enable Prodrug Solutions to Lower the Abuse Potential for Fast-Release Opioids</td>
<td>Travis Mickle, CEO, KEMPHARM</td>
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9:45 Risk Management and Monitoring Plans to Predict Abuse Potential
Getting the fullest picture of the abuse potential of your drug requires monitoring a diverse array of data through appropriately designed questions and pill-tracking programs. By determining which avenues of abuse are more and less likely, you can make a more convincing presentation to regulatory agencies.
- Remove ambiguity from new pill orders by predicting when refills would normally be requested
- Rank the best pain scales and measuring tools for your questionnaires
- Establish SMQs to seek out adverse events

Lisa Benaise, Head, Office of Medical Safety Evaluation, MITSUBISHI TANABE PHARMA

9:45 Advance Transdermal Patch Delivery Systems into Abuse Deterrence
Transdermal opioid patches have residual drugs left in them after use, which can be chewed, swallowed or smoked for abuse purposes. This is an underexplored area that needs further development of abuse-deterrent formulations.
- Build from successful ADFs of other delivery routes to reduce risks associated with topical patch abuse
- Add antagonists such as naloxone to patches to block the receptors
- Map the marketing future of both branded and generic ADF patches

Audra Stinchcomb, CSO, F6 PHARMA

11:00 Understand Regulatory Expectations and Optimize Submission and Post-Submission Discussions with FDA
Drug companies must thoroughly prepare for the pre-NDA meeting and smoothly orchestrate the NDA submission. By creating a rapid response team, you can be better positioned to respond to FDA questions in a transparent and direct manner in order to facilitate a clean review.
- Identify the biggest pre-IND considerations
- Discuss appropriate ADF Category 1 studies - formulation analyses and in vitro testing
- Design protocols for FDA review of ADF Category 2 and Category 3 studies

Penny Levin, Director, Global Regulatory Intelligence and Policy, TEVA

11:45 Proper Statistical Foundations for Human Abuse Clinical Trials
Sample sizes and endpoints are just some of the key statistical factors that are associated with the design and analysis of successful human abuse clinical trials. The selection of active controls and the placebo effect are among other factors that can sway trial outcomes.
- Re-envision HAL trial setup based on FDA guidance
- Prepare and account for missing data points
- Focus on the importance of statistical methods in study design

Vincent Yu, Director, Biometrics, UPSHER-SMITH

11:45 Analyze the Scientific and Market Potential for Kappa Opioids
Kappa opioids may represent the next breakthrough product in analgesic development. Since these drugs work on the dorsal root ganglion and other peripheral tissues instead of the brain and do not pass the blood brain barrier, they may be less prone to euphoric sensation, and by virtue of their pharmacology have the potential to be less addictive. How viable is this approach for your portfolio?
- Investigate the history of receptor-agonist products
- Compare and contrast oral versus IV delivery routes of kappa opioids
- Forecast the healthcare system's response to these new products

Joseph Stauffer, CMO, CARA THERAPEUTICS

12:30 Luncheon

1:30 Select Databases and Define Terms to Track Abuse
Retrospective cohort studies can be vital tools for tracking the actual abuse rates of specific drugs and separating their signals from those that are not abused. Proper selection of databases and terms is a must-have first step in evidentiary assessment of the risks of each drug and the successes of ADFs.
- Incorporate distance traveled to account for doctor shopping
- Differentiate between misuse and abuse of prescription drugs
- Scan insurance claim records, EMRs and national data indices

Soledad Cepeda, Director, Epidemiology, JANSSEN

1:30 Enable Prodrug Solutions to Lower the Abuse Potential for Fast-Release Opioids
While the industry is making progress toward mitigating abuse risks of extended release opioids, the greater challenge comes from avoiding the euphoria of rapid release drugs. The most efficient way of blocking the “high” from a fast-acting opioid is to design a prodrug formulation.
- Engineer opioids with prodrug features that cannot become addictive
- Distinguish between fast-release and extended-release products
- Stay up to date with the latest advances in prodrug science

Travis Mickle, CEO, KEMPHARM

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2:15 Re-Envision Abuse Liability Testing in the Context of Your Preclinical Pipeline

Preclinical drug safety tests must run the gamut of PK, safety pharmacology, toxicology, and animal dependency and withdrawal symptoms, among others. The broader industry and regulatory interest in clinical and marketing risks for drug abuse means your preclinical tests are more important than ever and must be correctly integrated into a broader testing timeline. Even if you begin to see early-stage clinical adverse events, continuing with animal research will give you a fuller picture of the drug’s properties and behavior.

- Target preclinical animal studies toward improving the design of eventual human abuse potential research
- Rely on specimen pharmacology to choose better comparators
- Keep to the preclinical testing regimen that regulators prefer

Mary Jeanne Kallman, CEO, KALLMAN PRECLINICAL CONSULTING; former Group Leader, Safety Pharmacology, ELI LILLY

New Subcutaneous Formulations to Reduce Oral Drug Abuse

Most ADFs aim to reduce the likelihood of success among drug abusers attempting to crush, snort or inject opioids. However, the most common route of abuse and starting point on the trajectory of addiction is through oral administration. Current guidelines do not address oral drug abuse in detail, so what is the best path forward to reduce the risks?

- Design subcutaneous time-release formulations that eliminate oral supply
- Quantify the benefits of removing physical access to drugs and accidental pediatric dosage risks
- Examine the possible countermeasures for extraction that addicts might employ

Nick Reuter, Manager, Risk Mitigation and Public Policy, RECKITT BENCKISER

3:00 Conference Concludes

“Nearly half of the nation's 38,329 drug overdose deaths in 2010 involved painkillers like hydrocodone and oxycodone... These narcotics now kill more adults than heroin and cocaine combined, sending 420,000 Americans to emergency rooms each year.”

—The New York Times, April 21, 2014

“Hydrocodone-based painkillers are the most-prescribed pharmacy drugs in the U.S. About 131 million hydrocodone products were dispensed in 2011.”

—Bloomberg News, March 12, 2014

“Across the country, more than 16,000 people died in 2013 from overdoses involving pain medications, and 1 in 20 people in the U.S. age 12 and older reported using prescription pain medicines for nonmedical reasons.”

—Forbes, March 3, 2015
Registration fees for attending ExL’s 2nd Human Abuse Liability & Abuse-Deterrent Formulations conference:

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<tr>
<td>ONSITE PRICING</td>
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**GROUP DISCOUNT PROGRAM**

Offers cannot be combined. Early Bird rates do not apply. To find out more on how you can take advantage of these group discounts, call 866-207-6528.

SAVE 25% per person when registering four

For every three simultaneous registrations from your company, you will receive a fourth complimentary registration to the program (must register four at one time). This is a savings of 25% per person.

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Can only send three? You can still save 15% off of every registration.

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Do you have a question that you would like to be addressed at this event? Would you like to get involved as a speaker or discussion leader?

Please email Production Team Leader Matt Greenbaum at mgreenbaum@exlevents.com.
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