Advancements and Challenges in Abuse Potential Evaluation 2023

Agenda

27-28 September 2023
Hilton Hotel and Executive Meeting Center, Rockville, MD

Organized by the Cross-Company Abuse Liability Council (CCALC),
With scientific support from Food and Drug Administration (FDA),
And participation by representatives of FDA

DAY 1	**Wednesday, 27 September 2023**
7:30-8:00	**Breakfast and Registration**
Welcome	
8:00-8:10	*Beatriz Rocha (CCALC, Fortrea)*
8:10-8:20	*Dominic Chiapperino (FDA/OCD/CSS)*
Topic #1: Exploring the Sensitivity of Pharmacodynamic Endpoints in the Human Abuse Potential (HAP) Study	
8:20-8:45	Considerations of Discordant Findings from Nonclinical, Clinical and Epidemiological Data. *Presenter: Silvia Calderon (FDA/OCD/CSS)*
	Panel Discussion
8:45-9:30	• For drugs with novel mechanism of action and for which nonclinical studies may be suggestive of no abuse potential: ○ Are there any approaches that could help us to identify and measure subjects' drug seeking preferences among drugs producing similar overall pharmacological effects? • Could HAP studies be used as a framework for drug preference questionnaires or other approaches? (e.g. money vs drug choice analysis or other parameters from a behavioral economics assessment) • Are there any key data gaps that may impact scheduling decisions and data interpretation? *Panelists: Kerri Schoedel (Altreos Research Partners), Beatrice Setnik (Altasciences), Jack Henningfield (Pinney Associates), Thomas Hudzik (ALA Biopharma Consulting), Beatriz Rocha (Fortrea), Chad Reissig (FDA/OCD/CSS), Rose Radin (FDA/OSE/OPE/DEPIII), Dominic Chiapperino (FDA/OCD/CSS), Silvia Calderon (FDA/OCD/CSS)*
Topic #2: Evolving Statistical Methodology to Assess HAP Studies	
9:30-9:45	Selecting Margins for Different Positive Controls (vs Placebo) – Does a One Size Fits All Approach Work? *Presenter: Denise Milovan (Altasciences)*
9:45-10:05	Enhancement of Enrichment on the HAP Study Population. *Presenter: Ling Chen (FDA/OTS/OB/DBVI)*
Morning Break	
10:05-10:20	
	Panel Discussion
10:20-10:50	• Evaluating margins for differentially scheduled positive controls • Best approaches to define a modified completer population • Handling variability on Drug Liking (effect size based on drug class)

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	Panelists: Qianyu Dang (FDA/OTS/OB/DBVI), Yu Ding (Altasciences), Beatrice Setnik (Altasciences), Denise Milovan (Altasciences), Ling Chen (FDA/OTS/OB/DBVI)
Topic #3: Identifying and Reporting Relevant Adverse Events (AEs) Related to Abuse Potential Across Clinical Trials	
10:50-11:05	Challenges of Capturing and Reporting Adverse Events to Assess Abuse Potential in Clinical Trials. *Presenter: Cynthia Arons (Pfizer)*
11:05-11:20	Identifying Relevant Adverse Events of Interest and Recommendations for Analysis and Presentation of Data in the NDA Submission. *Presenter: Steven Galati (FDA/OCD/CSS)*
	Panel Discussion
11:20-11:50	• What is the right list, how do we balance inclusivity and reducing noise • How is it determined which events need narratives, can this be done early enough to plan for the information needed • What events trigger a HAP study • Are there other methods to capture the events, i.e., checklists, questionnaires • How does diversion relate *Panelists: Joshua Lloyd (FDA/OCD/CSS), Thomas Sciascia (Trevi Therapeutics), Ryan Lanier (Pinney Associates), Steven Galati (FDA/OCD/CSS), Cynthia Arons (Pfizer)*
Lunch	
11:50-12:50	
Topic #4 Incorporating Behavioral Economic Assessments	
12:50-1:20	Exploring Behavioral Economics Outcome Measures in Animal and Human Abuse Potential Studies. *Presenter: Neil Varshneya (FDA/OCD/CSS)*
1:20-1:35	Behavioral Economics for Abuse Potential Assessment. *Presenter: Steven Hursh (Institutes for Behavior Resources)*
	Panel Discussion
1:35-2:05	• *What are the benefits of this model over existing models, does it fill a gap* • *The role of currently available measures (e.g., Subjective Drug Value, Money vs Drug Choice) vs novel approaches* • *Pragmatic considerations in study design* • *Validation for broader use* • *Market economics-external factors* *Panelists: Beatrice Setnik (Altasciences), Thomas Hudzik (ALA Biopharma Consulting), Chad Reissig (FDA/OCD/CSS), Justin Strickland (Johns Hopkins University School of Medicine), Sandra Comer (Columbia University), Dominic Chiapperino (FDA/OCD/CSS), Neil Varshneya (FDA/OCD/CSS), Steven Hursh (Institutes for Behavior Resources)*
Topic #5: Methodological Considerations for the Abuse Potential Evaluation of Psychedelics	
2:05-2:30	A Regulatory Perspective on the Preclinical and Clinical Abuse Potential Evaluation of Psychedelics. *Presenter: Katherine Bonson (FDA/OCD/CSS)*
2:30-2:45	Current Approaches to the Preclinical Abuse Potential Evaluation of Psychedelics. *Presenter: David Heal (DevelRx)*

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2:45-3:00	Current Approaches to the Abuse Potential Clinical Evaluation of Psychedelics. *Presenter: Beatrice Setnik (Altasciences)*
	Panel Discussion
3:00-3:30	Panel Discussion Part 1 (preclinical) • Comment on methodological approaches and limitations • Differentiating required elements of the abuse potential assessment for known psychedelics vs NMEs *Panelists: Jamie DaSilva (Pfizer), Paul Kruzich (PTC Therapeutics), Thomas Hudzik (ALA Biopharma Consulting), Katherine Bonson (FDA/OCD/CSS), David Heal (DevelRx)*
Afternoon break	
3:30-3:45	
	Panel Discussion

3:45-4:45	Panel Discussion Part 2 (clinical)
	• Scenarios/ psychedelics for which a conventional HAP study may/may not be required
	• HAP study methodological considerations for psychedelics
	  ○ Identifying appropriate positive controls for HAP studies
	  ○ Considerations for dosing and repeat exposure
	  ○ "(At the Moment) Drug Liking" as a primary endpoint for psychedelics
	  ○ Considerations for most informative primary and secondary endpoints
	  ○ Additional questionnaires and scales
	  ○ Appropriate selection of subjects
	  ○ Defining the role of the facilitator for Phase I psychedelic trials
	  ○ Environment/setting in a HAP study
	• Risk management issues for a potential postmarket setting
	Panelists: Denise Milovan (Altasciences), Steven Galati (FDA/OCD/CSS), Heddie Martynowicz (Neokee Pharma Consulting), Naama Levy-Cooperman (Altreos Research Partners), Ryan Lanier (Pinney Associates), Sophia Raitsin (Biopharma Services), Beatrice Setnik (Alta Sciences), Katherine Bonson (FDA/OCD/CSS), Joshua Lloyd (FDA/OCD/CSS), Silvia Calderon (FDA/OCD/CSS)

Day 1 Summary and Closing Remarks	
4:45-5:00	*Beatriz Rocha (CCALC, Fortrea)*
Networking Reception	
5:30-6:30	

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Day 2	**Thursday, 28 September 2023**
7:30-8:15	**Breakfast and Networking**
Opening Remarks and Overview	
8:15-8:20	*Beatriz Rocha (CCALC, Fortrea)*
Topic #6: Evaluating Physical Dependence and Withdrawal	
8:20-8:35	FDA Perspective on Best Practices for the Preclinical Evaluation of Physical Dependence and Withdrawal (PDW). *Presenter: Jovita Randall-Thompson (FDA/OCD/CSS)*
8:35-8:50	Proposal for Preclinical Evaluations of PDW. *Thomas Hudzik (ALA Biopharma Consulting)*
	Panel Discussion
8:50-9:50	• Incorporation of learnings from clinical WD syndromes (e.g., sleep disturbances for stimulants, anhedonia) when selecting endpoints for preclinical PDW studies • Stand-alone studies vs Add-on to general toxicology studies; study design considerations for positive control and dose selection. • Utility of preclinical dose tapering for informing clinical strategy • Appropriate duration of monitoring during the WD period (PK/PD driven vs. fixed) • Demonstrating model sensitivity and interpretation of WD vs. rebound/recovery in the context of a positive control. *Panelists: Jamie DaSilva (Pfizer), Paul Kruzich (PTC Therapeutics), Chad Reissig (FDA/OCD/CSS), David Heal (DevelRx), Thomas Hudzik (ALA Biopharma Consulting), Jovita Randall-Thompson (FDA/OCD/CSS)*
9:50-10:05	Regulatory Requirements for Assessing Physical Dependence and Withdrawal in Human Subjects. *Presenter: Emily Deng (FDA/OCD/CSS)*
10:05-10:20	Pragmatic Considerations for Assessing Physical Withdrawal in Phase 2/3 Studies. *Presenter: Thomas Sciascia (Trevi Therapeutics)*
Break	
10:20-10:35	
	Panel Discussion
10:35-11:35	• Timing and duration of physical dependency assessments in Phase 2/3 trials • to identifying adverse events related to withdrawal • Pragmatic data collection in patient studies – how to include PK and other in clinic assessments • Demonstrating model sensitivity and interpretation of WD vs. rebound neuroadaptation in the context of a positive control. • Assessment for abuse potential vs safety (CSS/OND) • Best practices

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	Panelists: Beatrice Setnik (Altasciences), Kerri Schoedel (Altreos Research Partners), Michael Klein (Controlled Substance Scientific Solution), Beatriz Rocha (Fortrea), Joshua Lloyd (FDA/OCD/CSS), Emily Deng (FDA/OCD/CSS), Thomas Sciascia (Trevi Therapeutics)
Topic #7: Discussion of Preclinical Assessments and Best Practices	
11:35-11:50	Defining Controls, Variables and Conditions for Preclinical Evaluations of a Novel Drug Entity. *Presenter: Sharon Rowton (Labcorp)*
11:50-12:05	Regulatory Perspective on Positive Controls vs Comparators in Preclinical Drug Discrimination and Self-Administration Studies, Other Updates in Considerations for Design of these Studies. *Presenter: Chad Reissig (FDA/OCD/CSS)*
Lunch	
12:05-12:50	
	Panel Discussion
12:50-1:50	• Which controls, variables and conditions are required to validate assessment of a NME in self-administration and drug discrimination (e.g., higher responding for training drug vs vehicle under FR schedule and >80% appropriate responding for training drug in generalization testing) • Positive Controls vs comparators; study validation vs. NME differentiation (e.g., between a C-II and C-IV) *Panelists: Jamie DaSilva (Pfizer), Paul Kruzich (PTC Therapeutics), Thomas Hudzik (ALA Biopharma Consulting), David Heal (DevelRx), Chad Reissig (FDA/OCD/CSS), Sharon Rowton (Labcorp)*
1:50-2:05	Design Considerations and Interpretation of Preclinical studies – An Overview of Current Challenges. Presenter: *Thomas Hudzik (ALA Biopharma Consulting) [for Anton Bespalov]*
	Panel Discussion
2:05-2:55	• Best practices for preclinical study design and analysis • Importance of true randomization and blinding in preclinical study design and analysis versus current practice • How do we standardize and implement *Panelists: Jamie DaSilva (Pfizer), Paul Kruzich (PTC Therapeutics), David Heal (DevelRx), Chad Reissig (FDA/OCD/CSS), Ling Chen (FDA/OTS/OB/DBVI), Thomas Hudzik (ALA Biopharma Consulting)*
Closing Remarks	
2:55-3:00	*Beatriz Rocha (CCALC, Fortrea)*