



Breakout Sessions and Working Groups

Breakout Session I

Session Chair: Steven Bird, MD

Evidence for Neurological Effects in Humans: Discussion of the evidence for short- and long-term sub-lethal effects from OP exposures in humans, including neuropathological effects and functional deficits (cognitive, sensory, motor). What is the evidence, and what is the relationship between these chemical exposures and the effects observed (causal, correlational, association, none)?

Points of discussion include but are not limited to the following:

1. What is the evidence in humans for neurological effects after sub-lethal exposure to OP nerve agents? What are the sources of human data?
2. What are the prevalent signs and symptoms?
3. What is the linkage to clinical exposure (eg. cholinesterase levels, residues measured, etc.)?
4. What clinical outcomes are best suited for studying in an animal model or other models?

The discussion during this session will be driven by several spreadsheets that capture information on potential sources of human data and prevalent clinical observations. These spreadsheets, and all other spreadsheets mentioned in this document, will be sent out to workshop participants two weeks in advance of the workshop meeting so that information can be collected both prior to and during the breakout session. This is voluntary, but we believe it will help facilitate discussion during the in-person meeting.

Roundtable Participants:

Mark Kirk, MD
Roger McIntosh, MD
Kent Anger, PhD
Luciana Borio, MD
Amy Snipes, PhD
Steve Bird, MD
Paul Wax, MD
Tetsu Okumura, MD, PhD
Tom Bleck, MD
Charles C. Engel, MD
Daryl Hood, PhD
Diane Rohlman, PhD

Frederick Henretig, MD
Nick Buckley, MD
Mike Rogawski, MD, PhD
Marti Jett, PhD
Walter Koroshetz, MD
David Siegel, MD
Ernie Takafuji, MD
Brandy Fureman, PhD
Francesca Bosetti, PhD
David Jett, PhD
Margaret Ochocinska, PhD

Breakout Session II

Session Co-Chairs: Douglas Cerasoli, PhD and Pamela Lein, PhD

Evidence for Neurological Effects in Animals

Discussion of what animal models exist for short- and long-term sub-lethal effects from chemical exposures, including neuropathological effects and functional deficits. What is the predictive value of animal models, both in terms of the effect of the chemical toxin, and the efficacy of potential therapeutics in humans?

Some points of discussion include but are not limited to the following:

1. What animal models exist for neurological effects after sub-lethal exposure to OP nerve agents?
2. What are the optimal parameters for these animal models? What are the optimal doses used? What is the optimal timing? Pretreatments/co-treatments needed?
3. Should protocols be standardized?
4. What are the sub-lethal effects of OPs in animal models? What do most people see – behavior, neuropathology? Other?

The discussion during this session will be driven by several spreadsheets that capture information on the design of animal models, and the prevalent sub-lethal effects observed.

Roundtable Participants:

Franck Dhote, DVM, PhD

Edson Albuquerque, MD, PhD

Alvin Terry, PhD

Pamela Lein, PhD

Lucy Lumley, PhD

John McDonough, PhD

Doug Cerasoli, PhD

Maria Braga, DDS, PhD

Joe Hanig, PhD

Robert Delorenzo, MD, PhD

Rick Rotundo, PhD

Cary Pope, PhD

Deborah Yourick, PhD

Samba Reddy, PhD

Phil Bushnell, PhD

Karen Wilcox, PhD

Wendy Pouliot, PhD

Ray Dingleline, PhD

Byron Ford, PhD

Eng Lo, PhD

Miguel A. Perez-Pinzon, PhD

Anthony Choo, PhD

C. Edward Dixon, PhD

Mike Babin, DVM, PhD

Jim Blank, PhD

Elizabeth Maull, PhD

David Yeung, PhD

Rajesh Ranganathan, PhD

Comparison of Human and Animal Data

Session Co-Chairs: Mark Kirk, MD and Kent Anger, PhD

Discussion of differences and similarities between the effects seen in humans, and the data from animal models of OP toxicity. These will be discussed in the context of developing animal models that are more predictive of the effects seen in humans.

1. Direct comparison of effects – seizures, pathology, behavioral?
2. Which of these effects in animals can be extrapolated to humans?
3. Can animal models be used to study mechanisms or target engagement learned from human studies, rather than a direct effects observed in humans?
4. Are animal models the best tools for determining efficacy of drugs? Should we explore in vitro technologies such as organ, body-on-a-chip?

The one-hour discussion during this session will be driven by a spreadsheet that facilitates the direct comparison of data and identification of outcomes that can be used in animal models.

Participants: open to all (held during general session)

Working Group I

Session Co-Chairs: Pamela Lein, PhD and John McDonough, PhD

Working Group on Animal Model Best Practices Session

The discussion during this session will be driven by a spreadsheet that describes requirements under the FDA Animal Rule Draft Guidance Document.

Participants: open to all (held during general session)

Working Group II

Session Co-Chairs: Maria Braga, PhD and Mark Kirk, MD

Working Group on Research Gaps

The discussion during this session will be driven by a spreadsheet that facilitates a research gap analysis and prioritization.

Participants: open to all (held during general session)