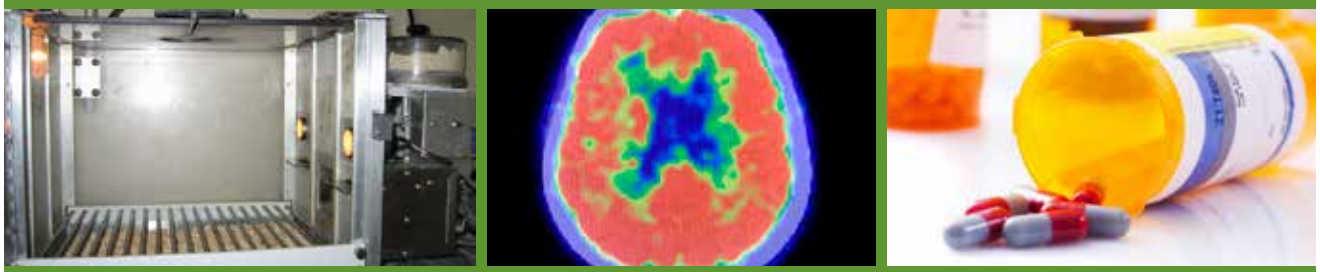


Substance Abuse Liability Assessment



RTI International offers substance abuse liability assessment services to help clients develop safe and effective medications for treating disorders of the central nervous system. Our experienced neurobehavioral pharmacology researchers work closely with the pharmaceutical industry to design thorough, confidential evaluation approaches that are tailored for specific new molecular entities.

Overview

According to the 2010 National Survey on Drug Use and Health conducted by the Substance Abuse and Mental Health Services Administration, 7 million Americans reported non-medical use of a prescription psychotherapeutic (e.g., pain reliever, tranquilizer, stimulant) within the past month. One major step toward preventing prescription drug abuse is appropriate scheduling under the Controlled Substances Act. Whether or not a new molecular entity (NME) falls within the act's purview is determined by analyzing eight distinct factors, including scientific evidence of the drug's pharmacological effects and its psychic or physiological dependence liability. When analysis indicates that a candidate medication may have abuse liability, an assessment of abuse liability must be included in any New Drug Application submitted to the Food and Drug Administration.

In January 2010, the Food and Drug Administration issued draft guidance for industry specifying the types of information that should be included in this assessment. Specifically, under the Animal Behavioral and Dependence section, the guidance recommends a battery of behavioral assays that includes self-administration, drug discrimination, psychomotor tests, and evaluation of tolerance and dependence. RTI researchers are experienced and well-positioned to support this battery of testing.

Capabilities

RTI offers the expertise and facilities required to conduct thorough and customized substance abuse liability assessments. Specific capabilities include the following:

- **Self-administration**—This procedure is an animal model of the rewarding effects of a psychoactive drug. The basic procedure involves training rats to press a lever in order to receive an intravenous infusion of a known drug of abuse (e.g., cocaine) and then substituting the NME. Reliable responding for infusions of the NME indicates potential abuse liability.
- **Drug discrimination**—This procedure is an animal model of the subjective effects of a psychoactive drug. The general procedure involves training a rat to press one of two levers, depending upon whether it is administered a particular training drug (e.g., morphine) or vehicle. The rat is then administered the NME. Pressing the lever associated with the training drug (and not pressing the vehicle lever not associated with the training drug) suggests that the NME may produce interoceptive effects similar to those of the training drug.
- **Psychomotor tests**—Psychomotor testing may include a variety of procedures, the most common being examination of effects of the NME on locomotor activity.

Substance Abuse Liability Assessment

Increases or decreases in motor activity can provide information about the similarity of the effects of the NME compared to known drugs of abuse, as well as about its acute toxicity.

- **Tolerance and dependence evaluation**—This evaluation examines the pharmacological effects of the NME following repeated dosing. Tolerance is suggested by decreased efficacy of the NME with repeated administration. Physical dependence is characterized by withdrawal signs that occur after termination of repeated dosing with the NME, whereas psychic dependence refers to reduced control over drug use (e.g., craving). Assessment of tolerance, physical dependence, or psychic dependence is part of the safety evaluation of an NME.

Client Focus

RTI's technical, research, and development services meet the highest standards of professional performance to satisfy the unique requirements of our clients. We work closely with our clients to identify their requirements and clarify their expectations, including cost and time constraints.

RTI extends its excellence in research and technical services to its business systems and processes, making it easy for clients, subcontractors, and vendors to partner with us. We have the contractual, legal, and business structures to serve any client with projects of all sizes. RTI is a 501(c)(3) nonprofit corporation.

Leadership Team

Jenny L. Wiley, PhD—Dr. Wiley has more than 20 years of experience in behavioral pharmacology and toxicology. She oversees the design of behavioral studies, including preclinical assessment of abuse liability, and coordinates parallel *in vitro*, pharmacokinetic, and safety toxicology studies, as necessary, for comprehensive assessment of candidate medications.

Julie A. Marusich, PhD—Dr. Marusich earned her degree in behavior analysis at the University of Florida. She has extensive experience in designing and conducting self-administration studies and in developing animal models of factors related to substance abuse or psychiatric disorder (e.g., impulsivity). She uses her expertise in a variety of behavioral techniques to develop experimental methods consistent with the client's goals.

More Information

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RTI International is an independent, nonprofit research institute dedicated to improving the human condition. Clients rely on us to answer questions that demand an objective and multidisciplinary approach—one that integrates expertise across the social and laboratory sciences, engineering, and international development. We believe in the promise of science, and we are inspired every day to deliver on that promise for the good of people, communities, and businesses around the world. For more information, visit www.rti.org.

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