

International Society for CNS Clinical Trials and Methodology

Session II: MATRICS Challenge

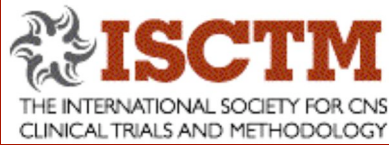
Industry Challenges for Assessing Cognition in Schizophrenia

Larry Alphas, MD, PhD

Industry Challenges for Assessing Cognition in Schizophrenia

- **Pre-MATRICS era**
 - **No consensus on**
 - **the definition of cognitive dysfunction in schizophrenia**
 - **the affected cognitive domains and nature of deficit**
 - **the clinical relevance of cognitive dysfunction**
 - **how to differentiate specific effects from non-specific therapeutic effects**
 - **the test batteries to assess these domains**
 - **indications that might be achievable if a drug-treatment were successful**
 - **'Registration quality' efficacy work was difficult**

- **MATRICES era**
 - **Greater field consensus on**
 - **the definition of cognitive dysfunction in schizophrenia**
 - **the affected cognitive domains and nature of deficit**
 - **the clinical relevance of cognitive dysfunction**
 - **how to differentiate specific effects from non-specific therapeutic effects**
 - **the test batteries to assess these domains**
 - **indications that might be achievable if a drug-treatment were successful**



Industry Challenges for Assessing Cognition in Schizophrenia

- **Post-MATRICS Era—INDUSTRY's Challenge**
 - **To develop safe and effective treatments for cognitive dysfunction in schizophrenia and related psychotic disorders**

- **Post-MATRICS Era—Outstanding Problems**
 - **Test Batteries**
 - **Can other batteries be used e.g., computerized? If so, how are they identified?**
 - **How should batteries be scored and endpoints be specified?**
 - **How well do the batteries work in non-Western cultures?**
 - **Can the batteries be validly translated to non-English languages? If so, what validation work is necessary?**

Industry Challenges for Assessing Cognition in Schizophrenia

- **Post-MATRICS Era—Outstanding Problems**
 - **No global consensus on approach to treatments to cognitive deficits**
 - **No ICH guidance**
 - **Given the consensus on cognitive domains, specifically how should efficacy be demonstrated...how much efficacy is enough to be clinically and regulatorily meaningful?**
 - **To what populations does this work apply? Schizophrenia? Schizoaffective Disorder? Bipolar? Psychosis?**
 - **What stages of illness are appropriately studied?**

- **Post-MATRICS Era—Outstanding Problems**
 - **What about co-primaries? Are they sensitive? specific? relevant to this indication?**
 - **How can broad spectrum treatments best be developed?**
 - **What labeling can be achieved as a consequence of these studies?**
 - **How can this be communicated to the field?**