

Advancing the Methods to Evaluate Abuse and Dependence Potential in Clinical Studies for CNS-Active Drugs and Novel Psychedelics

During this working group session, study methods and current practices were discussed concerning the human abuse potential evaluation of psychedelics and the clinical physical dependence evaluation of CNS-active drugs. The session highlighted several key areas that require further consideration, including 1) the need for adaptations of study methods, including the primary endpoint, for HAP studies evaluating psychedelics, and 2) outlining a pragmatic approach to assessing physical dependency of CNS-active drugs that is achievable for patient trials. The group considered the current primary and secondary endpoints in the HAP studies and discussed the limitation of the visual analog scale (VAS) for at-the-moment Drug Liking. The group agreed to undertake further discussions to review current endpoints and provide recommendations for primary and secondary endpoints based on emerging data from psychedelic trials. In addition, the group discussed some of the limitations of assessing physical dependency in late-stage trials involving patients. Frequent assessments of withdrawal symptoms are limited by questionnaires and scales that are often clinician rated and include questions initially validated in drug abusing patients that are not relevant to patients in clinical trials. The group agreed to work together to draft a strawman of assessments that can be reasonably assessed at frequent intervals to provide robust measures of drug withdrawal symptoms and rebound effects that can be administered in a less burdensome manner. The working group will meet throughout the year to work on the objectives and present their recommendations at next year's annual meeting.