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KEY OPERATIONAL CONSIDERATIONS FOR SUBSTANCE USE DISORDER TRIALS

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A DEVELOPMENT LANDSCAPE THAT DEMANDS OPERATIONAL PRECISION

Substance use disorders (SUDs) remain a major public health challenge. In 2022, 46.3 million people aged 12 or older in the United States met criteria for an alcohol or drug use disorder.¹ Yet the scale of need tells only part of the clinical development story. Sponsor developing treatments for opioid, alcohol, stimulant, nicotine, and other substance use disorders must translate rapidly evolving science into trials that are feasible for sites, workable for participants, and credible to regulators.

Bringing this evolving science into clinical development is difficult because SUD studies rarely involve a single operational variable. Substance use patterns may fluctuate. Co-occurring psychiatric and medical conditions can complicate eligibility and safety oversight. Participants may face transportation, housing, employment, legal, or caregiving pressures that make rigid visit schedules unrealistic. Biological measures, self-report, clinician ratings, and functional outcomes may all contribute to the evidence package, creating a need for careful alignment across protocol design, site training, data systems, and monitoring.

The practical question for Sponsors is therefore, not simply whether a protocol is scientifically compelling. It is also whether every element of that protocol can be executed consistently across the sites and communities where eligible participants receive care.

DESIGN ENDPOINT AROUND MEANINGFUL CHANGE, THEN PROTECT THEM OPERATIONALLY

Endpoint strategy in SUD development is evolving beyond a single, universal definition of success. FDA guidance for opioid use disorder identifies several possible clinical endpoint domains, including adverse outcomes, change in disease status using diagnostic criteria, changes in use patterns, and patient reported outcomes.² In alcohol use disorder, measures related to heavy drinking and abstinence have long served as standard efficacy measures. More recent scientific discussion has also emphasized the clinically meaningful reduction in use may matter even when complete abstinence is not achieved.³

This creates opportunity, but it also raises the operational stakes. A trial may combine toxicology, self-reported use, craving measures, withdrawal assessments, treatment engagement, and broader activities of daily functioning. Each source answers a different question and carries a different risk of missing data points, bias, or inconsistent administration. Before the first site is activated, the study team should be able to explain how each endpoint is collected, how discrepancies are handled, what windows are clinical and statistically acceptable, and which data streams drive eligibility, dosing, safety, or efficacy analysis.

OPERATIONAL ENDPOINT PROTECTION AT A GLANCE

ENDPOINT DOMAIN	RISK	MITIGATION STRATEGY
Substance use pattern	Inconsistent collection windows, discordance with self-report	Define collection windows, reconciliation rules, escalation pathways, and participant reminders before activation
Craving and withdrawal	Rater drift or bias, participant fatigue, timing effects	Use role-based training, qualification and certification where appropriate, clear source document expectations, and ongoing data review.
Function and recovery	Measures may not align with the target population or study duration	Ensure endpoint measurement tools are relevant and minimize participant burden.
Digital measures	Device malfunction, participant compliance, connectivity issues	Implement robust helpdesk support, program alerts to monitor for missing assessments

PRIORITIZING A PATIENT CENTERED APPROACH IN RECRUITMENT

Strong enrollment begins with a realistic map of the treatment ecosystem. Depending on the indication and protocol, appropriate sites may include academic addiction programs, community treatment centers, outpatient psychiatry practices, medication treatment programs, primary care networks, or research sites with established referral relationships. A high-enrolling site in one SUD indication may not be suitable for another if it lacks the patient mix, prescribing authority, pharmacy controls, laboratory infrastructure, behavioral intervention capability, or overnight observation resources required by the protocol.

Feasibility should therefore test more than investigator interest. It should examine the site's accessible population and referral pathways, competing studies, standard of care treatment patterns, access to controlled medications where relevant, lab sample-handling and processing capabilities, staffing coverage, rater experience and capacity, and ability to respond when participants miss visits or experience relapse. Medpace's neuroscience model combines therapeutic input with operational feasibility and established site relationships to help Sponsors select sites that can both recruit and execute.

Community engagement can expand reach, but it must be tailored to the protocol and population. Recruitment language should be respectful and non-stigmatizing. Referral partners should understand the study's eligibility criteria. Digital recruitment campaigns should connect interested individuals to responsive prescreening pathways rather than simply generate volume of respondents. The objective is not the largest funnel. It is a funnel of qualified candidates that sites can manage without compromising participant experience or data quality.



TREAT RETENTION AS A DATA-INTEGRITY STRATEGY

In SUD trials, missed visits and early study withdrawals may reflect the condition under study, the burden of participation or both. A retention plan should anticipate instability rather than respond to it after data are lost. Participant-facing materials need to set clear expectations without judgment. Visit schedules should distinguish procedures that truly require on-site attendance from those that can be completed remotely when the protocol and local regulations allow. Transportation support, flexible scheduling, rapid outreach after a missed contact, and continuity in site-participant relations can reduce attrition.

The strongest retention plans are individualized but controlled. Sites need clear boundaries for permitted contact methods, escalation timing, privacy protection and re-engagement after relapse or temporary loss to follow-up. Teams should know whether a relapse is an endpoint, an adverse event, a treatment failure, a reason for additional assessment, or some combination of these. That distinction should be resolved in the protocol and study plans, not improvised by the site.

Hybrid and decentralized elements can reduce burden when they are used for a defined purpose and supported by reliable oversight. FDA's guidance on decentralized clinical trials emphasizes appropriate investigator oversight, participant safety, data reliability, and clear boundaries for trial-related activities conducted outside of the research clinic.⁴ Digital health technologies used for remote data collection also require fit-for-purpose selection, risk management, and attention to how data are collected and used.⁵

BUILD SAFETY AND ELIGIBILITY OVERSIGHT FOR REAL-WORLD COMPLEXITY

Concurrent maladies such as depression, anxiety, trauma-related disorders, attention deficit disorder, chronic pain, and polysubstance use may be common in potential study populations. Overly broad exclusions can make recruitment impractical and reduce operational feasibility. Insufficiently considered inclusions can create avoidable safety risks. The solution is not a generic inclusion or exclusion philosophy. It is early review by clinicians who understand both addiction psychiatry and drug development.

Study teams should align on diagnostic criteria, intoxication and withdrawal thresholds, concomitant therapy rules, suicidality assessment, overdose risk, rescue treatment, pregnancy consideration, and escalation pathways. Where independent eligibility review or centralized assessment is use, the workflow should be timed such that it supports sites rather than creating a late-stage enrolment bottleneck. Medpace's embedded neuroscience physicians can support protocol planning, investigator engagement, medical monitoring, and regulatory interactions throughout the study lifecycle.

USE TECHNOLOGY TO CONNECT THE TRIAL, NOT COMPLICATE IT

Technology can improve SUD trial execution when it reduces friction and creates timely visibility. ePRO or eCOA can support repeated craving, withdrawal, mood, and function assessments. Electronic reminders may reinforce visit and dosing routines. Central laboratory and bioanalytical services can support safety testing, pharmacokinetics, biomarkers, and toxicology. Imaging or cardiovascular core laboratories may be relevant when a mechanism, route of administration or safety profile requires specialized assessment.

The operational advantage comes from systems integration. When study management EDC, IRT, eCOA/ePRO, laboratory, and imaging information are connected, study teams can identify missing data, delayed or missed assessments, enrollment barriers, and safety follow-up needs earlier. Medpace's full-service model includes ClinTrak study management platform inclusive of EDC, IRT, TMF, and ePRO/eCOA capabilities.



Additionally, Medpace offers in-house services for central and bioanalytical laboratories, imaging and cardiovascular core laboratory services, and a Phase I unit. The intent is to reduce vendor fragmentation while maintaining clear ownership and human review of study decisions.

Technology selection should remain participant and site-centered. A device or application is not operationally useful if participants cannot access it reliably, sites cannot support it, or the protocol does not specify how its data will be interpreted. Every digital element should have a defined purpose, a user-friendly interface, robust technology support services, and a contingency plan.

WHAT SPONSORS SHOULD EXPECT FROM A CRO PARTNER

SUD programs benefit from a CRO partner that can connect scientific intent to execution across medical, regulatory, operational, data, laboratory, imaging, and participant-engagement functions. The differentiator is not simply access to each capability, but rather whether those capabilities operate as one seamless study team, with risks proactively identified and mitigated throughout the project lifecycle.

Medpace brings a therapeutically focused neuroscience model, embedded physicians, experienced operational teams, global regulatory support, integrated laboratories, proprietary clinical trial technology, and customized participant recruitment and retention planning. Medpace offers:

- Comprehensive project evaluation that tests whether endpoints, visit schedules, safety requirements, and more can function together to protect participant safety and data integrity.
- Country and site selection strategy grounded in therapeutic fit, accessible populations, referral pathways, competitive landscape, and execution capacity.
- Rater and assessment oversight designed to protect consistency across subjective and objective endpoints.
- Integrated data and service delivery that reduces handoffs and gives study teams a more complete end-to-end operational picture.
- Embedded medical leadership that can guide complex eligibility, safety, and regulatory questions throughout the drug development lifecycle.
- Participant-focused recruitment and retention planning that accounts for the realities of SUD care and recovery.

SUBSTANCE USE DISORDER STUDY EXPERTS: FROM SCIENTIFIC AMBITION TO EXECUTION

Innovation in SUD development is expanding the range of mechanisms, endpoints, and delivery models available to Sponsors. Success will depend on more than adopting the newest biomarker or digital tool. It will depend on designing studies around meaningful clinical questions, selecting sites that can execute the protocol, supporting participants through periods of instability, and integrating data quickly enough to guide action.

For a Sponsor, the right operational partner can make that complexity manageable. By combining neuroscience expertise with integrated services and disciplined study execution, Medpace helps transform promising SUD development strategies into trials that are practical for sites, designed to minimize participant burden, and positioned to deliver robust clinical endpoint data.



Serving as therapeutic team leaders, our in-house neuroscience physicians apply years of psychiatric drug development experience and are embedded throughout every study, providing a greater depth of expertise and the ability to tackle the complex challenges often associated with substance use disorder trials. Our subject matter experts provide strategic direction for study design and planning, train operational staff, work with Investigators, provide medical monitoring, and meet with regulatory agencies as well as our global regulatory affairs experts to provide strategic guidance on the best pathways to accelerate approvals.

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REFERENCES

1. Substance Abuse and Mental Health Services Administration (SAMHSA). Key Substance Use and Mental Health Indicators in the United States: Results from the 2022 National Survey on Drug Use and Health (HHS Publication No. PEP23-07-01-006, NSDUH Series H-58). Center for Behavioral Health Statistics and Quality; 2023.
2. U.S. Food and Drug Administration. Opioid Use Disorder: Endpoints for Demonstrating Effectiveness of Drugs for Treatment. Guidance for Industry. Center for Drug Evaluation and Research (CDER); October 2020.
3. National Institute on Drug Abuse (NIDA). Advancing Reduction of Drug Use as an Endpoint in Addiction Treatment Trials. Nora's Blog. March 18, 2025. National Institute on Drug Abuse, National Institutes of Health
4. U.S. Food and Drug Administration. Conducting Clinical Trials With Decentralized Elements: Guidance for Industry, Investigators, and Other Interested Parties. Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), Center for Devices and Radiological Health (CDRH), and Oncology Center of Excellence (OCE); September 2024.
5. U.S. Food and Drug Administration. Digital Health Technologies for Remote Data Acquisition in Clinical Investigations: Guidance for Industry, Investigators, and Other Stakeholders. Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), Center for Devices and Radiological Health (CDRH), and Oncology Center of Excellence (OCE); December 2023.

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MAKING THE COMPLEX
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