ACI CLINICAL

Independent Committees

Endpoint Adjudication Committees

Data Monitoring Committees

Safety Assessment Committees

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ACI Clinical was founded in 2001 as a niche specialty company within the clinical research industry. For more than a decade, we have focused on driving best practices in managing Independent Expert Committees by combining internal expertise with our strong academic relationships to deliver a fully integrated approach. ACI Clinical operates globally having supported more than 600 projects with more than 100 compounds for Pharma, biotech, academia, device, and CROs in nearly all therapeutic areas. Our proprietary technologies help to facilitate committee interactions and our global network of more than 500 medical, statistical and safety experts that can serve as committee members and advisors for clients in order to deliver high-value solutions that enhance trial integrity.

Expert Committees for Clinical Trials

Safety Assessment Committee FAQs

A Quick Guide of What You Need to Know

What is a Safety Assessment Committee?

A Safety Assessment Committee (SAC) is a group of individuals chosen by a clinical development sponsor to review unblinded safety information in a development program in order to make a recommendation to the sponsor regarding whether the safety information must be reported in an IND safety report.

Where does the term 'Safety Assessment Committee' come from?

This term was defined in the FDA's December 2015 Draft Guidance to Industry on IND Safety Reporting requirements.

When is a Safety Assessment Committee needed?

The FDA recommends a Safety Assessment Committee should be implemented on ***every drug development program*** that will be part of an IND filing.

What is the intended purpose of using a Safety Assessment Committee?

The use of a Safety Assessment Committee is intended to significantly reduce uninformative expedited safety reports as there is a serious concern that true safety risks are obscured by the high volume of unnecessary safety reports.

What type of members should comprise a Safety Assessment Committee?

Safety Assessment Committees can be comprised of medical experts that are internal to the sponsor, external to the sponsor, or a mix of both. Additional member criteria can be found within this packet.

When do companies need to outsource their Safety Assessment Committees?

This depends on a sponsor's in-house resources and their availability. Most pharma companies can manage SACs internally using medical staff from other programs, whereas most biotech and smaller companies need to supplement or fully outsource their SAC members because their medical staff would have a conflict-of-interest in performing unblinded reviews of a program in which they are involved.

How does a Safety Assessment Committee compare to a Data Monitoring Committee?

SACs and DMCs are both comprised of medical/statistical experts that are independent of a clinical trial's operations and responsible for review of ongoing, unblinded data in order to make a recommendation back to the sponsor. However, the SAC recommends whether individual safety events should be reported, whereas a DMC recommends trial-level actions based on summary data. SACs are tasked with analyzing aggregate data across a drug program whereas traditional DMCs oversee one study. In addition, SACs tend to meet much more frequently due to the reporting time boundaries (i.e. weekly or bi-weekly) whereas DMCs tend to meet less frequently (i.e. quarterly or bi-annually).

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Safety Assessment Committees

About Safety Assessment Committees

A **Safety Assessment Committee (SAC)**, as defined by the FDA's December 2015 Draft Guidance for Industry, is a group of individuals chosen by the sponsor to review safety information in a development program and tasked with making a recommendation to the sponsor regarding whether the safety information must be reported in an IND safety report. The guidance also explains that a safety surveillance plan should describe processes and procedures for assessing serious adverse events and other important safety information. Safety Assessment Committees, when combined with a safety surveillance plan, create a systematic approach for safety monitoring and reporting. SACs provide a critical oversight role for analysis of clinical trial safety events and can help to lower the over-reporting of expected safety events to regulatory agencies in order to focus more clearly on serious and unexpected events that may occur.

ACI Clinical's Safety Assessment Committee Expertise

As an industry leader in managing Expert Committees for clinical trials, ACI Clinical brings clients the largest committee dedicated staff in the industry, our own global network of more than 500 vetted medical, safety and statistical experts who can serve as committee members or advisors to clients, and a technology-enabled methodology designed specifically for efficient, user-friendly committee workflows. ACI's SAC services focus on delivering a fully integrated approach to unblinded safety analysis and management in order to satisfy the FDA's safety reporting requirements.

ACI's executive leadership remains deeply involved in public-private thought leadership efforts that focus on shaping Expert Committee best practices. We work with clinical trial sponsors, academic experts and regulatory agencies to focus on providing the best independent committee solutions on the market to enhance trial integrity and ensure the most appropriate analysis, documentation and reporting of clinical trial safety events.

When to Implement

A Safety Assessment Committee is used to ensure vigilant oversight and analysis of safety data so that a reliable, consistent and transparent methodology can be used to determine which events to report to regulators and the scientific community.

SACs are recommended for use in every development program and is thought to be especially helpful when analyzing trends across the aggregate program-level data. The FDA recommends and expects that sponsors implement SACs early in a IND program's development. At this time, it is also important that the SAC review any event rates and historical safety data from earlier clinical studies, epidemiological studies and animal or in vitro testing. This aggregate analysis can help to establish reporting thresholds for expected event rates as the development program continues through Phase II and Phase III studies on the path to regulatory submission and approval.

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SAC Implementation

How to Implement

ACI Clinical's Safety Assessment Committee solutions are largely focused on proper establishment of the process. In order to provide consistent and efficient safety assessment services, we have created detailed "Best Practice Guides" to help clients navigate through the critical decisions that should be made upfront in the design of the process. Additionally, ACI structures our processes around current regulatory thinking. The draft FDA guidance includes several recommendations for the SAC process that we include in ACI's standard practices:

1. Establish Safety Assessment Committee
2. Establish Safety Surveillance Plan
3. Define prospective identification strategy for anticipated serious adverse events
4. Define SAC charter development
5. Define roles and responsibilities between SAC, sponsor and data monitoring or adjudication committees
6. Create tables for aggregate analysis of safety data
7. Define process for determining causal relationships between drug and event (i.e. adjudication)
8. Standardize coding
9. Close monitoring of established reporting thresholds to ensure appropriate IND safety reporting

For any given project or program, ACI focuses our services into three categories: Startup, Maintenance and Closeout

	Goal	Deliverables

Start Up	To have all of the components in place so that the SAC is ready to review safety events	• Initial assessment of the safety components the sponsor has in place
		  • Integrate SAC procedures into established PV/safety process
		  • Where limited procedures exist, define new safety procedures in collaboration with sponsor
		• Process development to create a systematic approach for safety reporting with regulatory consulting
		• Committee member recruitment, vetting, selection and contracting
		• Precise charter development
		• Configuration and training on ACI's committee-focused technology

Maintenance	To have timely and accurate review of events and reporting recommendation to sponsor	• Independent web-based SAC discussion meetings • Statistical aggregate analysis as needed • Committee member management, payments and payment reporting • Metric reporting and trend analysis • Adjudication consulting as needed
Closeout	To have a complete regulatory-grade package as robust support for a submission	• Final reconciliation • Master file archival and transfer

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Committee Members

The ACI Clinical approach to member relationships is a core part of our SAC service. We have a department that is dedicated to relationship management and support of our global experts throughout the entire time that they serve within our network. We offer full-service member activities (from committee composition, to preparing and paying their invoices, to HCP payment reporting) that focus on reducing administrative burden so the experts can focus on what really matters. We believe in designing committee services to meet the needs of our clients and the committee members, and we regularly work with our network to solicit their feedback on our services and any suggestions for improvement.

ACI's Expert Network

ACI's global network of 500+ medical, safety and statistical experts represents more than 25 countries, 75 therapeutic sub-specialties and approximately 250 global academic institutions. Each of our experts are personally vetted by ACI Clinical's MDs for any conflicts of interest and to ensure their understanding and availability for a project. ACI views committee composition as a collaborative process with our clients, and we are happy to accept any sponsor recommended candidates or to suggest experts within our network that are appropriately qualified for a project. We use the following criteria as a general basis for member selection requirements to ensure the Safety Assessment Committee is multidisciplinary. ACI can also collaborate with the sponsor to determine committee members as well as ad hoc discipline consults (i.e. epidemiology, toxicology).

SAC Member Criteria

- At least one physician familiar with the therapeutic area for which a drug is being developed
- Additional clinicians with general or specific safety experience (i.e. cardiology, hepatology)
- No direct responsibility for the conduct or analysis of trials in the development program
- Knowledge about the drug, epidemiology of the disease and subject characteristics or familiarity with the standards of care in current practice
- Understanding of the role of a SAC within the context of the regulatory approval process
- Recognized competence in the area for which member is selected (i.e. therapeutic area), as evidenced by academic appointment or other teaching activities, relevant publications or competence; may be demonstrated by active clinical practice in the area of interest
- Able to understand evidence needed to support Charter criteria for evaluation of safety events
- Willingness and ability to perform responsibilities in a timely fashion on an ongoing basis

Committee Chair Suggested Requirements

- Must meet all requirements listed above for the appropriate type of committee
- Prior experience as a Member on at least 2 previous committees
- Knowledgeable about the FDA and EMA monitoring and reporting guidances related to safety events
- Able to manage other clinical experts as evidenced by previous DMC, EAC, SAC or Trial committee chairmanships or leadership roles at academic or professional venues
- Agreement with sponsor about the role of the committee and the role of the chairman

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Partnership Solutions

Performance Metrics

As part of ACI's mission to be an industry leader in Expert Committee services, we believe in tracking ourselves against performance metrics and making these transparent to our clients. Our staff's expertise in committee management along with their deep experience working across so many client therapeutic areas allows us to consistently deliver on performance targets:

- 1-2 weeks for member identification and vetting
- 2-4 weeks for member contracting
- Less than 48 hours for ad hoc member consulting on an unexpected safety issue
- Average 5 days from event posting to SAC recommendation to sponsor

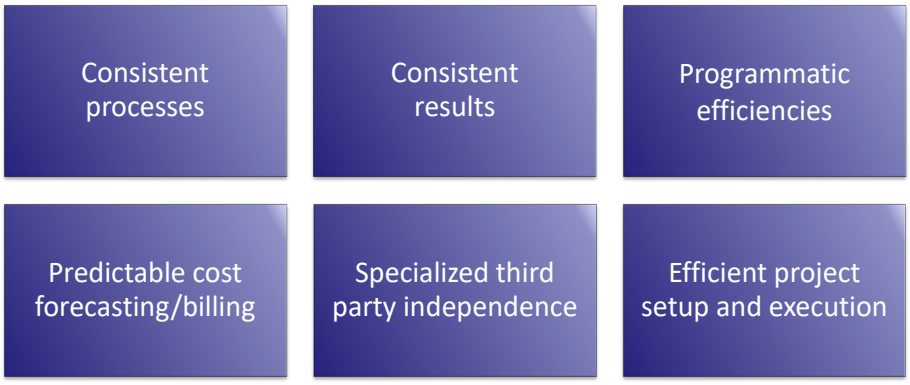
Our Technology

Our proprietary AIMS® technology is built for committee management. AIMS® streamlines processes and diminishes administrative burden, allowing committee members to focus on providing their expert assessments. AIMS® makes online data review and communication as seamless as possible for committee members, sponsors and other personnel spanning the globe.

The ACI team administers the system, managing all data and content to ensure appropriate review and a complete audit trail for all activity. With the power of AIMS® and the support of our experienced project oversight, ACI makes communication and overall committee management as straightforward, efficient and constructive as possible.

Partnership Goals

ACI Clinical constantly strives to work with our clients to drive efficiencies, where possible, within our service offerings. We create best practice guides to serve as a central guide for all parties involved in the operation of a Safety Assessment Committee, and we use a simple deliverable-based budget to align incentives and easily track progress against spending. Appointed relationship managers work with each of our client partners to achieve the goals below and monitor for improvement opportunities.



Contact ACI Clinical today to discuss any Safety Assessment Committee needs or questions.

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