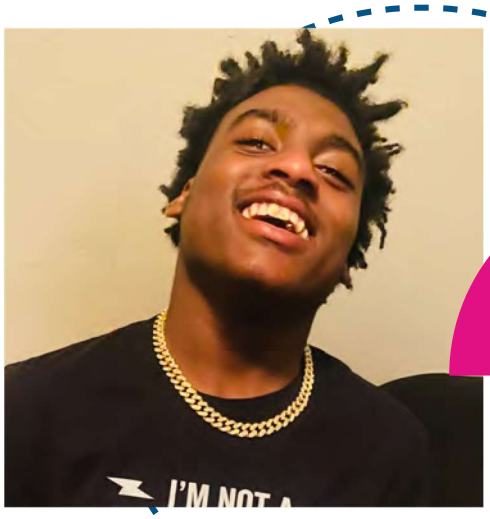

Part 4:
Patient Experience & Practical Considerations

Practical Angelman Syndrome Guidance for Site and Hospital Staff

What Every Staff Member Should Know

Not every person interacting with an Angelman family will be a principal investigator or study coordinator. Front desk staff, anesthesia teams, PACU nurses, transporters, phlebotomists, EEG techs, security staff, inpatient nurses, and rotating personnel may all influence the safety and experience of a trial day.

For many families, the quality of these interactions matters just as much as protocol execution.

This section is intended as a practical reference for any staff member who may encounter an individual with Angelman syndrome during a trial visit.

Common Behaviors and Presentations Staff May See

- Individuals with Angelman syndrome may:
- Smile or laugh frequently, even when anxious, overstimulated, or uncomfortable
- Have limited or no verbal speech
- Communicate through vocalizations, gestures, AAC, facial expressions, or behavior
- Show excitement through movement, grabbing, reaching, flapping, vocalizing, or sudden activity
- Have short attention spans or difficulty tolerating waiting
- Seek movement or resist stillness
- Be highly sensory-sensitive to lights, sounds, transitions, touch, or unfamiliar environments
- Have difficulty expressing pain, fear, nausea, dizziness, or discomfort clearly
- Escalate quickly when routines change or when they do not understand what is happening

Staff should not assume that smiling means comfort, that quiet means calm, or that distress will always look obvious.

What Families Want Staff to Know

Families are usually the best source of practical guidance for that individual child or adult. Parents and caregivers often know:

- What anxiety looks like for their loved one
- How pain is expressed
- What sensory triggers may escalate distress
- What calms, comforts, or redirects effectively
- Whether touch, separation, noise, bright lights, or waiting are likely to be difficult

When in doubt, ask the caregiver first.

Practical Tips for Staff

Small adjustments can make a major difference.

Helpful Approaches

- Smile warmly and greet both the caregiver and participant respectfully
- Use simple language, short phrases, and visual or gestural cues
- Give one direction at a time
- Allow extra processing time
- Follow the caregiver's lead on interaction style when appropriate
- Offer movement breaks or space to walk, when safe
- Provide estimated wait times and keep families updated
- Reduce unnecessary transitions when possible
- Prepare rooms, supplies, and staff before bringing the family in
- Consider texting or calling families when the room is ready, if it is safer and easier than prolonged waiting room time
- Ask what works before problems arise

Things to Avoid

- Long, unexplained waits
- Bright, noisy, crowded, or overstimulating spaces when avoidable
- Separating the participant from the caregiver without preparation
- Assuming nonverbal means unaware
- Speaking only to the caregiver and not acknowledging the participant
- Leaving tempting objects within reach, such as phones, badges, lanyards, stethoscopes, or dangling items
- Wearing long loose hair or unsecured accessories if grabbing is likely
- Expecting the participant to remain idle for long periods in prep, PACU, or waiting areas
- Changing plans abruptly without explanation

Questions Staff Should Feel Comfortable Asking Parents

To prepare appropriately, site staff should feel empowered to ask caregivers practical questions such as:

- What does anxiety look like for your child?
- How does your child show pain or discomfort?
- What usually helps calm them?
- Are there common triggers we should avoid?
- Is touch helpful or upsetting?
- How do they usually respond to waiting?
- What communication methods work best?
- Are there words, routines, songs, or objects that help?
- Is separation from you likely to be distressing?
- What should we know before we begin?

These questions signal respect, improve planning, and reduce preventable distress.

Trial Implications for Ancillary Staff

For ancillary staff such as PACU nurses, anesthesia teams, transport staff, front desk personnel, and rotating hospital teams, Angelman syndrome may present differently than other neurologic or neuromuscular conditions they have encountered.

For example, a site may have prior ASO experience in SMA and feel highly comfortable with lumbar puncture workflows or inpatient monitoring. However, the lived experience of Angelman syndrome can differ substantially in ways that affect the day:

- Communication barriers may make pain or side effects harder to detect
- Sensory sensitivities may heighten distress in routine hospital environments
- Behavioral responses may be misread if staff are unfamiliar with Angelman syndrome
- Waiting, transitions, recovery, and separation may be more disruptive than anticipated
- Parents may need to remain central throughout the visit to support regulation and communication

What this means for site teams:

- Operational readiness alone is not enough. Site preparedness should include basic Angelman-specific education for all staff who may interact with the family that day.
- Where possible, sites should consider a brief in-service or reference sheet for staff that reviews:
- Common Angelman behaviors and communication differences
- Sensory and anxiety considerations
- Parent-guided calming strategies
- Safety considerations in waiting, pre-op, procedure, and recovery settings
- The importance of avoiding assumptions based on smiling, age, or nonverbal status

Resources for Families Participating in Clinical Trials

Role of the Angelman Syndrome Foundation (ASF)

ASF serves as a trusted bridge between families and the research ecosystem. Many families turn to ASF first, not sponsors, when they are deciding whether to participate or when challenges arise mid-trial.

Clinical Trial Education and Navigation

ASF provides families with:

- Plain-language explanations of trial phases and goals
- Clear descriptions of placebo, randomization, and blinding
- Realistic expectations around timelines and uncertainty
- Support in preparing questions for investigators

Why this matters:

Families who understand the why behind a protocol are more confident, less anxious, and better retained.

Clinic and Care Coordination

ASF supports:

- Coordination with specialty clinics familiar with Angelman syndrome
- Guidance for local providers supporting trial-related care
- Education to prevent conflicting medical decisions

Why this matters:
Trials rarely replace routine care, coordination prevents gaps and risk.

Family Support Resources
ASF helps families manage:

- Travel logistics
- Scheduling strain
- Educational disruption
- Caregiver overwhelm
- Mental Health Support

Best practice:
Investigators should proactively share ASF resources at screening, not only when challenges arise.

Standards of Care in Angelman Syndrome
Angelman syndrome standards of care are built on decades of collective clinical and family experience. Many families have spent years stabilizing medication regimens, sleep routines, therapies, and communication supports.

Why This Matters for Trials
Protocols that disrupt standard care, even unintentionally, can:

- Trigger seizure instability
- Worsen sleep deprivation
- Cause regression in skills
- Increase family distress

Investigator Responsibilities

- Design protocols that respect medication stability
- Avoid unnecessary therapy interruptions
- Coordinate with existing providers
- Clearly explain why deviations are required

Ignoring standards of care does not just increase burden, it risks safety and data integrity.

Mental Health and Psychosocial Support for Trial Families
Clinical trial participation in Angelman syndrome is emotionally layered and psychologically demanding. For many families, enrolling in a trial is not simply a research decision, it is a deeply personal act shaped by years of caregiving, advocacy, and lived experience with uncertainty.

A Dynamic Emotional Landscape
Families often experience multiple, sometimes conflicting emotions throughout the trial lifecycle, including:

- Hope tied to the possibility of improvement or stabilization
- Fear of adverse effects, regression, or unforeseen complications
- Guilt related to decision-making on behalf of a nonverbal loved one
- Grief when expectations are not met or when outcomes fall short

These emotions are not static. They often intensify at key moments, screening, first dosing, adverse events, protocol changes, unblinding, or trial close-out, and may fluctuate even during periods of clinical stability.

The Weight of Decision-Making
Caregivers often carry the emotional burden of making irreversible decisions for someone who cannot consent for themselves.

Accumulated Grief and Loss
For families who have participated in multiple studies, each trial outcome, especially those that fail or end early—can add to a growing sense of cumulative grief.

Ethical Trial Practice Requires Psychosocial Awareness
Supporting mental health is not separate from scientific rigor, it is integral to ethical research conduct.
Ethical trial practice includes:

- Normalizing emotional responses and explicitly acknowledging that mixed feelings are expected
- Checking in with families beyond clinical endpoints, particularly after stressful events or major milestones
- Recognizing sibling impact, including anxiety, disrupted routines, and emotional strain
- Referring families proactively to ASF mental health and psychosocial support resources rather than waiting for crisis points

Why This Matters for Trial Outcomes
Unaddressed psychosocial strain can:

- Contribute to missed visits or protocol deviations
- Increase withdrawal rates unrelated to safety or efficacy
- Undermine trust between families and study teams
- Shape community perception of research programs

Conversely, families who feel emotionally supported are more likely to:

- Remain engaged through trial completion
- Communicate concerns early and clearly
- Participate in follow-up studies
- Serve as informed advocates for ethical research

ASF Mental Health Support Access

The Angelman Syndrome Foundation offers free mental health counseling to individuals with Angelman syndrome, caregivers, and siblings across the community.

Trial teams are encouraged to:

- Inform families of this resource early in the trial process
- Normalize use of mental health support as part of comprehensive care
- Refer families proactively, not only in moments of crisis

Burden Awareness and Protocol Flexibility

Trial participation often requires families to absorb:

- Long-distance travel
- Missed work and lost income
- School disruption
- Sibling caregiving logistics
- Sleep loss and physical exhaustion Thoughtful design includes:
- Flexible visit windows
- Remote or hybrid assessments when possible
- Minimizing duplicative procedures
- Recognizing cumulative burden over time

Reducing burden improves both ethics and data quality.

Communication Expectations

Families value honesty over optimism.

Effective communication means:

- Clear timelines, even when uncertain
- Prompt updates when plans change
- Avoiding exaggerated promises
- Transparent discussion of risks and unknowns

Silence or delayed communication erodes trust faster than bad news.

Historical Context and Community Memory

Some families enter trials with:

- Extensive trial experience
- Strong scientific literacy
- Past trauma or disappointment Others are new and overwhelmed.

Best practice:

Ask about prior trial experience

Acknowledge what families bring with them

Create space for concerns rooted in history

This awareness creates safer, more respectful engagement.

Post-Trial Considerations and Follow-Through
The conclusion of a clinical trial is not merely a procedural milestone, it is often an emotionally significant moment for families who have invested time, energy, hope, and trust in the research process.

Families frequently leave a trial asking:

- What happens now?
- What did our participation actually contribute to?
- Did this help our child, or help others?

Ethical Follow-Through Extends Beyond Data Collection
This includes:

- Sharing results in accessible, plain-language formats
- Providing realistic timelines for data analysis, publication, and regulatory steps
- Communicating clearly when results are inconclusive or negative
- Clarifying post-trial access options, compassionate use pathways, or follow-on studies when applicable

Acknowledging Emotional Impact
Trial teams should recognize that families may experience grief, frustration, anxiety, or loss at close-out.

Closing the Loop as an Act of Partnership
Families who feel respected and informed at trial close-out are more likely to engage in future research and remain trusted partners in the field.

Angelman Syndrome Patient-Focused Drug Development (PFDD)
ASF's PFDD process centered lived experience across the lifespan and identified:

- Symptoms that matter most to families
- Outcomes beyond traditional endpoints
- Risk tolerance shaped by real caregiving realities

PFDD findings offer a roadmap for ethical, family-centered trial design grounded in real life, not theory.

Resources You Can Share With Families to Prepare for the Trial Pre-Visit Checklist for Families: Preparing for Interventional Clinical Trials
Participating in a clinical trial is a big step, and we want to help make your experience as smooth and informed as possible. Please review and complete this checklist before your visit.

1. Understand the Trial Basics

- Review the informed consent form and bring any questions with you
- Know the trial phase, purpose, and what the investigational treatment is intended to do
- Confirm whether this is a blinded or open-label trial
- Understand randomization, if applicable, and what group your child may be assigned to

2. Gather Documentation

- Bring a copy of your child's most recent medical records, including:
  - Neurology notes
  - Seizure logs
  - Therapy reports such as PT, OT, and speech
  - Genetic testing results
  - Growth charts and immunization records
- Print and bring a list of current medications and supplements, including doses and times
- Create a seizure diary or behavior log from the last 2–4 weeks, if required by the protocol

3. Prepare for Assessments

- Be aware of any baseline evaluations your child will undergo, such as bloodwork, EEG, MRI, or behavioral assessments
- Talk to your care team about how to prepare your child for these assessments, including sedation or fasting
- Bring comfort items, snacks, and sensory supports for long wait times

4. Coordinate With the Trial Site

- Confirm your appointment date and time and expected duration of the visit
- Ask about pre-visit fasting, medication restrictions, or special instructions
- Verify clinic location, parking information, and where to check in
- Request contact info for a study coordinator or nurse in case you need support day-of

5. Plan for Travel and Accommodations

- Book hotel accommodations if overnight stay is needed and ask if the site offers discounts
- Bring a travel folder with:
  - ID cards
  - Insurance cards
  - Site contact info
  - Trial paperwork
- Pack essentials such as comfort items, extra clothes, headphones, snacks, medications, and sensory supports

6. Communication and Consent

- Review and bring all legal guardianship or custody paperwork, if applicable
- Prepare a list of questions to ask the principal investigator or study team
- Ask about how data will be shared, potential risks and benefits, and post-trial access to treatment

7. Reimbursement and Support

- Ask about travel reimbursement, per diem, or coverage for meals and hotels
- Inquire about compensation for participation, if applicable
- Confirm whether you need to save receipts for reimbursement

8. Emotional Preparation

- Talk as a family about what to expect and identify fears or concerns
- Bring a friend or co-caregiver for support if possible
- Schedule some time for fun or relaxation before or after the visit if travel is involved

If you have questions before your visit, do not hesitate to contact your study coordinator. You are not in this alone—we are here to support you every step of the way.

Suggested Add-On Resource for the Trial Readiness Binder

Based on site feedback, this document may be strengthened further by creating a short companion resource such as:

Angelman Syndrome: What Every Staff Member Should Know

A one-page or two-page quick reference for:

- PACU nurses
- OR staff
- Anesthesia teams
- Front desk staff
- Transporters
- EEG or imaging staff
- Rotating inpatient or procedural staff

This could include:

- Common Angelman behaviors and communication differences
- Sensory considerations and triggers
- Tips for successful interaction
- Things to avoid
- Questions to ask parents
- Reminders that parents are the best source of calming and communication strategies
- A brief note on chronological age versus cognitive/functional presentation