

**WHITE PAPER**

Special Considerations for Child Psychiatric Trials During a Global Pandemic



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INTRODUCTION

Children are a vulnerable population afforded **special legal protections** in all IRB-regulated research. **During a global pandemic such as the COVID-19 crisis, assuring protection of this population is especially important.**

Sponsors, investigators, and, importantly, **IRBs**, must determine the:

- Overall risk/benefit ratio of newly enrolling a child into a trial during the COVID-19 pandemic (many IRBs are disallowing this except in certain special circumstances).
- Overall risk/benefit ratio of discontinuing a child mid-study vs allowing a currently enrolled child to continue.
- Overall risk/benefit ratio of maintaining in-person visits vs switching to remote visits. The potential benefit of in-person clinical evaluation must be weighed against the potential risk of virus exposure to the child, accompanying caregiver, and others with whom the child may then interact in transit, at the clinic, and at home.

FOR CHILDREN TO BE CONTINUED IN A TRIAL THAT BEGAN PRIOR TO THE COVID-19 STUDY, A REMOTE ASSESSMENT PLAN IS OFTEN PROPOSED FOR AT LEAST SOME, AND SOMETIMES ALL, OF THE VISITS.

FACTORS TO CONSIDER WHEN EVALUATING THE FEASIBILITY OF A SWITCH TO A REMOTE ASSESSMENT PLAN

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SAFETY CONSIDERATIONS

- Will there be **access to emergency care** if needed (suicidality, other psychiatric and physical adverse events including exacerbation of disorder under study, and including symptoms of COVID-19); has a specific plan been established for safety issues that arise during and in between the remote assessment?
- Will there be a **responsible parent/caregiver at home during assessments** to provide additional safety information and ensure that child receives emergency care as directed

***NOTE: IN CONTEXT OF THE COVID19 PANDEMIC, THE HEALTH OF THE CAREGIVER SHOULD BE CONSIDERED AS SHOULD BACKUP PLANS FOR ALTERNATIVE CAREGIVER SHOULD CAREGIVER BECOME ILL**

2

PRACTICAL CONSIDERATIONS

- **Access to internet/telephone communication.** Does the family have internet or telephone access?
- **Access to video platform/camera** – Does the family have the equipment needed? Will equipment have to be provided?
- **Scheduling of visits** - How will logistics be handled? What will happen if there are **multiple raters** required per visit?
- **Access of rater(s) to rating scale** – When raters are working off-site, how will they gain access to the scales they need to conduct the assessments?
- **Access to ratings data for site staff responsible for global ratings (such as the CGI) and site staff responsible for dosing and medical decisions** – How will assessments by multiple raters be visible to PI and others involved in dosing and medical decision making?
- **Data entry** – How will collected assessments be captured in the study database?

3

VALIDITY/DATA INTEGRITY CONSIDERATIONS

PANDEMIC – EFFECT ON PSYCHIATRIC/PHYSICAL SYMPTOMS

- The **overall effect of the COVID-19 pandemic** on psychiatric illness in children is **unknown**.
- Fear, anxiety, grief, and social isolation may **exert unique effects that differ by age, study drug, psychiatric illness under study, and region of the world**.
- **For these reasons, even if there is NO CHANGE in administration method, we recommend that all assessments conducted during the COVID-19 pandemic be flagged as such for subsequent analysis of this cohort effect.**

MID-STUDY SWITCH TO REMOTE ADMINISTRATION

- **The effect on data of switching scale administration modalities midstream is not known; we recommend that such changes be flagged for subsequent analysis.**
- **For some scales, there may be published data** regarding scale equivalences across modalities; for others there may not.
- **For some scales, copyright holders have requested that permission be sought to switch administration modalities.**
- **Video preferred over phone** – We believe that video conferencing better approximates the in-clinic experience and note it may be required for certain scales/items.
- **Modifications may be needed to better approximate the in-clinic experience** – For example, the parent/caregiver might be asked to hold the camera of a video device so as to allow the rater to visualize a specific part of the child's body.
- **Consent/assent language** may need to be altered - The governing **IRB should be consulted**; typically, the child and parent/caregiver would be advised of the risks/ benefits of the remote assessment and any safety rules that would be enacted (calling police, reporting location, etc.) If audio or video recording is to occur, and is not currently in the consent/assent form, this would need to be clearly specified.



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GENERAL TIPS FOR REMOTE ASSESSMENT WITH CHILDREN DURING THE PANDEMIC

- **Begin with child and parent/caregiver in room together**
 - If applicable (if the child is cognitively able), explain that the interviews will be separate, but that it is **mandatory for the parent/caregiver to be physically present** to help out in case there's a technical problem and in case you need to ask additional questions or have any concerns about the child.
- **Allow time for the child to become comfortable** – Introduce the setup and technology; engage in neutral talk about the child's day as needed to promote the child's comfort.
- **Explain what will happen** – To ensure understanding it is often useful to have the child explain back to you what you'll be doing and why you and the child will now be doing things this new way.
- **Ensure that equipment is positioned to allow for capture of body parts that require visualization** - Note that many scales will require visualization of the full body so as to assess symptoms such as fidgetiness, tics, and hyperactivity/hypoactivity. Be aware (and explain to the child and parent/caregiver) that the parent/caregiver may need to be called in to adjust the camera angle for different scales or different scale items.
- **If the child is to be interviewed alone** – The parent/caregiver should be asked to leave the room but stay close by in case assistance is required.
- **Note that at some point during the remote assessment (often the end), a medically responsible investigator must interview child and parent/caregiver separately to determine:**
 - Adverse events,
 - Dosing or discontinuation considerations,
 - Compliance with study medication, and
 - Any known or suspected exposure to COVID-19
 - Note this may necessitate more than one rater interacting with the child and parent/caregiver during a remote visit



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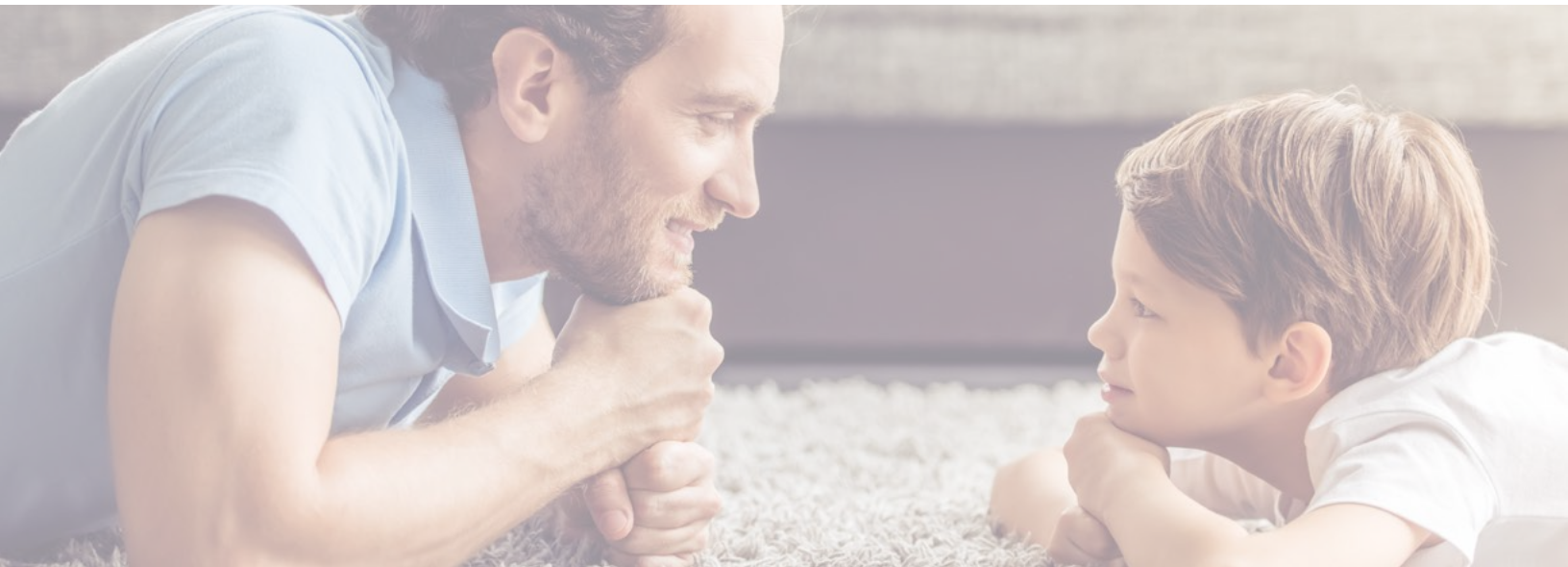
SPECIFIC GUIDANCE FOR REMOTE ADMINISTRATION FOR SELECTED COMMONLY USED SCALES IN CHILD PSYCHIATRIC TRIALS

- **K-SADS-PL** - This scale requires separate interviews with the parent/caregiver and the child. Although the copyright holder has indicated that a phone interview is acceptable, we recommend videoconferencing of the child portion if at all possible as some disorders (e.g., ADHD, tics, and psychosis, for some typical examples) benefit greatly from visualizing the child during the interview (motor activity, motor tics, and responding to internal stimuli, respectively, using the above example disorders).
- **C-YBOCS** - In non-remote settings, this scale is typically done with the parent/caregiver and child together in the room. Typically, the opportunity is given for either party to then speak alone with the interviewer. We recommend following this approach. As the scale does not rely on visualization, it is possible to administer this by phone.
- **CY-BOCS-ASD** - In non-remote settings, the scale is often administered solely to the parent/caregiver. If this is what has occurred in the trial previously, we would recommend that this be continued. As the scale does not rely on visualization, it is possible to administer this by phone.
- **YGTSS** - In non-remote settings, the scale is typically done with the parent/caregiver and the child together in the room. If this is what has occurred in the trial heretofore we would recommend that this be continued. The opportunity is given, typically, for either party to then speak alone with the interviewer. We recommend following this approach. Visualization of motor tics that might occur during the interview is important and often drives additional probes. For this reason, videoconferencing is recommended.
- **CDRS-R** - The interview requires separate interviews with the parent/caregiver and the child. The interview requires visualization of the child for some of the items, thus videoconferencing will be needed for the child portion of the interview.
- **ADHD-RS** - In most trials, the interview is done solely with the /caregiver, so telephone administration is possible.
- **CGI-S/I** - Regardless of the indication, the CGI-S and CGI-I requires the rater's overall consideration of all relevant information about the illness under study. The assessment must include, in addition to a review of collected relevant data, a clinical interview with the child. To best capture the full clinical picture, videoconferencing is clearly preferable to phone; for some conditions (e.g., ADHD, motor tics, among others) videoconferencing may be required.
- **PANSS** - The scale requires separate interviews with the parent/caregiver and the child. As many of the items require visualization of the child, we strongly recommend videoconferencing for the child interview.

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GENERAL GUIDANCE ABOUT RATING A CHILD'S PSYCHIATRIC SYMPTOMS DURING THE COVID-19 PANDEMIC

- Maintain rater consistency
 - Ideally the same rater who rated the child prior to the switch to remote assessment will continue to rate the child in the remote assessment phase
- Maintain caregiver/parent informant consistency
 - Ideally the same parent/caregiver who provided information prior to the switch to remote assessment will continue to provide information in the remote assessment phase
- "Rate as you see it"
 - Don't try to imagine what a symptom would have been if the pandemic hadn't occurred
 - Efforts to rate in the hypothetical are misguided and will result in poor data quality
 - Studies will track pre and post COVID19 data and effects on psychiatric symptoms will be examined statistically



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