In the face of the COVID-19 outbreak, Children's National Hospital (CNH) is implementing additional human subject protections guidelines for clinical research participation. These guidelines are designed to protect the safety of our research participants, healthcare providers, and staff. The current situation is fast-moving and updates to this policy will be provided as needed. These guidelines are effective immediately and will remain in effect until further notice.

As of 5/25/20, we are in Phase 0.5 of research allowable during COVID-19 response (Table 1 below).

GUIDELINES:

I. Applicability

These guidelines apply to all inpatient and outpatient research visits for active participants, as well as new enrollment in approved human subject research studies conducted by faculty and staff at Children's National Hospital. These guidelines apply to human subject research taking place at all CNH facilities and community enrollment sites and are based on best practices at peer institutions during this time.

II. Pause of certain research studies and/or in-person study procedures and/or new enrollment based on the potential for direct therapeutic benefit and phase of research preparedness.

EFFECTIVE IMMEDIATELY, certain research studies or activities must be paused until further notice. This pause is necessary because there is the potential for additional risk of exposure to the virus for research participants and staff in clinical environments, a need to prioritize personal protective equipment (PPE) for clinical operations, and to reduce the risk of viral transmission from person-to-person contacts.

Allowable research activities and those that will need to be paused will depend both on the tier of research and the phase of allowable research (see Table 1 below) that the Children’s National Research Institute has put into effect.

PIs must re-evaluate their research portfolio using the defined tiers of research below and determine, for each study, which tier applies to the research.

Defined tiers of research studies during the COVID-19 Pandemic

Tier 1 – High Prospect of Direct Benefit to Research Participants

- Research protocols involving treatments for acute, life-threatening health conditions (e.g. some treatment trials for cancer, malignancies/tumors, some rare diseases)
- Protocols where stopping the intervention (e.g., some investigational drugs or investigational devices or vaccines or preventative drug regimens) could be harmful
- All research protocols related to the surveillance, diagnosis, and treatment of COVID-19
- Some but not all studies that have been approved by an IRB as greater than minimal risk with the prospect of direct benefit (45 CFR 46.405 or 21 CFR 50.52) will fall into this category

Tier 2 – Moderate Prospect of Direct Benefit to Research Participants

Protocols which, if stopped, may pose a hazard to the research participant. For example:

- Protocols in which research participants are receiving interventions or clinical care that is very interrelated to their research participation (e.g., test results coming back that might have clinical implications for their care)
Some protocols evaluating treatments for chronic conditions (e.g., asthma, hypertension, depression, stabilization of high-risk mental health conditions, etc.)

Protocols involving assessment of the safety (such as Phase 1 studies) or efficacy (such as Phase 2 studies) of an intervention and which, if stopped, the potential societal benefit of the science would be significantly and adversely impacted. For example where a research assessment (blood collection or imaging study) is only valuable if collected at a very specific time. This must be measured against the risk to participants, including the risk of exposure of COVID-19

Some but not all studies that have been approved by an IRB as greater than minimal risk with the prospect of direct benefit (45 CFR 46.405 or 21 CFR 50.52) will fall into this category

**Tier 3 – Low Prospect of Direct Benefit to Research Participants/No Prospect of Direct Benefit**

- Studies not meeting criteria for Tiers 1 and 2 above
- Cohort and natural history studies where delays in data collection have limited impact on scientific objectives
- Protocols in which delays to starting or pausing of research do not have a substantive impact on the research objectives of the research protocol
- Protocols in which risks to research participants are higher (e.g., potentially exposing vulnerable individuals to COVID-19) and benefits of the study to the participants remain minimal
- Research with healthy volunteers
- Any minimal risk studies that require research subjects to travel, that involve undergraduate students, or that are in a community setting and require direct interaction with researchers
- Studies that have been approved by an IRB as greater than minimal risk with no prospect of direct benefit (45 CFR 46.406 or 21 CFR 50.53) will fall into this category
- Some studies that have been approved by an IRB as minimal risk (45 CFR 46.404 or 21 CFR 50.51) will fall into this category
<table>
<thead>
<tr>
<th>Response Phase</th>
<th>Example Criteria for Implementation – Based on local and national public health recommendations and direction of CRI leadership and IRB</th>
<th>Required Modifications/Pauses to Research by Tier of Research</th>
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</thead>
<tbody>
<tr>
<td>Response Phase 0</td>
<td>Potential, but no immediate threat of spread to local researchers and employees</td>
<td>Develop contingency plans</td>
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</table>
| Response Phase 0.5 (as of 5/25/20) | Regional community spread; minimal local & institutional cases; adequate PPE, social distancing & other protections in place for those involved in research | **Tier 1:** Research can continue if the PI agrees the research can be conducted in a safe manner that protects subjects, the research team and the community. In-person visits that can be transitioned to remote administration or delayed should be transitioned.  
**Tier 2:** In-person visits with potential for direct benefit that out-weighs risks, including the risk of exposure of COVID-19, to subjects may continue. Research components can be added to clinic visits when the research can be safely conducted at the point of care with minimal additional time and no participation by additional clinical or non-clinical staff. All other research activities must be transitioned to the Clinical Research Center (CRC), conducted via remote administration or paused.  
**Tier 3:** Direct participant contact must be paused. All remote visits may continue. |
| Response Phase 1 | Regional community spread; minimal local cases | **Tier 1:** Research can continue if the PI agrees the research can be conducted in a safe manner that protects subjects, the research team and the community. In person visits that can be transitioned to remote administration or delayed should be transitioned.  
**Tier 2:** Only those in-person visits with potential for direct benefit that out-weighs risks, including the risk of exposure of COVID-19, to subjects may continue. All other visits must be transitioned to remote administration or paused.  
**Tier 3:** Direct participant contact must be paused. All remote visits may continue. |
| Response Phase 2 | Local community spread; High absenteeism; Sporadic institutional closures | **Tier 1:** Research can continue if the PI agrees the research can be conducted in a safe manner that protects subjects, research, and the community. In person visits that can be transitioned to remote administration or delayed should be transitioned. **PIs must pause enrollment of new research participants unless there is a compelling reason for enrollment to continue.** PIs must petition the IRB if they have a compelling reason for not following this new policy.*  
**Tier 2:** Only those in-person visits with potential for direct benefit that out-weighs risks to subjects, including the risk of exposure of COVID-19, |
Requests must be submitted to the IRB using the OPHS exceptions request form and will be reviewed in order of priority (based on tier of research). These guidelines must be followed for studies seeking an appeal until such time as an appeal is granted.

III. Institutional Review Board

In the midst of the current COVID-19 outbreak, the Institutional Review Board (IRB) and Office of Protections of Human Subjects (OPHS) are fully operational.

The differences:

- The IRB has implemented triage procedures to prioritize reviews and manage workload. OPHS anticipates a large increase in submissions as investigators adapt their research to the measures being taken to limit the transmission of COVID-19.
- Highest priority will be given to emergency expanded access requests, new research related to the surveillance, diagnosis, and treatment of COVID-19, and modifications (amendments) prompted by COVID-19 to approved, ongoing, Tier 1 and Tier 2 studies. We regret that this may result in temporary delays in the processing of other types of submissions.
- While OPHS staff members are working remotely, the main OPHS phone line (301-565-8447) will be converted to a message-only line which will be checked on an hourly basis during core business hours. The OPHS main email box (OPHS@childrensnational.org) and the reliance mailbox (reliance@childrensnational.org) will continue to be monitored frequently throughout each work day.
- The OPHS office at the main hospital will be closed until further notice. OPHS office hours will be conducted via Zoom and email consultations. Please see the IRBear home page (www.IRBear.org) for a listing of office hours and staffing.

IRB FAQs below provide guidance on when and how to request IRB approval for changes to the protocol and associated documentation and reporting requirements.

IV. Investigational Drug Services

- The Investigational Drug Services will continue to support dispensing of investigational products for all inpatient and outpatient research visits for active participants. On a case-by-case basis, we can also explore shipping investigational products directly to participants, if allowed by the protocol.
• The Investigational Drug Services will prioritize the support of activities needed to open new protocols that are deemed essential and/or high priority. This may result in delays with support of other types of submissions.

• The Investigational Drug Services will conduct and/or participate in all meetings remotely, including pre-study visits, site initiation visits, and monitoring visits.

V. Sponsored Research

• For industry-sponsored studies, any procedural changes should be made in coordination with the sponsor.
• For sponsored research studies (government, foundation, or non-profit), PIs must notify the Office of Sponsored Research Administration (OSRA) so that OSRA can report to the sponsor.
• External sponsor visits: On-site external sponsor monitor visits are suspended, effective immediately. This includes pre-study visits, site initiation visits, and monitoring visits. Remote monitoring can be provided through the use of the Online Research Binder (ORB). In specific cases on-site monitor visits may be required by the sponsor to proceed with Tier 1 studies, utilizing one of the designated monitoring rooms for the approved time allotted. These on-site visits must be approved by Kerstin Hildebrandt, Vice President, Research Administration.
These FAQs have been created to share the answers to COVID-19 related IRB questions. It will be updated as needed.

Q1: Which studies or study visits must be paused?
A1: See descriptions for each tier and phase of allowable research in section II above.

Q2: Which studies with in-person interactions may continue?
A2: See descriptions for each tier and phase of allowable research in section II above.

In operationalizing clinic visits with added research components, PIs must follow current institutional guidance for use of clinical spaces, maintain required social distancing at all times, comply with PPE requirements, minimize additional time added to the visit due to research procedures, and eliminate involvement of additional clinical or any non-clinical staff in conducting consent and research procedures. The Clinical Research Center (CRC) should be leveraged to the extent possible for allowable research visits and activities.

Q3: What if my study doesn’t clearly fall into any of the three tiers?
A3: Contact the IRB to discuss the ethical basis/demonstrated need for continuing the study and a plan for minimizing person-to-person contact.

Q4: How can I minimize risks associated with in-person visits?
A4: Here are some recommendations:
   a. **Prior to a scheduled study visit**: Trained study team members should screen the participants (and accompanying parent/guardian) by phone for symptoms of fever, cough, congestion, and respiratory distress. If participants report symptoms, the visit should be rescheduled, with the participant returning once asymptomatic.
   b. **The day of the scheduled study visit**: Trained study team members should screen participants who present for study visits for symptoms of fever, cough, congestion, and respiratory distress. Study participants (and accompanying parent/guardian) with symptoms should be counseled to go home and seek medical care as they typically would with their current symptoms.
   c. **For participants (or accompanying parent/guardian) with severe respiratory symptoms**: The study team should isolate the individual in a room with a closed door and contact Infection Control and the Infectious Diseases COVID team (Pager 59980) for guidance.
   d. **If a participant/family/stakeholder meeting is needed as part of the investigative team’s research protocol**: Teams are currently recommended to conduct these study participant/family/stakeholder meetings by Zoom or reschedule them.

Q5: Must I inform the IRB if I am pausing a study or some or its procedures due to COVID-19? (Note: This represents a change to previous guidance dated: 3/13/20)
A5: Yes. There is a simple process for informing the IRB if you are pausing some or all protocol procedures/activities due to the current situation which does not require additional IRB review or approval. Go the study home page in IRBear and log a Public Comment. Check the box indicating that you are documenting a pause in research activities. Describe which procedures/activities are being paused and who initiated the pause (PI, external funding agency, industry sponsor, etc.). Attach any relevant documentation. You will receive a notification from
IRBear through Outlook acknowledging that you logged a comment. Also be sure to log a public comment when activities are resumed.

Q6: Can studies which do not involve in-person interaction continue?

A6: Yes. Studies that do not involve face-to-face interactions with participants, such as studies conducted entirely electronically, via telephone or by mail can continue. Studies involving data analysis only or involving secondary data analysis may continue.

Q7: If I need to modify my study procedures to occur remotely, what should I do?

A7: If your study is not exempt, the approved protocol specifies in-person visits, and you want to modify the study’s procedures – such as replacing in-person study visits with “remote” options for safety monitoring, questionnaires, surveys, check-ins, screening, or obtaining consent – you must submit a protocol amendment to the IRB before implementing any changes. Modifications to any study procedures should be approved in advance by the IRB. See the next Q&A for exceptions.

When applicable, PIs should create a note in the regulatory binder describing and providing rationale for any changes to planned study visits or approved visit windows.
Q8: Are there circumstances when study procedures can be modified without prior IRB approval?

A8: Yes. There are 2 scenarios when prior IRB approval is not required.

a. **Modifications which are necessary to eliminate imminent hazards to a participant and ensure their immediate health and safety** may be implemented right away if there is insufficient time to obtain prospective IRB approval. For non-exempt studies, if procedures are modified without prior IRB approval to eliminate immediate possible harm, it is considered a **protocol deviation**. Report the deviation to the IRB within seven (7) business days by using the reportable events process in IRBear, describing the modifications, circumstances, and corrective and preventive action plan.

b. You do not need to submit an amendment in order to hold visits remotely or change the schedule if the study is exempt or if the IRB application does not describe whether the visits will take place in person or remotely.

**Tip:** When reporting unapproved changes to study procedures, out-of-window visits, or other **minor** protocol deviations which are due to COVID-19, do not submit a separate report for each event. Rather, please include multiple occurrences of protocol deviations in one reportable event submission. Depending on the number of events, consider submitting a report on a monthly basis or at the time of the next continuing review.

If you have any questions about whether a remote option is possible or approvable (especially for consent), please contact the OPHS team at OPHS@childrensnational.org.

Q9: For FDA regulated research, how do I document out of window visits and other changes to the sponsor approved protocol in the regulatory binder?

A9: Research teams should use notes to file to indicate a pause in research of other modifications required to comply with this guidance. PIs should discuss this guidance with sponsors. Use of an electronic regulatory binder, when available, is encouraged.

Q10: May we initiate a new trial or enroll new subjects on existing studies not subject to the pause?
A10: New studies must follow the criteria in this guidance to begin enrolling patients. PIs should consult with sponsors and funders prior to implementing a new study. Some funders, such as NIH, have issued and are updating guidance for awardees, see: [https://grants.nih.gov/grants/natural_disasters/corona-virus.htm](https://grants.nih.gov/grants/natural_disasters/corona-virus.htm)

Additionally, PIs should ensure that the current COVID-19 circumstances and the availability of personnel and resources allow for implementation of new studies.

Q11: Should anyone else (e.g. sponsors, the FDA, NIH or other funding agencies) be notified about changes in IRB-approved study procedures in response to COVID-19?

A11: It may be necessary to notify the following parties of these changes:

- The study sponsor, for industry-sponsored trials, pursuant to the terms of the clinical trial agreement or other contract governing the study. Sponsors might call the pause to research or new enrollment a **protocol hold**.
- ClinicalTrials.gov, for studies registered there for which the institution is the “responsible party” under 42 CFR Part 11 if required by 42 CFR § 11.64, or for other studies that the institution has registered on ClinicalTrials.gov because of the funding source, Medicare reimbursement requirements, or journal publication policies.
- The FDA, for studies where the PI or institution holds the investigational new drug application (IND) or the investigational device exemption (IDE), pursuant to 21 CFR 312.30 (for drugs) or 21 CFR § 812.35 (for devices). The FDA has released a guidance with additional information about the conduct of clinical investigations at: [https://www.fda.gov/media/136238/download](https://www.fda.gov/media/136238/download)
- The NIH (if the study is NIH-funded), depending on the change in procedures, after consulting with the Children’s Office of Grants and Contracts and the Program Official at the NIH awarding Institute/Center. The NIH has a COVID-19 resource page with information for funding recipients at: [https://grants.nih.gov/grants/natural_disasters/corona-virus.htm](https://grants.nih.gov/grants/natural_disasters/corona-virus.htm)

Q12: Do I need to modify my consent form to include the risks of COVID-19 if there will be in-person interactions in studies not focused on COVID-19?

A12: At this time, OPHS does not believe that this is necessary for most studies.

Q13: I am modifying my research to replace in-person visits with remote visits. How can I modify my process for administering informed consent?

A13: There are several possible options available, depending on the study design, which can be requested through a protocol amendment:

a. Research teams can mail the informed consent/parental permission form to the participant/LAR, review the form by phone, and ask the participant to return the signed form to the research team.

b. Verbal consent can be obtained by telephone with documentation of verbal consent by the research team.

c. Some studies may qualify for a waiver of written documentation of consent (e.g. signature).

Research teams can reach out to OPHS to discuss options for specific studies.

Q14: Do we need approval from the IRB for communications to study subjects explaining the pause in activities?

A14: Yes. The IRB has approved a template letter that PIs can customize prior to sending to participants. The letter is available on the IRBear Home page under General Information > Forms and Templates. No additional IRB
review and approval is required if no changes are made to the templated text. If the letter template is altered in any way or if other communications are developed, they will require IRB review and approval.

Q15: If I am pausing study procedures on a project reviewed by an external IRB of Record, must I notify the external reviewing IRB?

A15: Yes, as soon as feasible, for their awareness. This guidance should be shared with the IRB of Record. The IRB of Record must review and approve any protocol amendments (unless required to remove a hazard to participants) prior to implementation. The IRB of record may also require review and approval prior to resumption of study procedures. Sponsors may also require changes to the research during this time.

Q16: If I am pausing study procedures on a multisite study where Children’s National IRB is the IRB of Record for multiple sites, must I notify the other participating sites of a pause or changes to the research protocol?

A16: Yes, as soon as feasible, the PI should notify the sites relying on the Children’s National IRB about the approved changes to the study protocol. If those participating sites require IRB approval of study changes based on their institution’s COVID-19 guidance, these requests will need to be submitted to the Children’s IRB for review. Please reach out to OPHS if you need additional information or guidance in these cases.

Q17: If I am part of a multisite study, either as the lead site or as a participating site, does this guidance apply to other sites?

A17: These guidelines are specific to our institution, although most institutions now have some level of COVID-19 related research restrictions in place. Each site must follow institutional guidelines and directions of the reviewing IRB and study sponsor.

Q18: Does the pause include research conducted by Children’s National investigators in international locations overseen by a local IRB or Research Ethics Committee (REC)?

A18: Research projects conducted by CN researchers in international settings should consider the local COVID-19 situation, seek guidance from the local IRB or ethics review boards that may have oversight for the research, and share this information with our IRB.

Q19: Do I need to register modifications with ClinicalTrials.gov?

A19: Some studies registered at the federal site ClinicalTrials.gov are modifying their research procedures to include assessment of COVID-19 symptoms. The ClinicalTrials.gov information for the study should be updated to include these new procedures, if they are done for research purposes. If they are being added as public health surveillance activities in coordination with public health authorities, the registration information does not need to be modified. The federal requirement about modifications is that any research-related changes that are communicated to the subjects (past, ongoing, future) must be added to the study’s ClinicalTrials.gov registration with 30 days after IRB approval of the modification.

Q20: Given the Children’s National policy requiring a pause for certain studies/study visits, does this also impact research sites that have subawards? Each site has their own/local IRB approval and we only send money.

A20: As these sites are under the oversight of their local institutions/IRBs, they should be informed of the pause for certain studies conducted at Children’s, but they would make an independent decision as to whether to proceed with research activities at their site.

Q21: How can I provide ClinCards to research subjects who are participating in research remotely remote visits?
A21: ClinCards can be mailed to research participants. Once the research team confirms that the participant received the ClinCard, the allowable compensation amount can be loaded onto the card.

Q22: Has the process for single-patient emergency use changed?

A22: No. The procedure for Single Patient Emergency Use of an experimental drug or device remains the same during the COVID-19 situation. Requests for single-patient emergency use should be sent to: OPHS@childrensnational.org, nluban@childrensnational.org, jslotsman@childrensnational.org and adcook@childrensnational.org. Please include “Emergency Expanded Access Request” in the Subject line.

As a reminder to PIs, while FDA-approved emergency expanded access requests do not require prospective IRB approval, an appropriate consent form is required and FDA regulations require that outcomes be reported to the IRB within five (5) business days after drug administration. **OPHS has developed a new consent form template for expanded access studies which is available on the IRBear Home page under General Information > Forms and Templates.** For additional information, see Research Involving FDA-Regulated Products in IRBear.

Q23: Is my COVID-19-related project considered research?

A23: In some cases, IRB approval may not be required for COVID-19-related activities. For example, the activities may consist solely of public health surveillance activities, clinical care, or diagnostic testing for which an FDA emergency authorization has been obtained. OPHS can assess the circumstances, provide advice, and issue determination letters (if warranted). Contact OPHS@childrensnational.org for more information.

Q24: I am planning to submit a grant to the NIH under the NIH Notice of Special Interest related to COVID-19 or conduct other research on COVID-19. How can I work with the IRB to facilitate efficient review of such new research if it is funded?

A24: If you are planning to respond to the NIH request or do any coronavirus research and before you create an application in IRBear, **please take five (5) minutes to provide OPHS with the information described below.** This information is enough to enable us to work “behind the scenes” to: a) identify, prioritize, and set up the likely resources that will be needed for the IRB review, and b) establish the likely regulatory and ethical framework for the review.

The following information will help OPHS prepare for a more rapid IRB review of these studies. Simply send an email to OPHS@childrensnational.org with the subject line “COVID-19 Research Proposal.” Provide this information:

1. **Children’s National PI** name and department
2. **Research title**
3. **IRB review information**, for example:
   - If there is an existing approved IRB application you want to modify to include this research: Tell us the name of the PI and approved study.
   - If this will be multi-institutional research and you will obtain the IRB review from another IRB: Tell us the name of the IRB or the name of the lead PI’s institution.
4. **One- to two-sentence research description**, including whether you will interact with the subjects
5. **External funding** you already have or are requesting for the research
6. **Any public health agency** (local, state, federal) that will be involved in the research; for example, you might use a research protocol developed by NIH or you might plan to share data with the CDC

When you are ready to begin the IRB process, consider first contacting OPHS through OPHS@childrensnational.org. We can advise you about the specific information the IRB will need for an efficient review.
Updated FAQs will be available on the CNH Intranet site:
http://intranet.childrensnational.org/department/clinical-support/infection-control/Pages/Coronavirus.aspx

If you have additional questions or require more assistance/guidance, please contact the OPHS at OPHS@childrensnational.org or 301-565-8447 with your protocol number.