Human Subjects Research during the COVID-19 Outbreak

Updated 5/14/2020

Effective March 17, Ascension Wisconsin is implementing specific policies and procedures for the conduct of human subject research. **Currently, these policies and procedures are planned to remain in effect until June 1st.** AWRI leadership will be reviewing and updating this guidance frequently.

In-person study interactions may only occur if the research is essential for the health and well-being of the research participant. All other non-essential in-person research interactions should be postponed or conducted remotely when possible. No new sponsored trials or NCORP studies will be opened until further notice and will re-evaluated on an on-going basis.

For more information see: the Temporary Policy: Human Subjects Research at Ascension Wisconsin during the COVID-19 Outbreak and FAQs below.

Direct any questions or concerns about this page to Dr. Douglas Reding, Chief Academic Officer at Douglas.Reding@ascension.org (mailto:Douglas.Reding@ascension.org) (mailto:Douglas.Reding@ascension.org?subject=Research and COVID-19)or at 414-465-3709. This information is being provided by the Ascension Wisconsin Research Institute for research PIs, staff, and administrators and will be revised as appropriate based on new information and circulated to the Ascension Wisconsin research community.

Temporary Policy

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Temporary Policy: Human Subjects Research at Ascension Wisconsin during the COVID-19 Outbreak

Background

In the context of recent municipal and institutional statements on COVID-19 and the rapidly evolving outbreak, the Ascension Wisconsin Research Institute has established this guidance related to human subjects-related research. This is being implemented to protect research participants, researchers, and the larger Ascension Wisconsin community from risk of infection with COVID-19 as well as to ensure ongoing access to research which may provide essential support and care to participants.

This policy will be revised as appropriate based on new information and circulated to the Ascension Wisconsin research community.

Research Visits

Face-to-face human subject research that is not essential to the health and/or well-being of the subjects must be paused, effective immediately. See below for guidance on whether your study provides direct benefit, if you have questions you can contact IRB@Ascension.org (mailto:IRB@Ascension.org).

In-person study interactions may only occur if the research is essential for the health and well-being of the research participant. All other non-essential in-person research interactions should be postponed or conducted remotely when possible. If the patient is present in the clinical setting for active treatment, this should be considered an essential visit.
As a reminder, all modifications to study procedures require IRB approval prior to implementation.

Remote Visits

Research visits should be performed remotely (e.g., by phone, Google Hangouts) whenever possible.

Non-Essential Research Visits

Research visits that are not essential to a participant's health and/or well-being should be completed remotely, as described above. If they are not able to be completed remotely, they should be postponed until further notice. This will be re-evaluated regularly and updates provided as needed.

Currently, the determination of whether a research visit is "essential to the health and/or well-being" of a participant is determined by the principal investigator of the research study, the participant, and the participant's care provider, and should be informed by current public health guidance regarding the COVID-19 outbreak.

Examples of non-essential visits might include subject surveys, toxicity checks, etc.

Essential Research Visits

Research visits that cannot be performed remotely and are essential to a participant's health and/or well-being may be performed in person, with the following additional guidance:

- Participants should be provided with information regarding the current COVID-19 epidemic and how best to reduce their risk of infection. If possible, this information should be shared before the research visit. See the following CDC COVID-19 link for reference and materials: https://www.cdc.gov/coronavirus/2019-ncov/about/ (https://www.cdc.gov/coronavirus/2019-ncov/about/)
- All clinical patients, including research participants, will be screened for fever, cough and flu-like symptoms by clinical staff prior to research staff seeing the for the research visit if they present to the clinic area. For COVID-19 positive patients, check with the provider to determine if treatment will be delayed and reschedule research visit to that time interval. This may indicate a protocol violation, but a valid one in light of the clinical condition of the patient.

Examples of essential visits might include subjects active on chemotherapy or other treatments.

Enrollment of new research participants

Enrollment of new participants on a clinical trial or other human subject-related research should be allowed only if:
Participation in the trial is essential to a participant's health and/or well-being, as determined as

above; or

The enrollment and longitudinal participant management can be conducted remotely for the duration of the COVID-19 outbreak.

Study Sponsors

AWRI Directors and Principal investigators or their designees will be asked to contact study sponsors to notify them of this guidance and make appropriate arrangements. All sponsor visits for clinical trials or other human subject-related research, whether for site qualification, site initiation, or monitoring visits, should be postponed whenever feasible. Consideration for remote monitoring should be based on study need and resource availability.

New Research Studies

No new sponsored trials or NCORP studies will be opened for 30 days minimum and will re-evaluated on an on-going basis.

Institutional and Local Resources

Principal investigators and study teams are expected to adhere to institutional and local guidance regarding availability of resources. For example, if local lab, imaging, or pharmacy are not available due to closure or clinical needs, research activities for specific studies might need to be suspended. This should be evaluated regularly to ensure that there is not additional burden on the system.

Frequently Asked Questions (FAQs)

Should I implement COVID-19 screening?

Updated 4/2/2020

COVID-19 screening should occur for all in person study visits following the institutional guidelines. Screening procedures that may be mandated by the institution at which a clinical trial is being conducted do not need to be reported as modification to the protocol, even if done during clinical study visits, unless the sponsor is incorporating the data collected as part of a new research objective.

Can I continue to conduct study interactions with research participants?

Updated 3/16/2020

Face-to-face human subject research that does not provide a direct benefit to the subjects must be paused, effective immediately. If you have questions regarding whether your study provides direct benefit, contact IRB@Ascension.org. (mailto:IRB@Ascension.org.?subject=Question about Research and COVID-19)

Where possible, transition in-person interactions for all studies, regardless of benefit, to remote interactions to limit potential exposure.

Considerations for Face-to-Face Interactions

Those studies providing direct benefit requiring face-to-face interactions, consider measures that can be undertaken to minimize exposure during face-to-face visits. Some specific considerations include:

- Implement participant screening to minimize exposure risk. Refer to Institutional guidance for possible screening questions. Such screenings do not require IRB approval as long as the information will not be added to the research data set.
- Ensure that hand sanitizer and hand washing facilities are readily available and encouraged.
- Establish rigorous disinfecting protocols for any equipment, manipulative, or other study equipment that will be used with multiple participants.
- Implement extra precautions or postpone study visits especially for participants falling into a high-risk category.

Studies Not Providing Direct Benefit

For studies not providing direct benefit, consider whether some study interactions can be conducted remotely. Some specific considerations include:

- Study interactions such as interviews or simple study follow-up visits may be able to be done by phone or video.
- Reach out to study sponsors to inquire about procedures for modifying protocol schedules.

- If your study requires signed informed consent, consider whether you can modify study procedures by requesting a waiver of documentation of consent so that consent may be obtained without requiring a signature. To be approved to waive documentation of consent, the study must present no more than minimal risk of harm to participants and involve no procedures for which written consent is normally required outside the research context.

As a reminder all changes to current procedures will require an amendment be reviewed and approved by the IRB of record prior to initiating any changes (except those required to eliminate immediate risks).

What if my subject does not want to come in for their research related visit because of COVID-19?

Updated 3/16/2020

This should be handled in the same manner as it has in the past. Subjects may miss study visits for a variety of reasons. If this occurs, identify if missing a study visit would put the subject at additional risk. If applicable, notify the study sponsor. If necessary, reschedule the visit as soon as possible. Consider whether the study visit can be safely conducted in an alternate location or whether or not the schedule of study related events can be altered. If the missed visit has an impact on the risks or safety of the subject, it should be reported to the IRB as a reportable event (noncompliance).

If a participant elects to withdraw from a clinical research study, it is important to ensure that the participant understands (a) the decision will not impact any other clinical care and (b) what possible alternatives may be available for treating or managing the underlying condition.

Do I need a study-specific COVID-19 Risk Mitigation Plan for ongoing research?

Updated 4/2/2020

In general, investigators should develop a study-specific COVID-19 risk mitigation plan for their research unless one of the following is true:

- Research does not involve in-person interaction with research subjects.
- Research can be conducted as written while adhering to social distancing requirements and institutional COVID policies/requirements.
- Research is externally sponsored, and Sponsor has developed COVID-19 risk mitigation plan for the research.
- Research should be voluntarily placed on hold for recruitment and all research procedures (except for necessary follow up procedures to be done consistently with social distancing requirements and institutional COVID policies/requirements).

Are there tools and resources to help with developing study-specific COVID-19 Risk Mitigation Plan?

Updated 4/2/2020

Review the policy above and these SOPs for general guidance on developing study-specific risk mitigation plans.

The following resources are also available:

- Decision Guide for Study-Specific COVID-19 Risk Mitigation Planning (/-/media/Project/SXA---WI/AWRI/Files/RIP/IRB-Guidance/AW-HRP-106-FLOWCHART--Study-Specific-COVID-19-Risk-Mitigation-Plan.pdf?la=en&hash=D98E06730E6D52719D7A56F0AA8AE5FCF325079A)
- WORKSHEET: Protocol-Specific COVID-19 Risk Mitigation Planning (/-/media/Project/SXA---WI/AWRI/Files/RIP/IRB-Guidance/AW-HRP-350---WORKSHEET---Research-Specific-COVID-19-Risk-Mitigation-Plan_v3-24-20.docx?la=en&hash=E230266D044C6132E506F30C5F8C5BF7E4C57B15)
- For FDA-regulated research, consult FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic (https://www.fda.gov/media/136238/download) as well for further information.

Should I modify in-person safety monitoring visits that are essential for the conduct of a clinical trial?

Updated 3/16/2020

Some ongoing clinical studies require in-person follow-up visits to monitor participant safety. For example, a treatment and intervention trial may require physical examinations, laboratory tests, or interviews.

You should plan for the possibility that in-person visits may not be possible or practical. Consider some of the following as possibilities that may or may not work for your study:

- If your study is sponsored, contact the sponsor for recommendations and/or changes in procedures that are being implemented study-wide.
- Conduct interviews by phone, video, or email questionnaires.
- Consider conducting physical examinations at participants' homes or other alternative locations.
- Attempt to combine follow-up visit procedures with other clinical visits participants' may already be doing (i.e., visit with another physician specialist).

As a reminder, all changes must be reviewed and approved by the IRB record before being implemented.

Any changes to study procedures made to eliminate apparent immediate hazards to research participants, including those to reduce potential exposure to SARS-CoV-2, or to continue to provide medically necessary study care to participants who have been placed in isolation do not need prior approval by the IRB. All such changes should be reported to the IRB as an unanticipated problem involving risk to subjects or others within 5 days.

Should I place a voluntary hold on human research activities?

Updated 4/2/2020

Investigators may voluntarily elect to place all recruitment, enrollment, and research procedures on temporary hold if doing so will better ensure the safety of research subjects and would not create any additional risks to the safety and welfare of research subjects. Such voluntary holds on research activity do not require IRB notification or review.

Are the Research Integrity and Protection Office and Institutional Review Board (IRB) operating as usual?

Updated 3/16/2020

Yes, the staff in the Research Integrity and Protection office and IRBs are conducting business as normal. The Research Integrity and Protection office and IRBs are fully capable of conducting reviews via the online system (Mentor (https://www.axiommentor.com/login/axlogin.cfm?i=ascension)) from any location.

If I change my human subjects research activities, do I have to submit a modification to the IRB?

Updated 3/16/2020

Yes, all human subjects research regulations still apply. If a change to research related activities does occur, a modification is required. All modifications to research related activities require IRB for review and approval prior to implementation. This includes modification to procedures to replace in-person study visits with virtual or phone options for administering questionnaires, surveys, check-ins, screening, and consenting remember that these changes must be approved in advance by the IRB as a modification to the study, unless they are necessary to eliminate immediate apparent hazards to participants.

If the Ascension Wisconsin IRB is the IRB of record, researchers should use Mentor (https://www.axiommentor.com/login/axlogin.cfm?i=ascension) to submit an amendment as usual. If you do choose to submit a modification select the “COVID-19 Specific Changes” amendment type in Mentor (beginning 3/18/2020). The IRB will prioritize these modifications. See the Mentor User Manual (https://www.mywheaton.org/app/files/public/4723/IRB-Mentor_eIRB_ResearcherUserManual.pdf)for submission instructions, or contact IRB staff for assistance.

If another IRB is the IRB of record for the study, follow their guidance for updates.

Do I need to modify my consent document to address the risk of COVID-19 if my study involves in-person interactions?

Updated 3/16/2020

At the present time, the IRB does not believe it is necessary to require risks related to COVID-19 be added to the consent document.

What do I do if I have a single patient emergency use case?

Updated 4/2/2020

The procedures for a single patient emergency use of an investigational drug or device remains unchanged during this time. You can find the information, form, and SOP on the IRB website (https://ascensionwisconsinresearchinstitute.org/researchers/research-integrity-and-protection/irb/emergency-use). In the event an emergency use scenario arises, contact Jackie Kirchen, Director or Research Integrity and Protection at 414-915-3229 or Jackie.Kirchen@ascension.org (mailto:Jackie.Kirchen@ascension.org?subject=Emergency Use- COVID-19).

See the FDA website (https://www.fda.gov/news-events/expanded-access/expanded-access-how-submit-request-forms) for guidance and instruction for how to submit the appropriate IND to the FDA.

IMPORTANT: When completing FDA Form 3926 be sure to select box 10b to “Request Authorization to Use Alternate IRB Review Procedures” so the IRB can expedite the review of the Expanded Access Request.

Once complete, contact the IRB Office immediately to discuss the request and submit the treatment protocol reviewed by the FDA, the consent form (using TEMPLATE CONSENT DOCUMENT - Emergency or Compassionate Device Use to prepare your consent document), the eIND and completed FDA Form 3926.

Expanded Access Program (EAP) for Convalescent Plasma for the Treatment of Patients With COVID-19

Updated 4/17/2020

Ascension Wisconsin is participating in the Expanded Access Program (EAP) to Convalescent Plasma for the Treatment of Patients With COVID-19 through the Mayo Clinic.

Working collaboratively with industry, academic and government partners, Mayo Clinic will serve as the lead institution and IRB for the program registering participating providers and potential patients who may benefit from and qualify for this investigational treatment.

References and Contact Information

- For more information about the EAP program and process, review the Mayo Clinic EAP website (www.uscovidplasma.org (www.uscovidplasma.org)) or contact them at uscovidplasma@mayo.edu. (mailto:uscovidplasma@mayo.edu)
- The Ascension Wisconsin IRB/Regulatory contact is Jackie Kirchen (jackie.kirchen@ascension.org (mailto:jackie.kirchen@ascension.org); 414-915-3229).
- There are Physician leads available to provide guidance and assistance for physicians through Ascension Wisconsin.
    - Southeast Wisconsin- Dr Jonathan Treisman (jonathan.treisman@ascension.org (mailto:jonathan.treisman@ascension.org); 414-427-2360)
    - Fox Valley- Dr Anthony Zeimet (Anthony.Zeimet@ascension.org (mailto:Anthony.Zeimet@ascension.org); 920-730-7603)

Ascension Wisconsin Physicians Instructions to Request Convalescent Plasma

1. Review all of the information on the Mayo Clinic EAP website

The Mayo Clinic website, at: www.uscovidplasma.org, (www.uscovidplasma.org,) is updated frequently and is the one place physicians will need to refer to for information, registration and reporting.The site includes the protocol, eligibility criteria, consent forms, and clear instructions for sites and physicians to request participation, register patients, and record results.

The workflow (https://www.uscovidplasma.org/#workflow) on the EAP website outlines the process, but physicians should be familiar with the eligibility criteria and EAP protocol, which includes a study checklist for participation.

2. Complete the Physician Registration Form

Any physician who wants to request plasma for a patient must complete the PI registration form on the EAP website (https://www.uscovidplasma.org/#physicians). The physician registration form requires selection of a facility. The facility needs to be registered, before a physician can register. Physicians need to register only at one site, even if they are treating patients at multiple facilities.

Ascension Wisconsin has begun to register sites. DO NOT register your facility directly. If your site is not registered, email the Director of Research Integrity and Protection: jackie.kirchen@ascesnion.org (mailto:jackie.kirchen@ascesnion.org)to request the site be registered.

Please note, your site will not be activated until plasma is available. Sites with current plasma supply will be eligible for activation once the Physician/PI Registration and Patient Enrollment Forms are completed.

3. Obtain consent and register the patient

Informed consent must be obtained from the patient or their Legally Authorized Representative/ surrogate. Informed consent documents approved from the Mayo Clinic IRB are available on the EAP website (https://www.uscovidplasma.org/#consent).

Informed consent is available in English (https://www.uscovidplasma.org/pdf/EAP CP English Consent 20.00331200.pdf), Spanish (https://www.uscovidplasma.org/pdf/EAP CP Spanish Consent 20.00331201.pdf), Arabic (https://www.uscovidplasma.org/pdf/EAP CP Arabic Consent 20.00331201.pdf). For other languages, it is acceptable for clinicians to have someone verbally translate the information to the patient, then document that process in the medical record. The consent must be included in the patient medical record per local process.

After obtaining consent, the physician must register the patient on the EAP website (https://www.uscovidplasma.org/#consent).

4. Work with the Mayo Clinic and Ascension Transfusion services to obtain plasma

After the medical facility, patient and physician are registered, the online tool will create a patient identification number to match with plasma. Mayo Clinic will contact you to fill out short regulatory documents for you and your patient.

At Ascension Wisconsin Southeast Region Hospitals Versiti will provide convalescent

plasma as supply permits. Transfusion Services will submit orders to Versiti.

Submit the following to your facility Transfusion Services:

- Place an order for ABO Typing and 1 unit of plasma following normal ordering processes
- Provide the Versiti Request Form (/-/media/Project/SXA---WI/AWRI/Files/Versiti-COVID-plasma/COVID-19-Convalescent-Plasma-Request.pdf?la=en&hash=D8EE3C8034583BB41EC8E0F279F23ABA5B0C65CB) to Transfusion Service
    - .Unit is approximately 200 mL- labeled Convalescent Plasma.
    - Order one unit per patient per Mayo Protocol)

- IND and IRB approval Forms (Obtained from Mayo Clinic)
    - FDA approved eIND or IRB approved blanket IND
    - IRB approval statement

Versiti will coordinate with Ascension Wisconsin's Transfusion Services department to provide plasma. Products will be distributed as requests are received. There may be times when a product is not available. Orders will be filled as soon as possible. Transfusion Services may call to confirm if order is still needed.

Transfusion Services is exploring the ability to obtain plasma from other sources as well. Updates will be provided on this site. If you are requesting plasma at another site, work with your local transfusion services department.

5. Provide Mayo Clinic required follow up data

The treating physician is required by federal regulation to provide updates to the IRB (Mayo Clinic). Reports must be made at the following times, through the EAP website (https://www.uscovidplasma.org/#consent).

- 4-hour report with (1) unit number and (2) patient medical record number. This report must be completed even if the transfusion is not given, including the CoVID-19 Convalescent Donor Pre-Screening (/-/media/Project/SXA---WI/AWRI/Files/Versiti-COVID-plasma/CoVID-19-Convalescent-Donor-Pre-

Screening.pdf?
la=en&hash=0033737F01D68AD9DCC425342D2F39451958FF01) reason why it was not given.

- 7-day report form
- 30-day report form, if patient remains hospitalized.

Other information to be collected retrospectively will include patient demographics, acute care facility resource utilization (such as total length of stay, days in ICU, days intubated and survival to discharge from an acute care facility).

6. Notify the Ascension Wisconsin IRB after each use

Within 30 days of each use, send an email to the Ascension Wisconsin IRB at IRB@ascension.org (mailto:IRB@ascension.org):

1. Treating Physician Name:
2. Facility:
3. Date patient treated:
4. Was consent obtained using the Mayo Clinic consent form, and the form added to the patient's medical record? (Yes/No)
5. Was all required reporting to Mayo Clinic completed as applicable (4 hour, 7 day, 30 day); reports may be attached, but are not required? (Yes/No)
6. Provide a brief description of the use/outcome:

Information for Donors

If you are an Ascension Physician and have a patient that you would like to identify and refer to Versiti Blood Center of Wisconsin, follow these instructions (/-/media/Project/SXA---WI/AWRI/Files/Versiti-COVID-plasma/Versiti-Wisconsin-Donor-Information.pdf?la=en&hash=482DDAE57D359C0845B6D714C7F979550D7EFC93) and referral (/-/media/Project/SXA---WI/AWRI/Files/Versiti-COVID-plasma/COVID-19-Convalescent-Plasma---Identifying-Donors-for-Referral-UPDATE.pdf?la=en&hash=71CE266D32D0E9344121A31FADAA596310F2ED70)and donor pre-screen (/-/media/Project/SXA---WI/AWRI/Files/Versiti-COVID-plasma/CoVID-19-Convalescent-Donor-Pre-Screening.pdf?la=en&hash=0033737F01D68AD9DCC425342D2F39451958FF01) forms.

If you have a patient who tested positive for COVID-19 and has since tested negative, they may be eligible to donate plasma. If they would like to consider donating they can find more information about donation locations and the donation process at Versiti Blood Center of Wisconsin (https://www.versiti.org/covid19plasma) or the American Red Cross (https://www.redcrossblood.org/donate-blood/dlp/plasma-donations-from-recovered-covid-19-patients.html).

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Language Assistance (https://healthcare.ascension.org/Language-Assistance)