Research During COVID-19: Reflections From an Institutional Review Board Office

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The COVID-19 pandemic affected clinicians by placing extreme stress on professions that were already facing personnel shortages, burnout, stress, and mental health challenges.[1] In addition to the well-known impact on the entire health care system, clinical research also was affected dramatically by the pandemic. This commentary focuses on the effect of COVID-19 on human research through the lens of an Institutional Review Board (IRB) office. We will highlight how our institution managed the suspension of research, transition to virtual platforms and activities for research, transition of effort to minimal risk research projects, and virtual consenting options, followed by a summary of the changes that have continued since the emergence of the pandemic.

As COVID-19 spread throughout the world and the United States, representatives from the Medical College of Wisconsin Office of Research, including the Human Research Protection Program (HRPP), which includes the IRB, began developing plans to suspend research. On March 13, 2020, senior leadership from the Office of Research issued guidance assuring stakeholders that they were closely monitoring the spread of COVID-19. They noted that research at our institution is mission critical, seeking to continue clinical research whenever possible while balancing safety and mitigating risk. Leadership advised each clinical research department to review its portfolios and categorize studies into three groups, described below. Phase I, described as a "research slow down," was activated when community-based transmission of COVID-19 was detected in Wisconsin in mid-March. For human research, this meant that all nontherapeutic research – research that provides no or minimal benefit to participants (Group 3) and involves direct contact – was suspended. On March 28, MCW leadership took further steps to mitigate the risks of COVID-19. For human research, in-person activities for all studies that offered only moderate benefit to participants (Group 2) were suspended. Only research involving in-person activities for which ceasing study activities could cause immediate and possibly life-threatening risk to subjects (Group 1) was allowed to continue. By the end of March 2020, the framework described above coincided with MCW's mandatory work-from-home directive to limit face-to-face contact and protect both research participants and personnel from exposure to SARS-CoV-2. Leadership provided an avenue for principal investigators to appeal the suspension of specific studies by petitioning the Clinical Research Appeals Group to review the study and determine if in-person research visits could continue.

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As research was suspended, study teams were encouraged to transition to virtual activities whenever possible, which had the potential to inundate the IRB with amendments and possibly delay the review of pending urgent COVID-19-related research. Regulations that govern the conduct of research contain a provision that allows researchers to implement a planned deviation without prior IRB review

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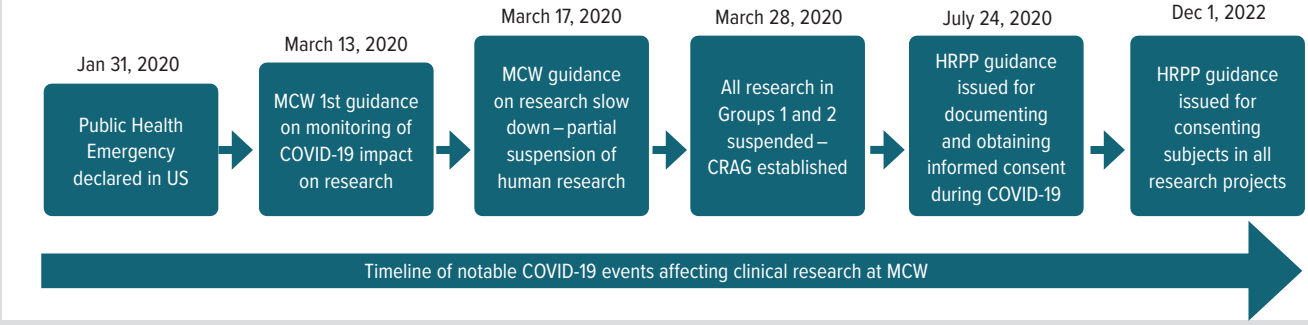
Figure 1. Timeline

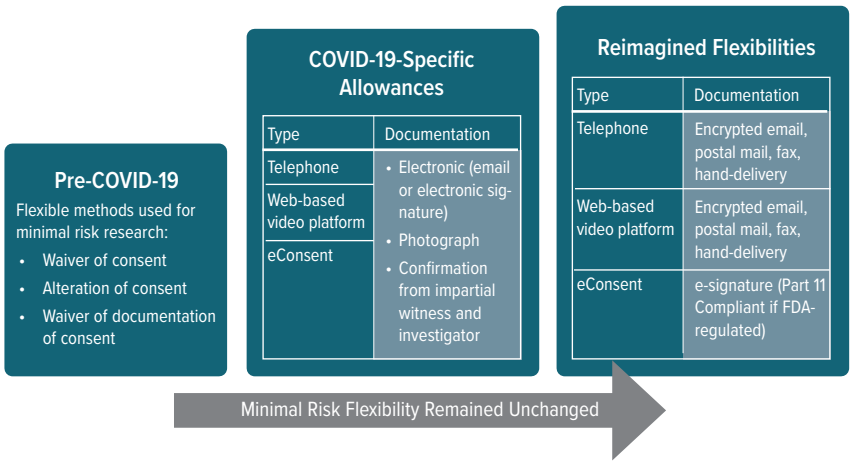


Abbreviations: MCW, Medical College of Wisconsin, CRAG; Clinical Appeals Research Group; HRPP, Human Research Protection Program

when those changes are "necessary to eliminate apparent immediate hazards to the subject."[2] Avoiding exposure to SARS-CoV-2 certainly met that criterion. However, making such changes would still require immediate reporting to the IRB. This, too, could inundate the IRB. When the National Institutes of Health (NIH) Clinical Center deferred all elective admissions and outpatient visits, including research visits, they, too, noted this challenge. The NIH IRB issued guidance that if a change was necessary to assure the safety of the research participant and given the expected volume of reports, only deviations that were "major deviations" needed to be reported immediately.[3] Major deviations are defined as deviations that could negatively impact the rights of research participants or substantively impact the scientific integrity or validity of the study. MCW followed this example and further stated that if the change was expected to be a temporary response to the COVID-19 pandemic and not a permanent change, this could be reported at the time of annual review instead of within 5 days according to institutional policy.

The transition to virtual activities also had implications for obtaining informed consent. Questions about consent were not at the forefront of the minds of researchers nor the MCW IRB committees since most research was suspended and the focus was placed on preventing immediate harm. During this time, the HRPP Office leaned heavily on US Food and Drug Administration (FDA) guidance when drafting its own guidance on how to obtain consent from individuals in quarantine or with suspected or confirmed COVID-19 infection.[4] Flexible methods were encouraged for documenting consent, even for FDA-regulated projects, due to the risk of infection during this early phase.

Figure 2. Evolution of Flexible Consenting Methods



When it became clear that we would be unable to "flatten the curve" and return to some semblance of normal operations in a few weeks, study teams began conducting remote, minimal-risk research. For example, an in-person study related to sickle-cell disease that offered minimal benefit to the participants – and so was suspended – could pivot to surveying their research participants about the impact of the COVID-19 pandemic on their quality of life and sickle-cell disease. For the IRB, this resulted in a massive volume shift from greater than minimal risk research to minimal risk research, which overwhelmed the committee dedicated to reviewing minimal risk research. We believe the ability of our committees to focus and specialize is a strength, but the pandemic prompted us to cross-train IRB staff quickly.

The results were not felt immediately, but we continue the practice of cross-training IRB staff so that they can shift focus as volumes change.

Similarly, another shift occurred in IRB operations to pivot to a remote video platform option for IRB meetings. This solution offered the opportunity to review the usual regulatory submissions (eg, continuing progress reports) without delay. While this shift offered a somewhat easy solution, technical issues encountered by some committee members and a lack of familiarity with social norms of interacting in the virtual space created new barriers to fruitful IRB meeting discussions.

As restrictions began to lift from non-COVID-19-related research, it became clear that consenting methods had changed for most research, whether by choice or necessity. As previously mentioned, the minimal-risk research portfolio grew during this time, and many minimal-risk projects already could employ consent methods not requiring a signature. The stark reality of a changing research enterprise led to a second consent guidance focused on all research rather than only COVID-19. Interestingly, all strategies could have been utilized prepandemic for most research, but as we functioned almost exclusively in-person, resources had not been allocated to pursue alternate strategies. The guidance not only highlighted possible consent methods, but it also detailed institutional requirements relating to embedded HIPAA (Health Insurance Portability and Accountability Act) authorizations for research and discrepancies in documentation resulting from alternate consenting strategies. See Figure 2.

Earlier, it was noted that attention rapidly shifted during the early pandemic toward the reduction of harm to subjects and research staff. During that time, the HRPP recognized that temporary changes were likely being made to research practices, but permanent changes required IRB review. MCW IRB has begun to see an increase in pandemic-related noncompliance being discovered at the time of continuing review and as part of routine reviews by the HRPP Quality Improvement office. One of the most common types of noncompliance is the incorrect application of information within the consent guidance, particularly for FDA-regulated research. Although the HRPP recognizes the hardships experienced throughout the pandemic, the regulations and ethical principles governing human research remain unchanged.

Additional adaptations have emerged from the pandemic experience, including home visits for research procedures and our virtual consent workflow. For some research participants, if a study visit only includes vitals and a physical exam, it is much easier if an in-home health care service visits them instead of traveling to a hospital. What began as a necessity when travel to a hospital was too risky has continued as a welcome convenience for some. We also have retained our guidance and workflow for virtual consent, as this offers convenience for both study teams and potential research participants. While we still seek to create a virtual consent option for FDA-regulated research compliant with the additional requirements for the FDA, this practice continues for non-FDA-regulated research.

Other practices that have continued include remote study monitoring visits, site initiation visits, and IRB meetings. While such visits from study sponsors became virtual at the onset of the pandemic, we have yet to return to in-person visits for this aspect of clinical research. Like many changes made during the pandemic, there are considerable cost savings associated with making these meetings and visits virtual, though the benefits of meeting in person – whether it be relationships established for the work moving forward or the ability to converse face-to-face – are diminished. Time will tell if these visits and meetings will return to in-person.

Overall, clinical research at our institution was able to continue, despite the added stress of COVID-19. Some activities have proven advantageous over previous workflows, including virtual IRB committee meetings, virtual monitoring and site initiation visits, home visits for research procedures, and virtual consenting procedures. While we reimagine the conduct of clinical research post-COVID-19, these activities will likely remain and provide flexible alternatives to research-related work that were underutilized prior to the pandemic.

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REFERENCES

1. Impact of the COVID-19 pandemic on the hospital and outpatient clinician workforce: challenges and policy responses. Office of the Assistant Secretary for Planning and Evaluation, US Department of Health and Human Services; 2022. Issue Brief No. HP-2022-13. Accessed July 6, 2023. https://aspe.hhs.gov/sites/default/files/documents/9cc72124abd9ea25d58a22c7692dccb6/aspe-covid-workforce-report.pdf

2. IRB functions and operations. 45 CFR §46.108(a)(3)(iii). Accessed March 20, 2023. https://www.ecfr.gov/current/title-45/subtitle-A/subchapter-A/part-46/subpart-A/section-46.108

3. Green J. NIH IRB Guidelines for protocol deviations during COVID-19 outbreak. National Institutes of Health, Office of Intramural Research, Office of Human Subjects Research Protection. March 11, 2020. Accessed March 15, 2023. https://irbo.nih.gov/confluence/display/ohsrp/COVID-19-IRB-1

4. Use of Electronic Informed Consent — Questions and Answers; Guidance for Institutional Review Boards, Investigators, and Sponsors. US Department of Health and Human Services, Office for Human Research Protections, Food and Drug Administration; 2016. Updated May 5, 2020. Accessed March 20, 2023. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-electronic-informed-consent-clinical-investigations-questions-and-answers

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