Human Research in the COVID-19 World: Boundaries, Obligations and Guidance

By: Debra A. Weinrich and Emily K. Silverstein
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The spread of the novel coronavirus (COVID-19), and implementation of assorted regulations and guidelines, raise concerns over the impact on clinical testing, data collection for virus tracking and seeking a cure. Institutions and investigators are left to ponder what is and is not within the legal boundaries of ongoing human research and clinical trials. In response to associated questions, the Office of Human Research Protection (OHRP) has provided guidance in the form of recommendations and reminders regarding preexisting requirements pursuant to the Department of Health and Human Services' (HHS) Human Subjects Protection regulations as set forth in 45 CFR 46. The recommendations do not create or confer rights and are not to be considered the only workable options in these unique pandemic circumstances. To the contrary, OHRP acknowledges that in these exceptional times, institutions may use alternative approaches as long as they are consistent with preexisting regulations and it will consider the institution or investigator's specific circumstances, and be flexible, when making decisions as steps are taken to protect public health while simultaneously protecting the research subjects.

Understanding the action's purpose is critical. Institutions and investigators should evaluate the purpose behind the conduct to determine whether the Institutional Review Board (IRB) must approve the actions before implementation. Specifically, "[a]ctions taken for public health or clinical purposes, and not for research purposes, are not research procedures." Therefore, IRB approval is unnecessary. Additionally, some restrictions and notification requirements are eliminated. However, to the extent that there is any ambiguity in purpose, best practices would include informing the IRB.

Public health surveillance activities are excluded from the definition of "research." These activities include "the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority," and are limited to those necessary for the public health authority to monitor, assess and investigate. (45 CFR 46.102(*l*)(2).) Thus, prior IRB approval for incorporation of these activities is unnecessary. Notably, an exception associated with FDA regulations applies if the activity involves the use of an *in vitro* diagnostic device. However, absent that context, general COVID-19 screening for surveillance purposes authorized by a public health authority can be incorporated into pre-existing research studies without prior IRB approval. As discussed above, any concern about notification should prompt the investigator or institution to err on the side of reporting to the IRB

The regulations do not prevent legally required reporting. The HSS' regulations on protecting human subjects, including sharing individually identifiable information, does not prohibit the dissemination of an individual's COVID-19 test results to public health officials where the law requires it. Such mandatory reporting may occur even if this action is inconsistent with research confidentiality documentation. Whether distribution of information is necessary is contingent upon state and federal law. The test subject should be informed of the reporting requirements. For instance, a subject should be informed if they test positive for COVID-19.

Implementing changes to eliminate immediate, apparent hazards is permissible prior to IRB approval. The OHRP expects investigators to be canceling or postponing non-essential in-person study visits and/or to conduct visits via telehealth means. Though prior IRB review is not required, the OHRP recommends that any such changes should still be reported to the IRB, when possible. (45 CFR 46.108(a)(3)(iii) under the 2018 Requirements, and 45 CFR 46.103(b)(4)(iii) under the Pre-2018 Requirements.)

Investigators may submit proposals to make minor or major changes to approved research studies. An IRB may use an expedited review procedure if such changes are minor. (45 CFR 46.110(b)(1)(ii) under the 2018 Requirements and 45 CFR 46.110(b)(2) under the Pre-2018 Requirements.)

OHRP must be notified where an IRB suspends or terminates approved research. However, an investigator or institution's decision to suspend or terminate an approved research project need not be reported to the OHRP consistent with 45 CFR 46.113.

Implementing The OHRP's Guidance

Naturally, an investigator and institution's goal is to attempt to continue to conduct medical research to meet funding and study deadlines, as well as make strides in providing the most evolved healthcare available. However, the welfare of study participants and public health and safety are of paramount importance and must be prioritized. Many institutions have already suspended in-person interactions with test subjects until the "stay-at-home" orders for their respective locations are lifted. However, that is not an absolute requirement. Consistent with previously released guidance from the FDA concerning medical products research, IRBs need to consider the specific risks and benefits associated with canceling or postponing research activities and interactions. For example, boards need to evaluate whether a subject's safety or wellbeing would be at an increased risk or would be deprived of a potential direct benefit absent timely interactions. *Id.* When implementing these exceptions, institutions and investigators should consider the ease of which personal protective equipment or medication is accessible, the manner in which medication or samples should be provided (maybe mailing would be the best option) and whether the research location does not increase the likelihood of exposure to COVID-19 (again, use of telehealth is encouraged). *Id.* Research procedures for non-essential trials that can be conducted remotely should also continue. The above applies to current COVID-19 research.

In ensuring participant health and safety during this global pandemic, institutions or investigators should consider contacting their respective IRBs for extensions. Financial concerns for current research may also arise. Institutions or investigators should examine whether their IRB may extend budgets, or to what extent unanticipated costs as a result of COVID-19 can be re-budgeted. Institutions and investigators should also look to their sponsors for additional issues regarding funding.

The above OHRP and earlier FDA guidance suggests that investigators and institutions should work in tandem, where necessary, with their respective IRBs to protect the health and safety of human subjects, but also allow critical research and clinical trials to continue, even in a slightly unorthodox manner. OHRP specifically invites questions about how the requirements of 45 CFR 46 apply to actions being taken or planned in response to the continuing and changing circumstances presented by COVID-19.

If you have questions or would like further information, please contact Debra A. Weinrich (weinrichd@whiteandwilliams.com; 215.864.6260), Emily K. Silverstein (silversteine@whiteandwilliams.com; 302.467.4527) or another member of our Healthcare Group.

As we continue to monitor the novel coronavirus (COVID-19), White and Williams lawyers are working collaboratively to stay current on developments and counsel clients through the various legal and business issues that may arise across a variety of sectors. Read all of the updates here.