IRB Reference:
Existing Regulatory Pathways and Processes Relevant to COVID-19

As institutional review boards (IRBs) continue to adapt to the new challenges associated with managing human research protection programs (HRPP) during the COVID-19 pandemic, IRB leadership should ensure that their administrators and reviewers are familiar with several categories of research that are infrequently seen at many institutions but may become more applicable during the coming months as the pandemic is managed.

Public Health Surveillance Activities

The revised Common Rule included additional carve-outs to the Department of Health and Human Services (HHS) definition of "research," one of which excluded certain public health surveillance activities. Specifically, the following activities are not considered research as defined by HHS:

- *Public health surveillance activities conducted by a public health authority, limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance.*
    - *Including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority.*
    - *Including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products.*
    - *Including those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).*

HRPP leaders are advised to remind IRB administrators and staff to be aware of these carve-outs in the event that your offices receive any questions or submissions involving applicable COVID-19 public health surveillance activities. And if you have not yet incorporated these carve-outs into your current policies and procedures, please do so.

Emergency Use of a Test Article[1]

Biomedical research institutions may experience an increase in requests from physicians/investigators for the use of an investigational drug or biological product with a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval (i.e., emergency use).

Biomedical IRBs that have limited prior experience with emergency use situations may need to refresh their understanding of applying these procedures. The Food and Drug Administration's (FDA) "Emergency Use of an Investigational Drug or Biologic" guidance provides additional information.

Whenever possible, physicians should notify the IRB of a proposed emergency use of a drug, biologic or device in a life-threatening situation in advance of the use. But when there is insufficient time to notify the IRB in advance of the use, FDA regulations do permit emergency uses to be reported to the IRB within five working days after the use.

[1] Please note that emergency investigational new drugs (INDs) and protocols are a subset of individual patient access.

Expanded Access

FDA regulations include pathways to allow access to investigational drugs and biologics outside of standard clinical trials. The expanded access pathways are available for serious or life-threatening diseases where there are no comparable or satisfactory alternatives, and where potential patient benefit from the investigational drug or biologic justifies the potential risks. Expanded access pathways are available for single patients, intermediate-sized patient groups, and broader access (treatment IND). FDA guidance on "Expanded Access to Investigational Drugs for Treatment Use" provides further clarification on the considerations associated with expanded access.

Single Patient Expanded Access

There is a unique IRB review pathway associated with some single patient expanded access requests. As described in the FDA's guidance on "Individual Patient Expanded Access Applications: Form FDA 3926," a physician submitting an individual patient expanded access IND may request authorization to obtain concurrence by the IRB chairperson or by a designated IRB member before the treatment use begins, in lieu of obtaining IRB review and approval at a convened IRB meeting.

Per Huron correspondence with the FDA, "concurrence" by the IRB chairperson (or designated IRB member) involves considering the same information that the full IRB would consider to determine whether to approve the treatment when reviewing and concurring for individual patient expanded access use.

Until recently, the investigational drug remdesivir had been available for use in COVID-19 patients under single patient expanded access. However, the manufacturer (Gilead Sciences) has announced that the drug will no longer be available under the single patient expanded access pathway except for pregnant women and children less than 18 years of age with confirmed COVID-19 and severe manifestations of disease.

Expanded Access (i.e., Treatment IND or Protocol)

It appears likely that drug manufacturers seeking to make investigational drugs intended for use in COVID-19 treatment will seek to use expanded access pathways on a larger scale than single patient expanded access pathways allow. This pathway is intended to accelerate access to specific medical products and to enable the collection of data from all participating patients.

Gilead now has a remdesivir expanded access protocol in place; please refer to the following for additional information:

- https://www.gilead.com/purpose/advancing-global-health/covid-19/emergency-access-to-remdesivir-outside-of-clinical-trials
- https://clinicaltrials.gov/ct2/show/NCT04323761

IRB administrators and reviewers should be reminded that standard IRB submission and review processes should be followed in cases of treatment INDs; the option for IRB chairperson concurrence in lieu of IRB review is not an option for this pathway.

Planned Emergency Research

Another possible regulatory pathway with potential future relevance to the COVID-19 pandemic is associated with "planned emergency research" for which exceptions to informed consent processes may be granted. This pathway is described in FDA regulations, Office for Human Research (OHRP) guidance and FDA guidance.

This pathway allows a waiver of the applicability of the regulatory requirements for obtaining and documenting informed consent for a strictly limited class of research, involving research activities that may be carried out in human subjects who are in need of emergency therapy and for whom, because of

the subjects' medical condition and the unavailability of legally authorized representatives of the subjects, no legally effective informed consent can be obtained.

Given the length of time typically required to address the public disclosure and community consultation requirements associated with this particular class of research, it is unlikely that IRBs will be called upon to review such research in the immediate future, but IRBs should remain aware of this category and the additional review responsibilities associated with this research, should such activities emerge in the future.

Emergency Use Authorizations

The emergency use authorization (EUA) authority, under section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act), allows for unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by chemical, biological, radiological or nuclear (CBRN) threat agents when there are no adequate, approved and available alternatives.

The FDA's EUA authority is separate and distinct from the use of a medical product under an investigational application (i.e., investigational new drug application (IND) or investigational device exemption (IDE)), section 561 expanded access authorities, and section 564A emergency use authorities][2]. Therefore, once the FDA issues an EUA, then subsequent use of the drug or device in the clinical setting is not considered research and subject to IND/IDE requirements, and is not subject to IRB review.

There have been many EUAs issued during the COVID-19 pandemic. One example of a therapeutic EUA that was issued permits the emergency use of hydroxychloroquine sulfate and chloroquine sulfate supplied from the Strategic National Stockpile to treat adults and adolescents "who weigh 50 kg or more and are hospitalized with COVID-19, for whom a clinical trial is not available, or participation is not feasible."[3]

IRBs may be asked questions about whether IRB review is required for COVID-19-specific diagnostic tests, other medical devices or therapeutics. One important question for IRBs to ask is whether the item or treatment in question has been issued an EUA or is applying for an EUA.

[2] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities
[3] https://www.fda.gov/media/136534/download