

For every application it reviews, whether during a convened board meeting or by expedited review, the IRB must make certain regulatory determinations. Determinations reached during convened board meetings are recorded in the meeting minutes, accompanied by citations from the Code of Federal Regulations, or CFR.

In approving an application, the IRB must determine

- that the study complies with all applicable federal regulations for human subject protections
- that the study identifies—and takes adequate measures to protect—any vulnerable subject populations
- that the study’s risk/benefit assessment is accurate
- as well as other determinations as they apply, such as
  - whether to grant any waivers of informed consent, assent, or HIPAA Authorization
  - whether a study-specific adverse event reporting plan is acceptable
  - whether an investigational medical device poses significant or nonsignificant risk
  - or whether a problem reported as an adverse event or ORIO meets the criteria for an unanticipated problem involving risk to subjects or others

With most submission types—including new study applications, amendments, scheduled continuations, and adverse events or ORIOs—the IRB must first of all determine that the research complies with applicable federal regulations governing the protection of human subjects. In most cases, this includes Department of Health and Human Services regulations, at 45 CFR 46.111; depending on the study at hand, Food and Drug Administration regulations, at 21 CFR 56.111, may also apply. Other federal agencies—such as the Department of Defense and the Department of Justice—have also published regulations in the CFR; studies sponsored by these agencies must comply with their respective regulations, as well. If a study involves the access, use, or disclosure of subjects’ protected health information, the IRB must also determine that the research complies with the Office for Civil Rights’ HIPAA Privacy Rule, at 45 CFR 160 and 164.

As part of its eResearch application, the study team identifies all vulnerable subject populations that it plans to enroll. This includes vulnerable populations as defined in federal regulations—women of child-bearing potential; pregnant women, fetuses, and neonates; prisoners; and children—as well as additional special populations recognized by the University of Michigan—such as patients of the study team, educationally or economically disadvantaged persons, cognitively impaired adults, and others. The IRB must determine whether the study team’s listing of vulnerable subjects is appropriate and, if not, which categories of subjects to add to or remove from the list. If minor subjects are involved in the research, the IRB must determine, based on the risk level and benefit type, whether parental permission documents need to contain one or two parents’ signatures.

The study team assesses its own study’s risk level and benefit type during the application process. The

# U-MIC TRANSCRIPT

## IRB Regulatory Determinations

IRB must make a determination either to confirm the study team's own risk/benefit assessment or, if it disagrees, to raise or lower the risk level or to change the benefit type.

With new study applications—and sometimes with amendments—the study team may request one or more waivers. Typical waivers include

- waivers of informed consent
- waivers of documentation of informed consent
- waivers of assent
- and waivers of HIPAA Authorization

A waiver may cover all study activity or may apply only to a portion of the study or only to certain subjects. In considering whether to grant a waiver, the IRB must verify that the research meets the federal criteria for the waiver, as defined by HHS, FDA, or—in the case of a HIPAA Authorization waiver—the Office for Civil Rights.

If an application includes a study-specific adverse event reporting plan, the IRB must determine whether the plan is acceptable.

If a study involves use of an investigational medical device, and FDA hasn't determined whether the device poses significant and or nonsignificant risk, the IRB must review the sponsor's own risk determination and decide whether it agrees. If it disagrees, it must modify the determination and instruct the sponsor to notify FDA of the IRB's determination. A past U-MIC presentation provides more detail about significant and nonsignificant risk devices.

It may also be necessary for the IRB to assess some adverse events and ORIOs, to determine whether they represent *unanticipated problems involving risk to subjects or others*, commonly referred to as UPIRSOs or UaPs. For an adverse event to constitute an unanticipated problem, it must be unexpected, must be either related or possibly related to the research, and must suggest that the study presents greater risk than previously recognized.

Contact the IRB for more information about IRB regulatory determinations.

*Posted:* DATE

*Revised:* DATE