Altered IRB Requirements for certain Low-Risk Research and other changes
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Introduction

In a significant policy change, starting now, the Human Research Protection Program (HRPP) has altered some requirements for low-risk human research. In the spirit of the changes in the federal regulations that were proposed last year, but that have not yet been finalized, the HRPP has reduced some regulatory burdens for minimal risk research. We are calling this “equivalent protections” since the requirements that were altered did not meaningfully add to the protection of human subjects. Because the federal regulations have not yet changed, as of now, the equivalent protections can only apply to research that does not have to follow the federal regulations.

There is an additional notable change that affects how to apply for IRB approval: investigators may reference page numbers in an attached separate protocol instead of cutting and pasting into some of the questions in the INSPIR application. This is to get ready for a requirement that will go into effect on August 1, 2016: all new submissions for clinical trials of drugs or devices must have a separate protocol.

EQUIVALENT PROTECTIONS

Which research is eligible for equivalent protections?

The HRPP is able to use the flexibility to adopt equivalent protections because in the Federalwide Assurances (the certifications required to be filed with the federal government), we have chosen not to state that we apply the federal regulations to all research reviewed by the IRB – to use jargon, we have “unchecked the box.” Therefore, as a starting point, to be eligible for equivalent protections, the research must:

- Not be supported by any federal funds (even a training grant)
- Not be a clinical investigation of a drug, device, or other product regulated by the Food and Drug Administration
- Not be required by the sponsor or funder to follow the federal regulations
- Not use any clinical services (because the services may be billed to a federal program)
- Have been initially approved after February 14, 2011, the date we “unchecked the
Specific additional criteria apply for each of the seven equivalent protections below.

Equivalent Protection #1 – extended approval period for minimal risk research

Most minimal risk research will now be approved for a three-year period instead of a one-year period. The reason is that the annual renewal for such research is not the best use of investigator or IRB resources. At the one- and two-year anniversaries of initial approval, notices will be sent reminding investigators of their obligations to report problems to the IRB, to submit for approval of research changes, to ensure investigators have up-to-date training, and to close the study when human subjects research activities have been completed.

Projects will generally be given a three-year approval period if they do not have to follow the federal regulations and:

- Are approved by the expedited process, including the new expedited categories in Equivalent Protection #3;
- Are approved by the full board when the board determines that the study is no greater than minimal risk; or
- Have reached a stage in the research where the study is closed to enrollment, interventions are complete, and the research remains active only for the long-term follow-up of subjects and/or analysis of identifiable data

What about already-approved research? If your study fits into one of these categories, the policy is not retroactive, so you still must submit the progress report six weeks prior to the current expiration date. However, your next expiration date will likely be in 2019.

What about new submissions? Investigators do not have to do anything differently; the IRB will set the expiration date based on the new policy for qualifying research.

Equivalent Protections #2 – new exempt categories

Research that is eligible for equivalent protections may be given an exempt determination (instead of expedited approval) if the research is no greater than minimal risk (including risks to privacy and confidentiality) and all research procedures fall into one of the following additional exempt categories (the numbering starts at 7 because there are 6 existing federal exempt categories):

7. Research with adults (who are able to consent for themselves) investigating individual or group characteristics or behavior. This includes most socio-behavioral research, including research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior; and including research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.
8. Research with children (with child assent and parental permission) involving surveys, interviews, and/or observation of public behavior where the investigator participates in the activities being observed.
9. Research involving identifiable data or specimens that have been or will be collected for non-research purposes.
10. Research involving data or specimens that have been collected for research purposes when the consent for the research does not preclude such additional research.
Such research can be approved by the expedited procedure under federal regulations, but making it exempt means that a shorter consent process can be used (for 7. and 8.) or the investigator does not have to justify the waiver of consent (for 9. and 10.). An exempt determination also means that changes in the research that do not affect the exempt determination can be implemented without prior IRB approval.

What about already-approved research? If you have a study that has already been approved that might qualify, you do have the option of submitting an amendment to ask for an exempt determination, but this is probably not worthwhile unless a shorter consent form would make a big difference going forward or if you are required to submit an amendment because you need approval for some changes to the study.

What about new submissions? Investigators who think their initial submissions qualify for exempt categories 7 and 8 can submit an exempt consent statement rather than a full consent form. Investigators who think their initial submissions qualify for exempt categories 9 and 10 will not have to justify a request for a waiver of consent.

Equivalent Protections #3 – new expedited categories

The federal regulations require some research with medical procedures to be reviewed by the full board rather than the expedited process, even though the procedures are minimal risk. Research that does not have to follow the federal regulations can be reviewed by the expedited process if it includes the following minimal risk medical procedures:

1. Collection of blood not exceeding 550 ml (or the lesser of 50 ml or 3 ml/kg in adults weighing less than 110 pounds or children) in an 8 week period
   a. via an indwelling catheter (federal regulations usually do not allow research collecting blood with an indwelling catheter to be expedited)
   b. more than 2 times per week (federal regulations do not allow research with blood collection more than 2 times per week to be expedited, even if it meets the 8-week totals above)

2. Collection of tissues using minimally invasive procedures (federal regulations only allow research using non-invasive procedures to be expedited). Examples are:
   a. Skin punch biopsies not requiring sutures (except facial or genital biopsies)
   b. Collection of additional tissues during procedures already performed for non-research purposes, such as additional biopsies during gastro-intestinal endoscopy, additional cerebrospinal fluid during lumbar puncture, or additional bone marrow during aspiration, without undue prolongation of anesthesia, sedation, or operating room time.

3. A single exposure of adults to ionizing radiation with an effective dose not exceeding 0.1 mSv (the dose from a typical chest x-ray, equivalent to 10 days of natural background radiation). Federal regulations do not allow any research involving ionizing radiation to be expedited.

What about already-approved research? You do not need to take any action, because when the full board initially approved such research, all future submissions were likely directed to be reviewed by the expedited process.

What about new submissions? No action is needed; the IRB will determine whether the new categories can apply.
Equivalent Protections #4 – Children

This applies to a specific category of child research where the federal regulations require that the IRB mandate permission be obtained from both parents: where the research is a minor increase over minimal risk, the child is not likely to receive a personal benefit from participating, and the research is nonetheless approvable because it is expected to yield important new knowledge. For research that does not have to follow the federal regulations, the IRB now has the flexibility to determine for a particular research project that approval of only one parent is sufficient for research in this category.

What about already-approved research? If your research requires permission from two parents and you are finding this burdensome, you may submit an amendment requesting that the IRB consider whether the research qualifies for this flexibility.

What about new submissions? If your project would require permission from two parents under the federal regulations and you can justify why permission of one parent would be sufficient, indicate this in your submission.

Equivalent Protections #5 – Prisoners

Federal regulations and guidance mandate that if an already-enrolled subject becomes incarcerated, all research interventions and interactions (except those required for the wellbeing of the subject) must cease until the IRB has made the prisoner determinations. Since the prisoner determinations primarily address preventing coercion or undue influence at the time of consent, they do not provide additional protections for subjects who have already been enrolled.

For research that does not have to follow the federal regulations, if an already-enrolled subject becomes incarcerated, the subject’s continued participation is handled by the investigator under his or her overall responsibility to protect the rights and welfare of subjects, and no submission to the IRB is required.

What about already-approved research? Effective now, if your research does not have to follow the federal regulations, you no longer have to submit to the IRB if an enrolled subject becomes incarcerated. The first time this happens, you may want to consult with the IRB to verify that there isn’t any requirement for your research to follow the federal regulations.

What about new submissions? You do not need to do anything differently. The exception is if you have been in the habit of routinely checking off prisoners in the INSPIR application as a vulnerable population on the chance that one of your enrolled subjects would become incarcerated. If so, you only need to do this if your research has to follow the federal regulations.

Equivalent Protections #6 – Pregnant women

There are two changes here: one that only affects the internal record keeping of the IRB, and the other that affects research designed solely to benefit the fetus of a pregnant woman.
The change for IRB record keeping consists of no longer requiring the IRB to make certain findings for minimal risk research on pregnant women (for research without funding from the Department of Health and Human Services). These federally-required findings are geared towards the protections that are needed when research is greater than minimal risk to pregnant women and/or their fetuses, so having the IRB document these findings for minimal risk research does not add to subject protections.

The change for research designed solely to benefit the fetus of a pregnant women is allowing the IRB to permit such research without mandating the consent of the father, when justified by the investigator and when the funder of the research does not apply the protections in Subpart B of the Common Rule.

What about already-approved research? If your research requires the consent of the father of the fetus, and is not federally funded, then you may submit an amendment with a justification for no longer requiring paternal consent.

What about new submissions? If your research involves fetal research where the procedures hold out the prospect of direct benefit to the fetus only, and is not federally funded, then you may include in the submission a justification for not requiring paternal consent.

Equivalent Protections #7 – Consent for screening

Similar to the first change in Equivalent Protections #6, this change only affects internal IRB record keeping. The IRB policy has been, and will continue to be, that a brief consenting process is required when screening involves obtaining information from prospective subjects. Under federal regulations, the IRB must make findings that a full signed consent form is not needed for such screening. The change is that going forward, the IRB will only have to make such formal findings for research that has to follow the federal regulations.

What about already-approved research? No change.

What about new submissions? No change.

INSPIR SUBMISSIONS WITH A SEPARATE PROTOCOL

A protocol is a document with a detailed description of what will happen to subjects in a study. In industry-sponsored research, the sponsor will provide a protocol. (Note that a grant application is NOT a protocol, see CR TIMES article April 2016).

If you have a separate protocol document, then when you complete the INSPIR application, you may list the pages where information is found instead of copying text into some or all parts of the following sections:

- Purpose
- Subjects
- Design/Procedures
- Data Safety and Monitoring
- Screening Procedures
- Confidentiality
Starting on August 1, 2016, initial submissions for drug and device clinical trials MUST have a separate protocol. Templates will be posted that you can use to write the protocol if you do not have one from the sponsor. The INSPIR application will be modified so redundant parts of the above sections may be skipped completely when there is a separate protocol.

OTHER CHANGES EFFECTIVE NOW

1. When an amendment is approved with a new or revised consent form, the approval letter will state whether already-enrolled subjects must be re-consented.

2. For research with adults who cannot consent for themselves (require a Legally Authorized Representative), the IRB can approve research that is a minor increase over minimal risk – even if the subjects are not expected to benefit – if the research is important to understanding the condition of this population.

3. The deadline for reporting Unanticipated Problems indicating new risks to subjects or others remains at 2 days if the Unanticipated Problem involved a fatal or life-threatening event; but the deadline has been increased to 7 days (5 business days) otherwise. The deadline for reporting major protocol deviations remains at 7 days (5 business days).

4. When you submit a translated consent form, you no longer are required to obtain the attestation of its accuracy from a second translator. Instead, the Principal Investigator lists the qualifications of the translator and acknowledges his or her responsibility for the accuracy of the translation.

5. Specified policies have been added for how the IRB will review planned protocol exceptions (single subject protocol modifications) and how the HRPP will be evaluated and improved.

Summary

The major change in the HRPP policies this month is decreased requirements for minimal risk research if it does not have to follow the federal regulations. An additional significant change is that certain information in INSPIR can be indicated by specifying page numbers in a separate protocol, to get ready for a requirement effective August 1, 2016 that all drug and device clinical trials must have a separate protocol.