**WORKSHEET: Primary Reviewer, Follow-on Submissions (Continuing Review/Modification)**

**INSTRUCTIONS:**

1. **Purpose:** This worksheet is for use by the Designated Reviewer (expedited reviews) and the Primary and Secondary Reviewer (convened IRB reviews) when preparing for the review of continuing review and/or modification applications for a study and for non-UW sites that are reviewed by the UW IRB per a reliance agreement. The Primary and Secondary Reviewers use this worksheet, together with the Pre-review Note prepared by HSD Staff, to review the application, identify and write down issues for discussion by the IRB. The Pre-review Note can be found in the Reviews tab of the ZIPLINE application. Filling out this form is not a requirement, but reviewers may wish to take notes on it to use as a guide during the IRB meeting.
2. **Review strategy:**
3. **Start with the assumption that the research, as previously approved, met all applicable criteria for approval.** Evaluate if the research continues to meet criteria for IRB approval by focusing on the considerations outlined in the table below.
4. Ask for additional information or clarification only when there is a regulatory or policy basis for the question.
5. Calibrate the level of review to the level of risk. Lower risk research does not require the same level of protections to meet the criteria for approval.
6. Do not impose changes or restrictions on the research if it qualifies for approval without the changes or restrictions.
7. Embrace flexibility in study design when the flexibility is allowable under the criteria for approval.
8. Be sure you understand the study design before requesting changes or placing restrictions.
9. Assess each application independent of other reviews.
10. HSD uses the acronym **P.A.U.S.E** as a framework to interrupt self- identified bias while reviewing applications. Don’t forget to- **P**: Pay attention to your reactions **A**: Acknowledge your assumptions **U**: Understand your perspective **S**: Seek different perspectives **E**: Examine your options and make a decision.
11. **Presentation to the convened committee:**
	1. Provide a short descriptive summary of the research, progress report and/or proposed changes.
	2. Present issues identified in your review to the other IRB members. Discuss one criterion of approval at a time and try to come to a resolution before moving on to the next.
	3. Discuss issues identified in the Pre-review Note. When possible, avoid re-stating the issue and indicate agreement or disagreement.
	4. Make a motion by proposing an IRB action, research risk level, and, for continuing reviews, an approval period.

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| **1. Study Information** |
| **Study Number:** |  | **Principal Investigator:** |  |
| **Study Title:** |  |
| **2. Modifications** |
| **Yes** | **No** | **Are there any changes to the research?** Consider whether the modified research continues to meet the criteria for approval. Consult the Pre-Review Note to see if the changes to the research alter prior determinations or call for new determinations (e.g., additional regulatory requirements for the inclusion of protected populations, or use of electronic signatures for consent). For modifications that involve substantial changes to the research, such as the addition of a new treatment arm or a new phase of the research, use the WORKSHEET Primary Reviewer, Initial Applications for reference as well. Consider whether the proposed modification warrants re-assessment of the requirement for, or frequency of continuing review.  |
|  |  | **If Yes,**identify thecriteria and determinations relevant to the changes and decide if there is a need for any additional information or any revisions to the research for the IRB to determine that criteria for approval are met. |
| **Discussion items:**  |
| **3. Risk Assessment and Monitoring** |
| **Yes** | **No** | **Is there any new risk information?**  For continuing reviews, consider any relevant information received since the last IRB review from the investigator, monitoring entities (e.g., the research sponsor, a coordinating or statistical center, an independent medical monitor, a DSMB etc.). Unanticipated problems are usually pertinent. For modifications, consider any new information in the submission or any related Report of New Information (RNI). |
|  |  | **If Yes,** decide how this information would affect the IRB’s previous conclusion that (1) risks to subjects are minimized, (2) the risks to subjects are reasonable in relation to anticipated benefits, if any, and the knowledge that may reasonably be expected to result, (3) data and safety monitoring are adequate, and (4) the assessment of the overall risk level (e.g., minimal risk versus more than minimal risk). |
| **Discussion items:**   |
| **4. Adequacy of Informed Consent Process** |
| **Yes** | **No** | **Do the informed consent document(s) and process require changes?** Consider whether the informed consent document(s) (including the Key Information section if there is one) and process still provide an accurate and up-to-date description of the reasonably foreseeable risks ([GUIDANCE Consent](https://www.washington.edu/research/hsd/guidance/consent/#r)) and discomforts of the research as well as appropriate alternative procedures or treatment. Assess whether any significant new information needs to be communicated to already enrolled participants and whether there is a need to re-consent participants. |
|  |  | **If Yes,** decide how this would affect the IRB’s previous conclusion that legally effective informed consent was being obtained or that the research met criteria for a waiver of the informed consent requirement. Assess whether there are adequate safeguards in place for vulnerable and protected populations. |
| **Discussion items:**  |
| **5. Adequacy of Privacy and Confidentiality Measures** |
| **Yes** | **No** | **Do the privacy and confidentiality measures require changes?** Consider any new information related to the sensitivity of information collected, methods of data collection, sharing of data, recruitment and consent procedures. Pay particular attention to problems involving breach of confidentiality. |
|  |  | **If Yes,** decide how this would affect the IRB’s previous conclusion that the research includes adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data, when appropriate. |
| **Discussion items:**  |
| **6. Investigator and Institutional Issues** |
| **Yes** | **No** | **Are there any new investigator and/or institutional issues?** Consider investigator and institutional issues that impact the research with regard to the criteria for approval, such as:* Changes in the investigator’s situation or qualifications (e.g., has left UW and is no longer managing the study)
* Evaluation, investigation, and resolution of complaints related to the conduct of the research
* Changes in resources (e.g., personnel, financial support, adequacy of facilities)
* Reports from any third party observations carried out (e.g. auditors)
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|  |  | **If Yes,**decide how this information would affect the IRB’s previous conclusion that (1) risks to subjects are minimized, (2) the risks to subjects are reasonable in relation to anticipated benefits, if any, and the knowledge that may reasonably be expected to result, (3) legally effective consent will be obtained, (4) privacy and confidentiality are adequately protected. |
| **Discussion items:**  |
| **7. Research Progress** |
| **Yes** | **No** | **Are there any concerns about the progress of the research?** Consider concerns raised by the DSMB about the enrollment rate. A marked difference between the actual and expected rates of enrollment may indicate a problem, such as the inability of a clinical study to achieve its objectives. For continuing review applications, consider whether the information provided in the status report is consistent with the research plan previously approved by the IRB. Review the number of subjects withdrawn and reasons for withdrawal for any indication of problems in the research. Evaluate the information provided about number of subjects enrolled.  |
|  |  | **If Yes,** decide how this information would affect the IRB’s previous conclusion that (1) risks to subjects are minimized, (2) the risks to subjects are reasonable in relation to anticipated benefits, if any, and the knowledge that may reasonably be expected to result, and (3) data and safety monitoring are adequate. For example, research risks may no longer be reasonable when interim results suggest that the research is unlikely to achieve statistical significance. |
| **Discussion items:**  |
| **8. New Information** |
| **Yes** | **No** | **Is there any new published or unpublished information that would:*** **Alter prior determinations (especially with respect to risks and benefits);**
* **Necessitate revisions to procedures, consent, or monitoring; or,**
* **Potentially affect a person’s willingness to continue to participate in the research?**
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|  |  | **If Yes,**decide how this information would affect the IRB’s previous conclusion that criteria for approval were met. |
| **Discussion items:**  |
| **9. Need for Verification** |
| **Yes** | **No** | **Is there a need to require verification of information from sources other than the investigator, to ensure that no material changes have occurred since previous IRB review?** **Factors the IRB considers include:*** **The complexity of the project;**
* **The types and magnitude of risks to subjects;**
* **Concerns about study resources or investigator oversight;**
* **Investigator history of noncompliance;**
* **Concerns about possible changes occurring without IRB approval, based on information received by the IRB.**
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|  |  | **If Yes,** decide what information needs to be verified and the method for obtaining verification. If there is a need for post-approval monitoring, auditing, or observation, please consult with HSD Leadership to determine an appropriate and feasible way to conduct such activities. Examples of verification may include:* An audit by the HSD Post-Approval Monitor.
* Obtaining copies of communications between the FDA and the sponsor (IND/IDE holder).
* Copies of communications from monitoring groups (e.g., DSMB; contract research organization).
* Information from other UW compliance offices.
* Communications with IRBs at collaborating sites.
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| **Discussion items:**  |
| **10. Observation of Consent or Research** |
| **Yes** | **No** | **Is there a need for the IRB or a third party to observe the consent process or research?** |
|  |  | **If Yes,**please work with HSD Leadership and the HSD Post Approval Monitor to identify specific concerns and the most appropriate way to address those concerns (e.g., post approval monitoring visit; sponsor monitoring observations, etc.). |
| **Discussion items:**  |
| **11. Motion** |
|  | **11.1 IRB Action**. Choose one: |
|  | **Approval:** The item is approved. The activity may be conducted within the constraints (if any) previously established by the IRB. All of the applicable criteria for IRB approval are met (or continue to be met) without any changes, requests for confirmation or additional information, or conditions that must first be fulfilled. |
|  | **Modifications required to secure approval (MRSA):** The IRB has determined that the applicable criteria for IRB approval have been met, based on the assumption that specific conditions will be met by the investigator and subsequently verified. **Note:** *when a continuing review application is conditionally approved, the IRB must specify whether enrollment can continue before conditions are met.* |
|  | **Deferral:** The IRB is unable to approve the research because the applicable criteria for IRB approval have not been met (or are no longer met). The IRB defers the item for further review at a future date after modifications and/or additional information have been provided by the investigator. |
|  | **Disapproval**: The criteria for IRB approval are not met, and the IRB is not willing to re-consider the item because the IRB believes that it is very unlikely that: (1) The applicable criteria for approval will be met even with substantial modifications and/or additional information; or (2) it is not possible to obtain (or the investigator is unwilling to provide) the substantial modifications or additional information that would be necessary to meet the applicable criteria for approval.**Note:***This action cannot be taken as part of the expedited review process. If the designated reviewer is concerned that the criteria for approval will not be met, the item in question must be taken to the full board for review.* |
|  | **11.2 Risk level.** Choose one: |
|  | [**Minimal risk**](https://www.washington.edu/research/glossary/minimal-risk/)**:**The probability and magnitude of harm or discomfort anticipated in the research ARE NOT greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.  |
|  | **More than minimal risk:**Does not meet the above definition of minimal risk.   |
|  | **11.3 Approval period.**  Choose one *(for Continuing Review or modifications that trigger the need for continuing review)*: |
|  | Requirements for future continuing review will vary depending on whether a study has federal support as well as IRB consideration of: the nature, magnitude, and probability of the risks; subject vulnerabilities; adverse events; complaints or compliance issues; the investigator’s experience; and other factors. If a modification to the study triggers the need for continuing review under the RCR, the approval period should begin the date the modification is approved by the IRB and should be ≤1 year in duration.Primary and Secondary Reviewers should refer to the **Pre-review Note** for information about continuing review regulatory requirements for a particular study. Designated Reviewers and HSD staff should refer to the table belowfor guidelines about continuing review requirements.  |
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| **Regulatory requirements for, and frequency of, continuing review** |
| **Regulatory Authority** | **Continuing Review Required** | **Frequency** |
| Revised Common Rule - RCR (2018 Requirements) | YES, if:* review by the convened IRB is required
* eligible for expedited categories 8b or 9
* the research includes prisoner populations
* the IRB or designated reviewer requires it and documents the reason, even if it meets the regulatory criteria for not requiring continuing review

NO\*\*, if:* eligible for expedited categories 1-7, 8a, or 8c
* remaining activities are limited to data/specimen analysis and/or follow-up of clinical care data
* approved under Limited IRB Review
 | ≤ 1 year\*n/a |
| Original Common Rule – OCR (pre-2018 Requirements)Food and Drug Administration (FDA)Department of Justice (DoJ) | YES | ≤ 1 year\* |
| OCR + Flexibility Policy\*\*\* | YES | ≤ 3 years |

 \* One year is the default for studies that must undergo continuing review but the IRB can grant approval periods of less than one year  if warranted by: the nature, magnitude, or probability of risks; subject vulnerabilities; adverse events; complaints or compliance  issues; the investigator’s experience; and other factors. Alternatively, the IRB may specify a specific enrollment number as a threshold  for when continuing review is to occur (e.g., after 5 subjects have experienced the study intervention or after six months, whichever  comes first). \*\* The IRB has the option to require continuing review at any time so long as the justification is documented. Examples of what might be  an appropriate justification for requiring continuing review include: the research involves complex issues that may rapidly evolve into  problems; the researcher has a significant recent history of compliance issues; the IRB determines that a Certificate of Confidentiality  (CoC) is required in order for the study to qualify as no greater than minimal risk and an expiration date will allow the IRB to track  expiration of the CoC; the application creates a registry or repository that will give out large amounts of data/specimens.\*\*\* Studies approved prior to January 21, 2019 that are eligible for the UW Flexibility Policy (**GUIDANCE Authority and Responsibilities**  **of HSD and UW IRB**) may receive an approval period of up to three years. Review **SOP IRB Review** for details about eligibility criteria. |

**Keywords:** Continuing review; IRB review; Modification