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| University of Washington Human Subjects DIvision | **WORKSHEET External Reliance,** **Follow-on Submissions** |

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| 1. **PURPOSE AND APPLICABILITY**
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This document is intended to be used as an aide for IRB Reliance Administrators on how to review follow-on submissions or additional information received after the initial authorization for external reliance is processed in Zipline (i.e., the application is in “Pending sIRB” state or beyond). It also addresses common issues with external study modifications and study updates. Most of the common issues are related to the Zipline functionality of the external reliance workflow.

This is not intended to be used to review initial requests for reliance or to perform any post-approval auditing (refer to **WORKSHEET External Reliance, Initial Submission** and the **WORKSHEET PAVE Consent Audit)**.

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| 1. **CHANGES TO APPLICATIONS WHILE IN PENDING SIRB REVIEW STATE**
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While in the *Pending sIRB Review* state, an application cannot be edited in Zipline by the study team because Zipline is designed this way. The application can be edited by HSD staff in this state, if needed. If a study team must make changes, they are instructed to communicate the need for those changes to hsdrely@uw.edu.

There are two situations in which changes to the application in the *Pending sIRB Review* state may be necessary because they need to be made before the external IRB can review the study:

* a change in UW PI and/or
* a change in the reviewing IRB

Most other changes to the application should be made after the application is moved to the *Active* state in Zipline, which is accomplished after the external IRB has approved the research.

**Identifying and Managing Changes**

Follow these steps if you receive a request from a study team to make changes to an application in the *Pending sIRB Review* state, e.g., the study team has let you know via email or comment or you have noticed it when performing other tasks in the application.

1. Assess the request for changes and identify whether the changes impact aspects of the reliance.
2. Examples of minor changes that likely **do not** impact aspects of the reliance:
* Adding study team members for access to Zipline.
* Changing the local study locations.
* Adding information about funding, e.g., updating the eGC1 number.
1. Examples of changes that likely **do** impact aspects of the reliance:
* Changing the reviewing IRB
* Changing the PI
* Any changes to the **REQUEST External IRB Review** form.
* Adding e-consent or changes to local context considerations.
1. If the changes do not impact the reliance arrangement:
2. Instruct the study team to submit the changes using the usual modification/update pathway after the external IRB has approved the research and the study has moved to the Active state, or
3. Gather the information the study team wishes to change and make the changes yourself using the Edit Study/Site function.
4. If the changes may impact the reliance arrangement:
5. Instruct the study team to Withdraw the application, which returns the application to the *Pre-Review* state. The study team can then make the changes and re-submit the application.
6. Follow the instructions in section 4 below to assess the acceptability of the changes and to perform any necessary actions, for example negotiating and executing a new reliance agreement.
7. Reissue an authorization letter if necessary (e.g., the content of the letter should be updated based on the changes).
8. Correct the external staff data entry or ct.gov data entry as necessary.

**Application Closure**

A small number of applications in the *Pending sIRB Review* state will need to be closed in Zipline even though approval from the external IRB has not yet been received. Study teams may contact HSD staff asking to close these applications, or HSD staff may find out that the study needs to be closed in communications with the study team. These closures typically occur because the study was cancelled by the funder or sponsor before UW could be approved as a site by the external IRB, or the UW study team chose not to pursue the study for a variety of reasons.

See Section 6 below for instructions on how to close studies in the *Pending sIRB Review* state.

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| 1. **PERFORMING POST-IRB APPROVAL CONSENT AUDIT**
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HSD staff perform a 100% audit of all consent forms for most industry-sponsored and initiated clinical trials and for all studies reviewed by WCG IRB or Advarra.

HSD staff monitoring HSDRely are responsible for monitoring for:

1. Any notifications received from WCG IRB or Advarra requesting Institutional Sign Off or Review after the IRB has performed its review, and
2. Any approval materials delivered by IRBs or study teams for industry initiated clinical trials reviewed by any other non-UW IRB (except Jaeb or Fred Hutch).

For any notifications or materials received, the staff member should initiate review of the consent materials using the **WORKSHEET PAVE Consent Audit** and **CHECKLIST PAVE Consent Audit**. Approval documents should not be uploaded into Zipline and Section 4 of this worksheet should not be completed until the audit has been completed.

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| 1. **RECORDING EXTERNAL IRB APPROVALS**
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HSD requires documentation of the initial approval for UW by the external IRB. This documentation can come in a wide variety of formats and depends on:

* UW’s role in the study (e.g., UW as a performing site or UW only has one engaged individual that will be obtaining individually identifiable data),
* when the UW is added to the study (e.g., soon after initial approval or in a modification to an ongoing study),
* the external IRB’s practices with citing what’s being approved on their approval letters.

Documentation may come directly from the external IRB or from the study team. HSD accepts documents from either source. Every six months, the UW study team is sent an automated reminder about providing approval documents applications that are in the *Pending sIRB Review* state.

**Identifying Acceptable Documentation**

The initial approval should either be an approval document from the reviewing IRB that explicitly states that UW is approved, or an approval document from the reviewing IRB with a written explanation from the reviewing IRB or lead study team that approval of UW is included with that approval document.

How an approval document explicitly states that UW is approved can vary. Acceptable ways include directly citing that UW as a site is approved, citing a UW site application or UW consent form on the reviewing IRB’s approval letter, or a modification submission that is stamped by the reviewing IRB as being approved—screenshots of the submission from the local IRB’s submission system are acceptable—which indicates in the modification summary that UW or UW personnel are being added. If it’s not clear whether the approval document explicitly states that UW is approved, consult the Sr. Reliance Administrator or Assistant Director of Reliances.

**Recording the Documentation in Zipline**

1. Double check that any required post-IRB approval consent audits are completed by reviewing the data entry in the **External Consent Audit** function in the study workspace. If not completed, refer to section 3.
2. Upload the documentation following the instructions for recording sIRB decision in the **INSTRUCTIONS Zipline for Staff**

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| 1. **MODIFICATIONS OR UPDATES**
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Applications in Zipline for reliance on an external IRB should only be modified or updated for a limited number of study changes, which are described in the **SOP External Reliance Agreements** and the **CHECKLIST External IRB for UW Researchers**. PIs receive an automated annual notification to update the study if any of the required elements have changed or to close the application if the study has been closed. Modifications or updates for items not on the checklist are typically not necessary; if you’re unsure, check with the Sr. Reliance Administrator or the Assistant Director of Reliances.

**Modification/Study Update Pathways in Zipline**

For externally reviewed studies, the options for submitting a modification or study update are dependent on whether the study type is “Multi-site or Collaborative study” or “Single-site study”. This is identified on the Basic Study Information page Question #4. Most externally reviewed studies created after January 7, 2020 will be “Multi-site or Collaborative study”. Most external studies created in Zipline before January 7, 2020 are listed as a “Single Site Study” on the Basic Study Information page and have a “SITEXXXXXXXX” study ID.

* **Single-site Studies.** There is one pathway for submitting changes to the application. In the study workspace for Single-site Studies, researchers select “Update Study Details” in order to create a study update.
* **Multi-site or Collaborative Studies.** In the study workspace for Multi-site or Collaborative Studies, users select either “Create Site Modification” or “Update Study Details” depending on change being made in Zipline.

The table in the **INSTRUCTIONS Zipline for Staff** under “INSTRUCTIONS Site Modifications and Study Updates” outlines which SmartForms are available for update for each type of modification or update.

**Additional Considerations**

Many updates to external studies have additional steps beyond those listed in the [Changing External IRB Studies](https://www.washington.edu/research/hsd/training/zipline-online-help-library/researcher-submission-guide/study-modifications/changing-external-irb-studies/) page in the Zipline Online Help Library. Zipline upgrades are the reason for the additional steps.

1. **Migrated Studies with 2020 Upgrade Changed Applications**

The January 2020 Zipline upgrade was the most significant upgrade. Due to this upgrade, all external studies created in Zipline before January 7, 2020 have a “SITEXXXXXXXX” study ID and a discarded “STUDYXXXXXXXX” study ID. Most of the study’s Zipline information was migrated to the “SITEXXXXXXXX” study ID from the “STUDYXXXXXXXX” study ID. Changes or additions to the study, including comments, should be made only to the active application with the “STUDYXXXXXXXX” study ID.

1. **New Required SmartForm Questions Since the Time of Initial Authorization.**

The January 2020 and subsequent Zipline upgrades added SmartForm questions in Zipline that must be answered before an update can be finalized. Studies which were submitted or updated by the study team prior to these questions being added must have the study team answer these questions before an update can be finalized. Reliance Team staff must check whether those questions have been answered. Researchers may need to be prompted to answer these questions.

Users submitting a modification versus update are prompted by the Zipline system to complete any new required questions added in Zipline. These submissions will not require a follow-up to instruct the completion of required new questions.

1. **No Submit Button for Study Updates**

Due to the functionality of Zipline, there is no way for study teams to submit Study Updates for review and HSD staff cannot identify whether or not changes to Study Updates are ready for review. Researchers are instructed by text in Zipline to email hsdrely@uw.edu to inform HSD staff that the changes are ready for review, however sometimes this does not happen. HSD staff should monitor for Study Updates for which an email has not been received and reach out to the study team to inquire about status.

1. **Combination Study Updates and Modifications**

Studies submitted in Zipline after January 7, 2020 require both an update and modification for some types of study changes. For example, implementing e-Consent that doesn’t involve UW’s Docusign or UW’s REDCap typically requires both a modification and an update. An update is needed to upload the revised **REQUEST External IRB Review** indicating e-Consent is being used, and a modification is needed to upload the supplemental documents related to the e-Consent method being used to the Local Site Documents page.

1. **Study Team Leaves UW**

Occasionally, the PI and/or PI Proxy will leave the UW without transferring the Zipline application to a new PI or PI Proxy. After separation from UW, individuals typically lose access to Zipline within 2 weeks to 2 months. When this happens, there is no way for the new study team to assume control of the application without the assistance of HSD. In these situations the Zipline Manager or Zipline Administrator should be contacted to either assign a new PI or grant an another individual access. Send an email to the S&I team at hsdinfo@uw.edu with the request. Provide them with whatever information you have, including any emails from the study team.

**Steps to Reviewing Study Updates and Modifications**

1. Identify whether there are any additional required Zipline Questions that should be answered at this time due to past Zipline upgrades.
2. Assess the acceptability of the changes.

Use the appropriate section of the **WORKSHEET External Reliance, Initial Submission** for full guidance on assessing the changes. This quick guide summaries the issues:

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| **Quick Guide to Assessing Changes** |
| Change of Study Team Members | Very little unless the study team roles description changes |
| Change of UW PI | Check Red Flag ListCheck CV is Present as requiredCheck qualifications  |
| Change of Reviewing IRB | Check that IRB is acceptable according to the terms of established cooperative agreements, etc.Check whether local context needs to be communicated |
| Addition of e-Consent Signatures | Assess whether the proposed system is acceptable according to UW policies. |
| Change to study team roles | Assess qualifications in line with UW policy |
| Other Changes | Assess whether the change materially impacts: * The terms of the Reliance Agreement
* Local Context Information that should be provided to the external IRB
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1. Request Clarifications and Changes from the Study Team. When requesting changes or follow-up from the study team, the communication method depends on the submission type.
* **Study Update.** This submission type does not have the Clarification Request option. The HSD reviewer should either post a comment to the study in Zipline or email the study team with instructions and then upload a copy of the email to Zipline.
* **Modification.** This submission type will have the Clarification Request option. The reviewer should use the Clarification Request function.
1. Generate and send:
	* an Acknowledgement of an External IRB Update letter if there is a new proposal to use eConsent or the study team requests one, otherwise a letter is not necessary.
	* a new Acknowledgement of Reliance on an External IRB letter if there is a change in the external IRB.
	* *NOTE: For study Updates, you must create the letter from scratch and upload as a comment. Use the* ***TEMPLATE External IRB Update Letter****. For modifications, you can use the Create and Send letter functionality in Zipline. Follow the steps in INSTRUCTIONS: Site Modifications and Study Updates in the document* ***INSTRUCTIONS Zipline for Staff*** *to**Create and Send the letter for Modifications.*
2. Finalize the Modification and/or Study Update.
3. Identify whether the changes modify the information in External Staff Data Entry and/or Ct.gov data entry. Some modifications or study updates may change information recorded in these (e.g., adding use of e-consent, changing the reviewing IRB). If applicable, when finalizing the modification or study update record any changes to this information.

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| 1. **REPORTS OF NEW INFORMATION**
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When a non-UW IRB reviews UW research, UW researchers are responsible for following the reporting requirements of the external IRB for events that might represent non-compliance or unanticipated problems. HSD does not require that any of these reports are submitted to HSD for review prior to or after review by the external IRB. Additionally, for studies reviewed by a non-UW IRB, HSD does not facilitate reporting to other UW offices, such as the CISO or UW Medicine Compliance. UW researchers are responsible for identifying when an event must be reported to those offices and for sending the reports, which is described in the **CHECKLIST External IRB for UW Researchers.**  HSD’s role in managing Reports of New Information for studies reviewed by external IRBs is therefore very limited.

**RNI in Zipline**

HSD should almost never receive Reports of New Information (RNI) in Zipline for research that is reviewed by an external IRB. If an RNI is received in Zipline, it will be initially fielded by the Regulatory Affairs team and the investigator will likely be instructed to discard the submission. However, if the RNI does require consideration by HSD, the assigned Regulatory Affairs coordinator will refer the submission to the Sr. Reliance Administrator or Assistant Director for Reliances for review. The Sr. Reliance Administrator or Assistant Director for Reliances will coordinate with the assigned RA coordinator to determine what steps should be taken.

**Researcher Questions about RNI**

Researchers with questions about RNIs should be directed to review the external IRB’s reporting criteria to determine whether a submission to the external IRB is needed. They should also be directed to the researcher responsibilities for reporting in the **CHECKLIST External IRB for UW Researchers**.

**Notices Received from External IRBs**

Safety or other compliance reports may be sent by the external IRB to hsdrely@uw.edu. These notifications are common for WCG and Advarra. When these reports are received, they should be forwarded to the Regulatory Affairs team at hsdreprt@uw.edu for tracking and filing. Once the emails have been forwarded to the RA team, the role of the Reliance Team is complete and the email can be filed as complete.

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| 1. **CLOSING APPLICATIONS**
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Zipline applications can be closed when IRB oversight of the activities by the external IRB have concluded. This can be accomplished with the IRB closure of the overall study or the ending of IRB oversite of UW research participation. This is known colloquially as “closure”, however it is different from what is known as “site closure” in FDA-regulatory research, which is typically synonymous with the cessation of all involvement of the site. Activities such as rectifying accounts and regulatory documents, final dispensation of study drug, etc., do not have to be completed in order to close an application in Zipline.

Due to Zipline functionality limitations, only HSD staff can initiate closure of an application in Zipline once it is past the *Pending sIRB Review* state. There is no closure request process in Zipline for researchers. Researchers are instructed to notify the HSD Reliance Team when a study (or UW’s involvement) has been closed by the external IRB. Notification of study closure can be received several different ways. Most common forms of notification are:

* Email from study team or reviewing IRB sent to either hsdrely@uw.edu or a reliance team member
* Comment posted to the application in Zipline
* Study update or modification submitted in Zipline
* *For WCG, Advarra and studies in IREx*: Email notification sent to hsdrely@uw.edu.

HSD accepts closure documentation delivered from any source. Closures received directly from the external IRB do not need to be verified with the UW study team.

**Identifying Acceptable Documentation**

The closure documentation should either be a document from the external IRB that explicitly states that UW or the entire study is closed, or a document from the external IRB with a written explanation from the external IRB or lead study team that closure of UW is included with that approval document.

**Recording the Closure in Zipline**

For all applications except those in the *Pending sIRB Review* state, follow the steps below:

* Upload documentation of closure to Shared Regulatory Documents.
* In the study workspace, click Close Site (Close Study (Admin) for single site studies).
* Include the following note in the closure dialogue box:
	+ “Notification of [Reviewing IRB] closure received on [XX/XX/XX]. Closure notification [and email] uploaded to Shared Regulatory Documents. Closing the study in Zipline.”
* Click OK.

For applications in the *Pending sIRB Review* state:

* Find out whether the external IRB has issued an initial approval for UW.
	+ If an initial approval for UW has been issued, follow the usual process to upload the initial approval in Zipline then upload documentation of the study closure following the steps above.

If an initial approval has not been issued, only the study team can close the application by discarding it in Zipline. To have the study team close the study, add a Comment to the study in Zipline indicating why the study needs to be closed at UW, attach any documentation from the study team, sponsor, or lead PI about why UW is closing, and then ask the study team in a Zipline Comment or an email to discard the study. **NOTE:** In situations in which the study team is unable to discard the application, for example the PI and PI Proxy no longer have Zipline access, are no longer affiliated with the study, or are unavailable for an extended period, the Zipline Manager or Zipline Administrator must discard the study. Send an email to the S&I team at hsdinfo@uw.edu with the request. Provide them with whatever information you have, including any emails from the study team.

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| 1. **RELATED MATERIALS**
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CHECKLIST External IRB for UW Researchers

[INSTRUCTIONS Zipline for Staff](https://www.washington.edu/research/forms-and-templates/instructions-zipline-for-staff/)

REQUEST External IRB Review

[RESEARCHER GUIDE Changing External IRB Studies](https://www.washington.edu/research/hsd/training/zipline-online-help-library/researcher-submission-guide/study-modifications/changing-external-irb-studies/)

SOP External Reliance Agreements

TEMPLATE LETTER External IRB Acknowledgement

TEMPLATE LETTER External IRB Update

WORKSHEET External Reliance, Initial Submission

WORKSHEET PAVE Consent Audit

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| **Version Number** | **Posted Date** | **Implementation Date** | **Summary of Changes** |
| 1.4 | 08.29.2025 | 08.29.2025 | Update information about post-approval consent audit. |
| 1.3 | 01.04.2024 | 01.04.2024 | Add instructions for auditing Advarra studies; allow use of prepare and send letter function in Zipline for external modifications |
| 1.2 | 11.02.2023 | 11.02.2023 | Changes to instructions about modifying applications in Pending sIRB, finalizing updates, and completing data entry for external consent audits. |
| 1.1 | 03.02.2023 | 03.02.2023 | Add information about process for requesting assistance from S&I Team |
| 1.0 | 01.04.2023 | 01.04.2023 | Newly implemented worksheet |

**Keywords:** External reliance; Multi-site; Pre-review