E&R

Ethical and Regulatory Concerns in Pragmatic Clinical Trial Monitoring and Oversight

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Figure 1.

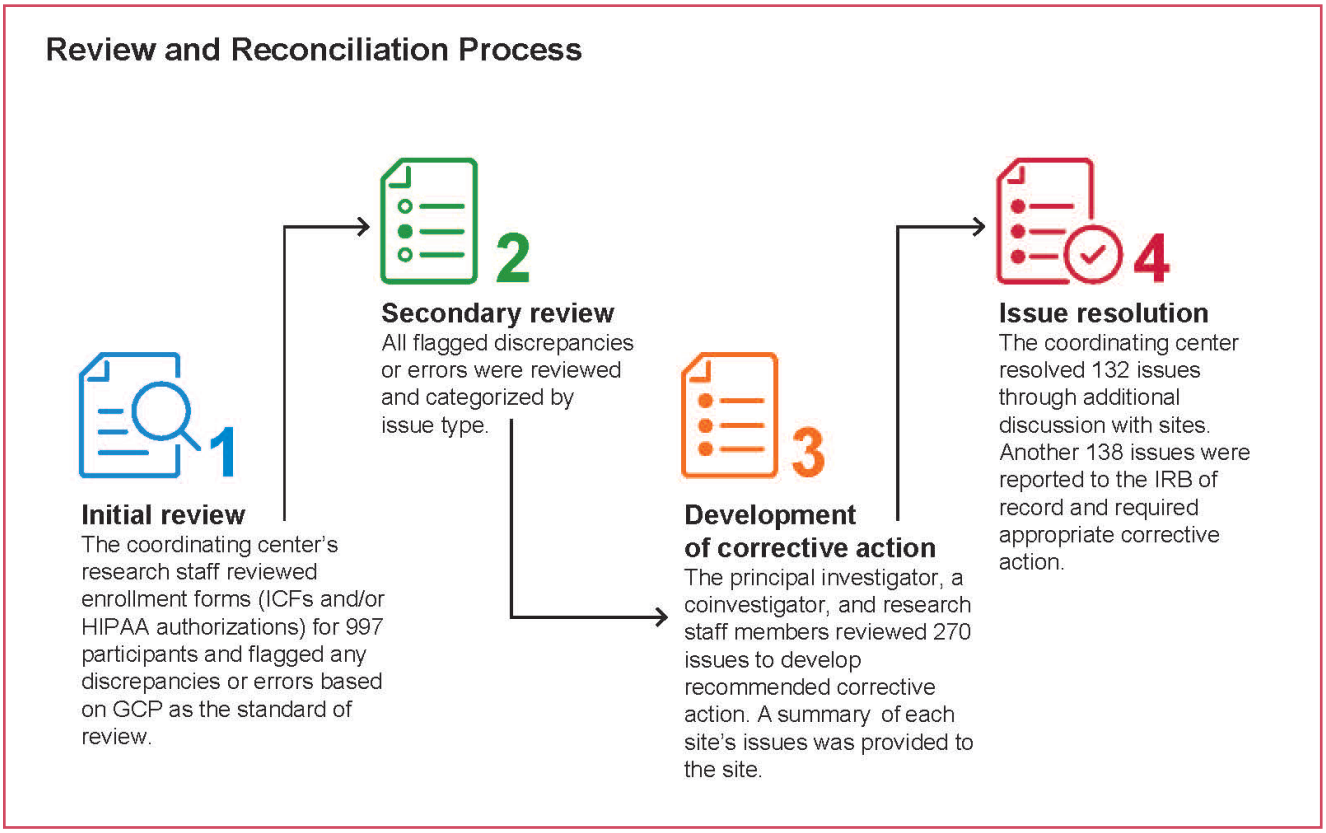

Table 1.
Participants' Issues Requiring IRB Report and Reconsent/Reauthorization

Issue type	*Total participants with issue type*	*Reconsent/ reauthorization required*	*Reconsent/ reauthorization completed*	*Participants retained*	*Participants withdrawn*
No HIPAA authorization form	41	23	0	25[a]	16[b]
Expired informed consent form and no HIPAA authorization form	25	25	5	5	20
Minor information missing or incorrect[c]	20	1[d]	0	19	1
Expired informed consent form	11	0	0	11	0
Participant signed as both the participant and the study staff member obtaining consent	10	0	0	10	0
Participant's data (including enrollment forms) not transmitted to the coordinating center	7	0	0	7	0
Study staff member who obtained consent signed in the wrong location on the form	6	0	0	6	0
Enrollment form missing the signature of the study staff member who obtained consent	4	0	0	4	0
Enrollment form missing the participant's signature	4	1	0	3	1[e]
Issue related to use or documentation of a witness	3	0	0	3	0
No informed consent form	2	0	0	2	0
No informed consent form and no HIPAA authorization form	2	2	1	1	1
Participant ineligible due to preferences marked on the HIPAA authorization form	2	0	1	1[f]	1
Participant incorrectly identified as a screen failure	1	0	0	1	0
TOTAL	**138**	**52**	**7**	**98**	**40**

[a] Twenty-two participants had patient-reported data retained only.

[b] Per the IRB, 15 participants needed to be withdrawn, not reconsented, because the participants were screen failures.

[c] Minor required information includes elements of an informed consent form and/or HIPAA authorization form (e.g., date, address, date of birth, printed name, and nonessential pages) not required per federal regulations but recommended to be included on forms per IRB of record.

[d] The issue requiring reconsent was a problem with the date on the HIPAA authorization form.

[e] Per the IRB, the subject needed to be withdrawn, not reconsented, since the subject was a screen failure.

[f] The participant was not supposed to be reauthorized, per the IRB, but reauthorization had been completed prior to the IRB determination.

Table 2.
Regulatory Review Results: Reportable Events, Corrective Action, and IRB Determination by Site

Sites with IRB submission required

Site no.	*Participants with IRB report required (n = 997)*	*Participants withdrawn after IRB report*	*Issue summary*	*Recurring issues*	*Corrective action required for participant retention*	*IRB determination*
1	4 (n = 37; 10.81%)	0 (n = 37; 0.00%)	Two participants had not been transmitted to the coordinating center, and 2 participants had minor information missing or incorrect.	None identified.	No reconsent/ reauthorization required.	Acknowledged.
8	5 (n = 31; 16.13%)	1 (n = 31; 3.23%)	One participant's forms had minor information missing or incorrect, 2 participants' ICFs were missing pages, 1 participant's ICF was missing the participant's signature, and 1 participant had an issue related to the use or documentation of a witness.	None identified.	Reconsent required for data retention for 1 participant.	Not serious or continuing noncompliance.
9	3 (n = 48; 6.25%)	0 (n = 48; 0.00%)	Three participants' forms had not been transmitted to the coordinating center.[a]	None identified.	None required.	No response received.
10	44 (n = 51; 86.27%)	17[c] (n = 51; 33.33%)	One participant signed an expired ICF, 38 participants had no HIPAA authorization form, one participant had no ICF and no HIPAA authorization form, 2 participants had required minor information missing or incorrect, and 2 participants enrolled were ineligible due to preferences marked on the HIPPA authorization form.	Thirty-nine participants had no authorization form on file.	Reauthorization required for the retention of data derived from the medical records for 22 participants; reconsent/ reauthorization required for data retention for 1 participant.	Neither serious nor continuing noncompliance.
11	1 (n = 36; 2.78%)	(n = 36; 0 0.00%)	One participant had an issue related to the use or documentation of a witness.	None identified.	None required.	No response received.[b]
12	7 (n = 40; 17.50%)	0 (n = 40; 0.00%)	Two participants had minor information missing or incorrect, 2 participants had signed expired ICFs, 2 participants had no ICFs, and 1 participant had no HIPAA authorization form.	None identified.	No reconsent/ reauthorization required for data retention.	Serious and continuing noncompliance.
16	5 (n = 17; 29.41%)	0 (n = 17; 0.00%)	Five participants signed expired ICFs.	Multiple participants consented on expired forms.	No reconsent required.	Acknowledged.

ICF = informed consent form

Table 2. Regulatory Review Results: Reportable Events, Corrective Action, and IRB Determination by Site *continued*

Site no.	*Participants with IRB report required (n = 997)*	*Participants withdrawn after IRB report*	*Issue summary*	*Recurring issues*	*Corrective action required for participant retention*	*IRB determination*
18	26 (n = 31; 83.87%)	20 (n = 31; 64.52%)	One participant had no ICF and no HIPAA authorization form, and 25 participants signed an expired ICF and had no HIPAA authorization form.	Site used an expired consent form and did not use the HIPAA authorization form for more than one year.	Reconsent and/or reauthorization required for data retention.	Serious and continuing noncompliance.
19	1 (n = 64; 1.56%)	0 (n = 64; 0.00%)	One participant was missing the signature page of the ICF.	None identified.	Verbal reconsent and/or reauthorization was required for data retention for 1 participant.	Approved.
20	2 (n = 32; 6.25%)	0 (n = 32; 0.00%)	One participant's ICF was missing the signature of the study staff member who obtained consent, and 1 participant had been incorrectly identified as a screen failure.	None identified.	No reconsent and/or reauthorization was required for data retention.	Acknowledged.
21	11 (n = 30; 6.67%)	0 (n = 30; 0.00%)	Four participants' forms had minor information missing or incorrect; 1 participant's ICF was missing the signature of the study staff member obtaining consent; 1 participant had no HIPAA authorization form; and 5 participants' ICFs had the signature of the study staff member who obtained consent in the wrong location.	None identified.	Reauthorization was required for retention of date derived from the medical record for 1 participant.	Noncompliance that is not serious or continuing.
23	1 (n = 36; 2.78%)	0 (n = 36; 0.00%)	One participant's forms had not been transmitted to the coordinating center.	None identified.	No reconsent and/or reauthorization was required for data retention.	Acknowledged, not serious or continuing noncompliance.
24	5 (n = 35; 14.29%)	1 (n = 35; 2.86%)	Two participants' forms had minor information missing or incorrect; 1 participant's ICF was missing the signature of the study staff member who obtained consent; 1 participant's ICF had such a signature in the wrong location, and 1 participant's HIPAA authorization form had a problem related to the use or documentation of a witness.	None identified.	One participant required reauthorization for retention.	Acknowledged.
25	3 (n = 60; 5.00%)	1 (n = 60; 5.00%)	One participant signed an expired ICF, 1 participant's ICF was missing the signature of the study staff member who obtained consent, and 1 participant did not have a HIPAA authorization form.	None identified.	Reauthorization was required for data retention for 1 participant.	Acknowledged.

ICF = informed consent form

Table 2. Regulatory Review Results: Reportable Events, Corrective Action, and IRB Determination by Site *continued*

Sites with IRB submission required as part of continuing review						
Site no.	*Participants with IRB report required (n = 997)*	*Participants withdrawn after IRB report*	*Issue summary*	*Recurring issues*	*Corrective action required for participant retention*	*IRB determination*
4	18 (n = 39; 46.15%)	0 (n = 39; 0.00%)	One participant had not been transmitted to the coordinating center, 4 participants' forms had minor information missing or incorrect, 1 participant signed an expired ICF, 10 participants' ICFs were not signed by study staff obtaining consent (participant signed as both the participant and study staff obtaining consent), and 2 participants' ICFs were missing the participants' signatures.	Study staff members who obtained consent did not provide the required signature or date. Participants signed, printed, and dated as both the participant and the study staff member obtaining consent.	No reconsent/ reauthorization required for retention.	Continuing review approved.
14	1 (n = 66; 1.52%)	0 (n = 66; 0.00%)	One participant signed an expired ICF.	None identified.	No reconsent/ reauthorization required for retention.	Continuing review approved.
15	1 (n = 36; 2.78%)	0 (n = 36; 0.00%)	One participant had minor information missing or incorrect.	None identified.	No reconsent/ reauthorization required for retention.	Continuing review approved.

ICF=informed consent form

Table 2. Regulatory Review Results: Reportable Events, Corrective Action, and IRB Determination by Site *continued*

Sites with no IRB submission required						
Site no.	*Participants with IRB report required (n = 997)*	*Participants withdrawn after IRB report*	*Issue summary*	*Recurring issues*	*Corrective action required for participant retention*	*IRB determination*
13[f]	0 (n = 31; 0.00%)	N/A	N/A	None identified.	N/A	N/A
2	0 (n = 22; 0.00%)	N/A	N/A	None identified.	N/A	N/A
3	0 (n = 63; 0.00%)	N/A	N/A	None identified.	N/A	N/A
5	0 (n = 34; 0.00%)	N/A	N/A	None identified.	N/A	N/A
6	0 (n = 40; 0.00%)	N/A	N/A	None identified.	N/A	N/A
7	0 (n = 34; 0.00%)	N/A	N/A	None identified.	N/A	N/A
17	0 (n = 61; 0.00%)	N/A	N/A	None identified.	N/A	N/A
22	0 (n = 23; 0.00%)	N/A	N/A	None identified.	N/A	N/A
	138 (n = 997; 13.84%)	**40 (n = 997; 4.01%)**				

ICF=informed consent form

[a] Participants' forms had not been transmitted to UW because baseline data (from the interview) was incomplete. Participants were withdrawn prior to randomization.

[b] Per the IRB's procedures, no response was provided unless additional clarification was required.

[c] For twenty-one retained participants, only patient-reported data was retained. Per the IRB, participants needed to provide reauthorization in order for data derived from the medical record to be retained, but patient-reported data was eligible for retention without reauthorization. Screen-failure participants were withdrawn without any attempt to obtain reauthorization from them.

[d] Although the IRB designated the reported deviations as serious and continuing noncompliance, the IRB determined that the data obtained from these participants could be retained. Per the IRB determination, destroying this data would result in the participants' having assumed the risks of the study without any benefit of contributing to science.

[e] For one retained participant, only patient-reported data was retained. Per the IRB, reauthorization was required from the participants to retain data derived from the medical record, but patient-reported data was eligible for retention without reauthorization.

[f] Three protocol deviations related to informed consent forms were discovered and reported to the IRB prior to study-wide review. In addition, the site had a recurring issue (not providing copies of consent forms to participants) resolved prior to regulatory review.