Guidance for Correcting Human Subjects Submission Validation Errors

1. Before submitting Research Performance Progress Reports (RPPRs), please keep notice **NOT-OD-22-008** (released on October 29, 2021) in mind. Failure to adhere to the guidance presented in this notice will prevent submission of the RPPR.

   a. The recipients should keep this in mind in particular:

> **Guidance for NIH Grant and Cooperative Agreement Recipients**
>
> Starting October 1, 2021, NIH has implemented new eRA RPPR submission system validations for clinical trial registration and results reporting. RPPRs that have associated clinical trials that are non-compliant with these requirements will receive errors preventing submission of the RPPR. To clear these errors and allow for submission of the RPPR, the recipient is required to take action to bring the clinical trial into compliance.

Figure 1: Screenshot from NOT-OD-22-008

2. The clinical trial registration error for RPPR submission or red bar to award will be resolved once the grantee completes the required registration and provides the NCT# (Clinicaltrials.gov identifier) on the Human Subjects Clinical Trial information form. The reporting error or award bar will be resolved after results are submitted to Clinicaltrials.gov. When registration or reporting is in progress, grantees may submit an exception document to resolve the error. Complete information on errors for noncompliance with clinical trial registration and reporting at time of award and in RPPR can be found on the **eRA.nih.gov website** (last updated on April 12, 2022).

3. If the HSS section is not in compliance, additional error messages will appear, but these are just warning messages, and the grantees will still be allowed to submit RPPRs. See Figure 2 below for a list of the triggering conditions and the yellow bar or warning message that may appear during RPPR submission. Grantees can see those warnings and error messages earlier than at the time of RPPR submission if they click on the **Check for Errors** button to run a validation check. This button is available for progress reports with a status of Work in Progress (WIP). Access is granted to any user with access to the grant. The RPPR can be validated at any time while in the status of WIP and can be validated multiple times. Detailed information on **Check for Errors** can be found in **5.4 Check RPPR For Errors and Warnings** of the **RPPR Instructional Guide** (last updated on June 23, 2022).

4. Additional information on compliance checks during RPPR submission, shown in Figure 2 below, can be found on the **eRA.nih.gov website** (last updated on April 12, 2022): New Errors for Noncompliance With Clinical Trial Registration and Reporting at Time of Award and in RPPR.

Compliance checks during RPPR submission

- **Display a warning message if the enrollment of the first participant was more than 21 days and less than or equal to 30 days ago and no NCT number was provided.**

Warning message: *Enrollment of first participant for <Study Title> was* ***more than 21 days ago and less than or equal to 30****, but a Clinicaltrials.gov identifier (NCT) has not been provided. Please complete Clinicaltrials.gov registration and use the Human Subjects link in G.4 to add the NCT number in the PHS Human Subjects and Clinical Trial Information Form item 1.5.*

An exception would be provided if one of the following conditions is satisfied:

- ◦ If no subject is enrolled (enrollment of first subject under Sec 6.3 of the Human Subjects Trial Information Form is null or set to anticipated).
  - ◦ If the recipient uploads a valid registration receipt as an attachment under Sec 5.1 Other Clinical Trials related attachments of the Human Subjects Trial Information Form. The file name should contain 'CTgov_registration_receipt' (without quotations; file name not case sensitive).
  - ◦ If the parent application was submitted in response to a Basic Experimental Studies Involving Humans (BESH) FOA.
- **Changed warning message to an error if the actual primary completion date was more than 12 months ago and the results have not been reported to Clinicaltrials.gov.**

Error message: *The study <study title> Primary Completion date is more than 12 months in the past and results have not been submitted to Clinicaltrials.gov. The responsible party should submit results in Clinicaltrials.gov or should have an approved extension to submit the results on a later date.*

An exception would be provided if one of the following conditions is satisfied:

- ◦ If the recipient uploads a valid Clinicaltrials.gov certification or extension receipt under Sec 5.1 Other Clinical trials related attachments of the Human Subjects Trial Information Form. The file name should contain 'CTgov_extension_receipt' (without quotations; file name not case sensitive).
  - ◦ If the parent application was submitted in response to a BESH FOA.
- **Display a new error message if the first participant was enrolled more than 30 days ago and no NCT number has been provided.**

Error message: *Enrollment of first participant for <Study Title> was more than 30 days but a Clinicaltrials.gov identifier (NCT) has not been provided. Please complete Clinicaltrials.gov registration and use the Human Subjects link in G.4 to add the NCT number in the Human Subjects and Clinical Trial Information Form item 1.5*

An exception would be provided if one of the following conditions is satisfied:

- ◦ If recipient uploads a valid registration receipt under Sec 5.1 Other Clinical Trials related attachments of the Human Subjects Trial Information Form. The file should contain 'CTgov_registration_receipt' (without quotations; file name not case sensitive).
  - ◦ If no subject is enrolled (enrollment of first subject under Sec 6.3 of the Human Subjects Trial Information Form is null or set to anticipated).
  - ◦ If the parent application was submitted in response to a BESH FOA.

Note: The above warnings and errors will be triggered only if the studies were submitted in FORMS-E or later form versions and Clinical Trial Code is set to 'Yes.'

Figure 2: Screenshot the eRA Website on New Errors for Noncompliance With Clinical Trial Registration and Reporting at Time of Award and in RPPR

5. Additionally, keep in mind the requirements for uploading PDFs to eRA Commons. It is important that all PDFs are flattened before upload. More information can be found on the **eRA.nih.gov website** (last updated on May 19, 2021). If a PDF submitted on or after May 25, 2021, is not flattened before it is uploaded to eRA Commons, an error may occur. There are several methods for flattening a PDF, the easiest of which is to print it as a PDF (also see the **eRA Commons Frequently Asked Questions** webpage).

To do this, go to File>Print, select the printer option from the menu that has a PDF option. Click the Print button and name the file.

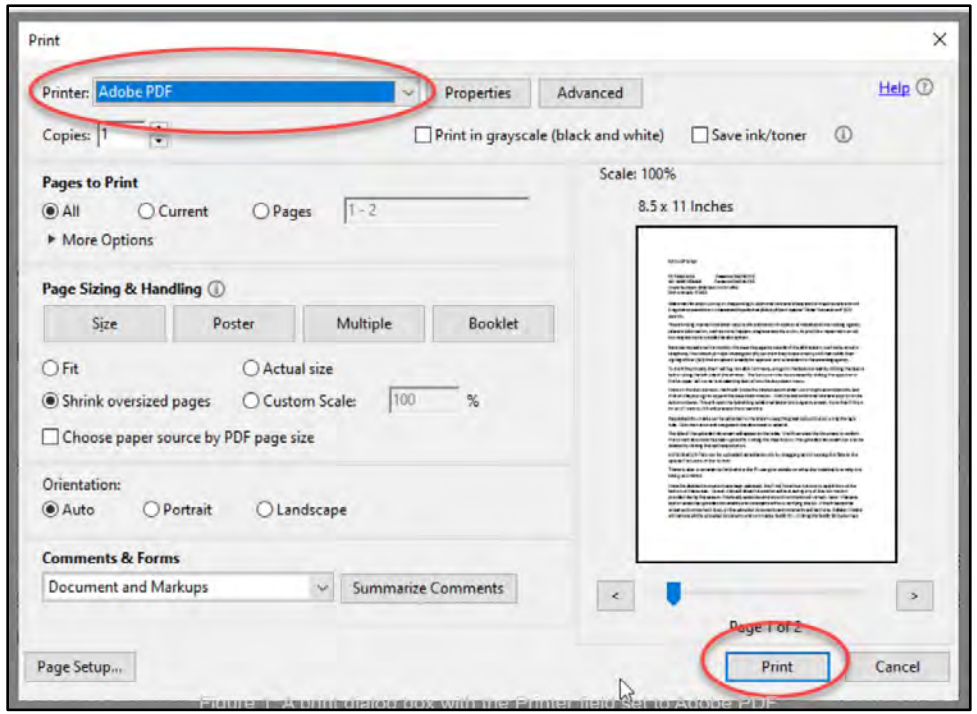

Figure 3: Screenshot From the eRA Website About Reminder to "Flatten" PDFs for Just-in-Time and RPPR Before Uploading to eRA Commons

In this process, you are exporting the layered PDF to the printer and saving it as a simple (flattened) PDF.

Depending on the software available to you, your options may vary from the one shown above. Other options are available with an Internet search.

6. Other validations in the Human Subjects System (HSS) when submitting RPPR can be found in the table below (Figure 4). This table also can be found on the **eRA.nih.gov website** (last updated on March 20, 2019).
   a. Enrollment and randomization will be required when submitting an RPPR.
   b. Principal investigators (PIs) and signing officers (SOs) submitting an RPPR with studies that are still in WIP status will receive a warning.

	Scenario	RPPR Response
1.	When application has studies in WIP	***Warning message:*** The following study(s) <Study Title> have some updated information that have not yet been submitted to NIH. If you would like to provide the latest updated version to NIH, please click on Human subjects link in G.4 and submit the study(s) that are in Work in Progress status.
2.	If Sec 6.6 Enrollment of the First Subject is missing. ***Note:*** This validation is valid only if the CT code of the study is set to 'Yes' and the application was received in FORMS-E format. Ignore Actual/Anticipated value and check if a date is provided	***Error Message:*** Enrollment of the First Subject date is missing for <Study Title>.Please click on the Human Subjects link in G.4 to update Enrollment of the First Subject date in section 6 of the Human Subjects and Clinical Trials Information form.
3.	If Sec 6.6, 25% of planned enrollment recruited by is missing. ***Note:*** This validation is valid only if the CT code of the study is set to 'Yes' and the application was received in FORMS-E format. Ignore Actual/Anticipated value and check if a date is provided	***Error Message:*** 25% of planned enrollment recruited by date is missing for <Study Title>. Please click on the Human Subjects link in G.4 to update the 25% of planned enrollment recruited by date in section 6 of the Human Subjects and Clinical Trials Information form.
4.	If Sec 6.6, 50% of planned enrollment recruited by is missing. ***Note:*** This validation is valid only if the CT code of the study is set to 'Yes' and the application was received in FORMS-E format. Ignore Actual/Anticipated value and check if a date is provided	***Error Message:*** 50% of planned enrollment recruited by date is missing for <Study Title>. Please click on the Human Subjects link in G.4 to update the 50% of planned enrollment recruited by date in section 6 of the Human Subjects and Clinical Trials Information form.
5.	If Sec 6.6, 75% of planned enrollment recruited by is missing. ***Note:*** This validation is valid only if the CT code of the study is set to 'Yes' and the application was received in FORMS-E format. Ignore Actual/Anticipated value and check if a date is provided	***Error Message:*** 75% of planned enrollment recruited by date is missing for <Study Title>. Please click on the Human Subjects link in G.4 to update the 75% of planned enrollment recruited by date in section 6 of the Human Subjects and Clinical Trials Information form.
6.	If Sec 6.6, 100% of planned enrollment recruited by is missing. ***Note:*** This validation is valid only if the CT code of the study is set to 'Yes' and the application was received in FORMS-E format. Ignore Actual/Anticipated value and check if a date is provided	***Error Message:*** 100% of planned enrollment recruited by date is missing for <Study Title>. Please click on the Human Subjects link in G.4 to update the 100% of planned enrollment recruited by date in section 6 of the Human Subjects and Clinical Trials Information form.

Figure 4: Screenshot From the eRA website on New Validations and Messages for RPPR

Additional information on Warning and Error Messages for Clinical Trials, shown in the tables below (Figures 5a, and 5b), can be found on the **eRA.nih.gov website** (last updated on April 13, 2022).

Scenario	RPPR Validation
Study's inclusion Monitoring code is marked as Yes, but there is no planned enrollment data and the study is not an existing dataset or delayed onset.	***Warning message:*** "Planned counts are required to be greater than zero for Inclusion Enrollment Reports <IER#, IER#> under Study<Study#>, Inclusion Enrollment Reports<IER#,IER#> under Study <Study #>. Please click on the Human Subjects link in G.4 to update the Inclusion Enrollment Report(s) in Section 2 of the Human Subjects and Clinical Trials Information form.
Enrollment of first participant was more than 21 days ago, but a Clinicaltrials.gov identifier (NCT) has not been provided.	***Warning message:*** "Enrollment for <study title> has begun but no Clinicaltrials.gov Identification Number (NCT) has been provided. Please complete Clinicaltrials.gov registration and use the Human Subjects link in G.4 to add the NCT number in the Human Subjects and Clinical Trial Information Form item 1.5."
The actual Primary Completion Date is more than 12 months ago and results have not been reported to ClinicalTrials.gov.	***Warning message:*** "The study <study title> Primary Completion date is more than 12 months in the past and results have not been submitted to ClinicalTrials.gov. The responsible party should submit results to Clinicaltrials.gov."
Project level and study level clinical trial codes are discrepant	***Warning messages:*** ***When project-level CT code is No:*** "One or more study records is listed as a clinical trial; however, this grant has a clinical trial indicator of No. Please contact your NIH Program Officer." ***When project-level CT code is Yes:*** "None of the study records are listed as clinical trials; however, the grant has a clinical trial indicator of Yes. Please contact your NIH Program Officer."
Sec 6. Study Primary Completion Date is missing on the form	***Error Message:*** Study Primary Completion Date is missing for Study<Study Title>. Please click on the Human Subjects link in G.4 to update the Study Primary Completion Date in section 6 of the Human Subjects and Clinical Trials Information form.
Sec 6. Study Final Completion Date is missing on the form	***Error Message:*** Study Final Completion Date is missing for Study<Study Title>. Please click on the Human Subjects link in G.4 to update the Study Final Completion Date in section 6 of the Human Subjects and Clinical Trials Information form.

Figure 5a: Screenshot From the eRA website on New Validations for HSS Form When Completing an RPPR

Scenario	RPPR Validation
Sec 6. Completion of primary endpoint date analyses is missing	*Error Message:* Completion of primary endpoint data analyses date is missing for Study<Study Title>. Please click on the Human Subjects link in G.4 to update the Completion of primary endpoint data analyses date in section 6 of the Human Subjects and Clinical Trials Information form.
Sec 6. Reporting of results in ClinicalTrials.gov is missing.	*Error Message:* Reporting of results in ClinicalTrials.gov date is missing for Study<Study Title>. Please click on the Human Subjects link in G.4 to update the Reporting of results in ClinicalTrials.gov date in section 6 of the Human Subjects and Clinical Trials Information Form.
Sec 6. Is this an applicable clinical trial under FDAAA answer is missing.	*Error Message:* Is this an applicable clinical trial under FDAAA answer is missing for Study<Study Title>. Please click on the Human Subjects link in G.4 to update Is this an applicable clinical trial under FDAAA in section 6 of the Human Subjects and Clinical Trials Information Form.
Completion of primary endpoint data analyses date is more than 12 months after the Primary Completion Date	*Warning Message:* Completion of Primary endpoint data analyses date cannot be later than 12 months from Primary Completion Date for Study <Study Title>. Please click on the Human Subjects link in G.4 to update the Primary endpoint data analyses date in section 6 of the Human Subjects and Clinical Trials Information Form.
Reporting results in Clinicaltrials.gov date is more than 12 months after the Primary Completion Date	*Warning Message:* Reporting of results in Clinicaltrials.gov date cannot be later than 12 months from primary completion date for Study<Study Title>. Please click on the Human Subjects link in G.4 to update the Reporting of results in ClinicalTrials.gov in section 6 of the Human Subjects and Clinical Trials Information Form.

Figure 5b: Screenshot From the eRA website on New Validations for HSS Form When Completing an RPPR

7. Other resources available
   a. **RPPR Instructional Guide**
   b. Warnings and Validations During RPPR Submission
      i. Guidance eRA RPPR Submission Validations for Clinical Trial Registration and Results Reporting: **NOT-OD-22-008**
      ii. **New Validations for HHS Form When Completing an RPPR**
      iii. **New Validations and Messages for RPPR**
   c. HSS Resources for SOs and PIs
      i. **HSS User Guide PDF**
      ii. **HSS Online Help**
      iii. Inclusion Help Desk email: **inclusion@od.nih.gov**

d. **Human Subjects Addendum**

e. **Inclusion Policies for Research Involving Human Subjects**

f. **Inclusion on the Basis of Sex/Gender and Race/Ethnicity FAQs**

g. **ASSIST (Application Submission System & Interface for Submission Tracking) User Guide**