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# Reference Material: NOTIS eCRF Guidelines



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## Overview

- This reference material provides a general overview of Northwestern Oncology Trial Information System (NOTIS) and details the submission of clinical trial data via electronic case report forms (eCRF).
- NOTIS can be subdivided into two main parts: NOTIS Rails and NOTIS eCRFs. This document will focus primarily on NOTIS eCRFs. However, data used for reporting purposes (i.e. patient screening and registration) will also be captured in Rails and it is important that data entered here is consistent with what is reported in eCRFs.
- NOTIS is regularly updated to better the user experience. Most changes will be behind the scenes and may not impact your day-to-day work, while others may. Check the Release Notes at the top of the NOTIS toolbar to see recent changes. If the Release Notes display is the color red, that means there have been new releases you have not reviewed.
- NOTIS is best used in the following browsers: Mozilla Firefox, Chrome, and Edge.

Technical support: [notis-support@northwestern.edu](mailto:notis-support@northwestern.edu)

Access support: Multi-Site Research Department (affiliates)  
[NUAffiliates@northwestern.edu](mailto:NUAffiliates@northwestern.edu)

Catie Humphreys (internal)  
[catherine-collins@northwestern.edu](mailto:catherine-collins@northwestern.edu)

Data Entry support: Quality Assurance Department  
[croqualityassurance@northwestern.edu](mailto:croqualityassurance@northwestern.edu)

## NOTIS Access

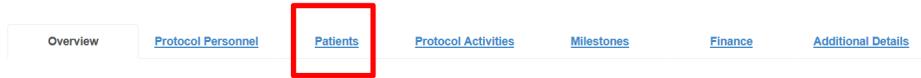
- A valid Northwestern University NetID is required to access NOTIS.
  - For internal, CTO employees, your Manager will provide access.
  - For internal, non-CTO employees, reach out to the Catie Humphreys for access.
  - For external affiliates, reach out to the Multi-Site Research Department. They will provide you with a Northwestern University NetID and access.
- Access to specific studies in NOTIS will be granted to delegated study staff.

## Access to eCRFs

- Additional training is required prior to accessing eCRFs. This access is required for any personnel who will be screening patients, registering patients, or performing data entry.
  - Reach out to the appropriate contact listed in NOTIS Access
- The user must complete the required training and submit the quiz. After a passing result, the user will receive a Training Certificate of Completion.
- Users that have met these conditions will be granted eCRF access. Access to specific studies in NOTIS eCRFs will be granted to delegated study staff.

## Screening and Registration

1. Log in to NOTIS and go to the protocol page of the study you are screening the patient. Click on the “Patients” tab. All patients currently screened and registered at your site will appear on this page.



2. To screen a new patient, click the green “Screen Patient” option on the right-hand side. If you do not see this option, reach out to your COM (if internal CTO employee), or the Multi-Center Research Department if you are an affiliate or non-CTO employee. They will need to verify your access.



3. You will be taken to the patient search page.
  - 3.1. If you navigated from a Northwestern Medicine site, the patient search will search EPIC for the patient. Select the appropriate MRN type in the drop-down menu and then enter the corresponding MRN. If you do not know this information, you may “Search by Demographics.” Last Name, First Name, Birth Date, and Gender are all required fields needed for patient search.
  - 3.2. If you navigated from a non-Northwestern Medicine site, the patient search will be by expanded demographics. Enter as much information as you can about your patient. Last Name, First Name, Birth Date, Sex, and Zip Code are the minimum required fields needed for patient search.

*Image 3.1 by MRN*

Patient Search for Screening on NU 10C03 at Northwestern Memorial Hospital

MRN Type  
Please select

MRN  
MRN

Fill out both MRN fields to perform Epic patient lookup.

Search by Demographics

Search Patients

*Image 3.1 by Demographics*

Patient Search for Screening on NU 10C03 at Northwestern Memorial Hospital

Search by MRN

Last Name  
Last Name

First Name  
First Name

Birth Date  
MM/DD/YYYY

Gender  
Please select

Fill out all demographics fields to perform Epic patient lookup.

Search Patients

Image 3.2-4

Patient Search for Screening on NU 10C03 at Beaumont Hospital

Last Name

First Name

Birth Date

Sex

MRN Type

MRN

Survival

Zipcode

Protocols

Spaces don't matter.  
 You can list as many protocols with complete protocol name  
 i.e. protocol type followed by protocol code as you'd like, separated by comma.  
 e.g. "hufda93u3, ecog 1487"

4. After entering search criteria, select the blue "Search Patients" button.
  5. On the right hand side will display patients that match the search criteria entered.
    - 5.1. If the patient displays in this area, select the patient to continue by clicking "Screen this patient." If you need to see more information to ensure the right patient before selecting, this button has a drop down arrow to "Go to patient" or "View all demographics". If you navigated from a Northwestern Medicine site, and the patient was found, the demographics will be imported from EPIC. If you navigated from a non-Northwestern Medicine site, and the patient was found, the demographics were previously entered.
- You may proceed to Step 6.**

Image 5.1

Patient Search for Screening on NU 10C03 at Northwestern Memorial Hospital

Last Name  Clear all filters Showing 1 patients out of total 1

| Last Name, First Name | Date of Birth | Sex  | MRN   | Zipcode | Survival  | Protocols |
|-----------------------|---------------|------|-------|---------|-----------|-----------|
| Wayne, Batman         | 10/01/2020    | Male | 10001 | Alive   | LCH 14C03 |           |

No more results to show.

First Name  Screen this patient

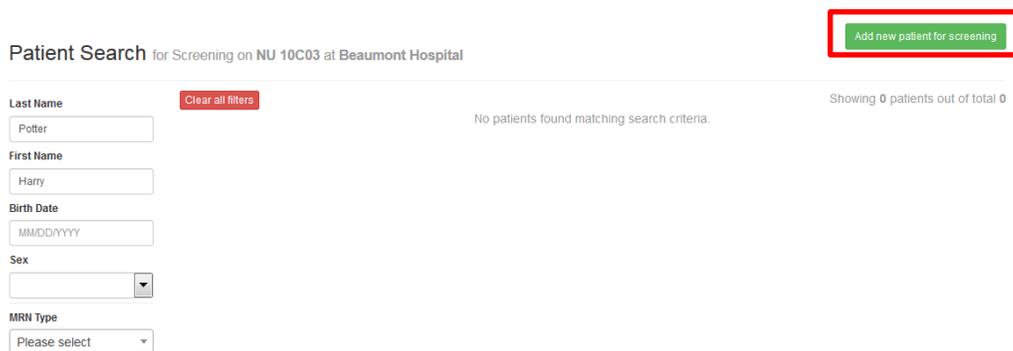
Birth Date

Sex

MRN Type

- 5.2. If the right hand side displays “No patients found matching search criteria”, click the green “Add new patient for screening” button.
  - 5.2.1. After your selection, you will be taken to the Patient Demographics page.
  - 5.2.2. Anything previously entered in the search boxes will be populated to this demographics page. You may enter any additional information. Last Name, First Name, Date of Birth, Sex, and Zip are all required fields.
  - 5.2.3. Once all information has been entered, click the blue “Submit” button.

Image 5.2



Patient Search for Screening on NU 10C03 at Beaumont Hospital

Clear all filters

No patients found matching search criteria

Showing 0 patients out of total 0

Last Name: Potter

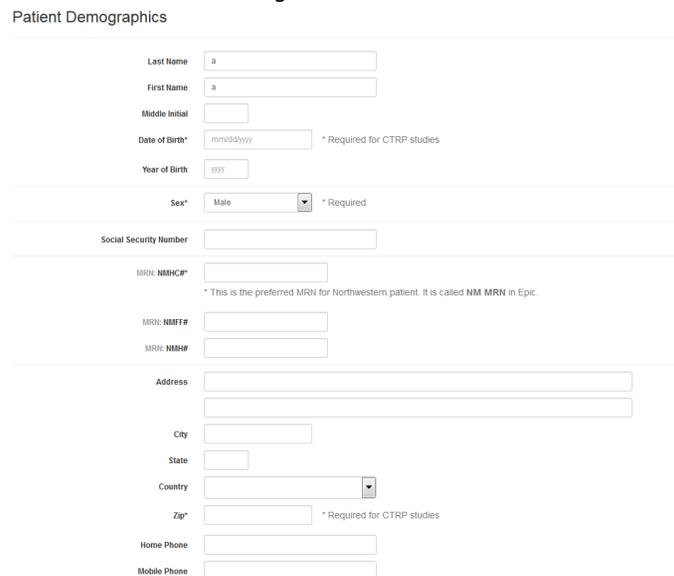
First Name: Harry

Birth Date: MM/DD/YYYY

Sex: (dropdown)

MRN Type: Please select

Image 5.2.1 – 5.2.2



Patient Demographics

Last Name: a

First Name: a

Middle Initial:

Date of Birth\*: mm/dd/yyyy \* Required for CTRP studies

Year of Birth: yyyy

Sex\*: Male \* Required

Social Security Number:

MRN: NMHC#

\* This is the preferred MRN for Northwestern patient. It is called NM MRN in Epic.

MRN: NMF#

MRN: NMB#

Address:

City:

State:

Country: (dropdown)

Zip\* \* Required for CTRP studies

Home Phone:

Mobile Phone:

6. After your selection, you will be taken to the Screening Information page.
7. Ensure the appropriate affiliate is selected. Screening Date is a required field on this page. This usually corresponds to the date of signed informed consent. Race and ethnicity are also required fields on this page.
8. Once all information has been entered, click the blue “Submit” button.

Image 6-8

Screening Information for **Batman Wayne** on **NU 10C03** at Northwestern Memorial Hospital

\* Required fields

Patient's Affiliate: Northwestern Memorial Hospital

Screening Date\*: 11/15/2020

Potential Start Date: 11/15/2020

Treating Physician:

Result: N/A

Screening Number:

Comments:

Race Not Reported/Refused

Race\*:  \* Required unless the checkbox above is checked

Ethnicity Not Reported/Refused

Ethnicity\*:  \* Required unless the checkbox above is checked

Sex Unspecified/Refused

Cancel Submit

9. You will now be navigated back to the patient demographics. Towards the top of the page, next to “Patient Demographics”, you should see a tab for the study you just entered screening information. If patient was previously screened for any other trials, those trials will also be listed here. Click on the appropriate study for which you are screening the patient. **If the trial you are screening and registering a participant does not require registration by the Northwestern University Quality Assurance team, after screening the participant (Step 9), proceed to Step 110 to Register the participant.**
  - 9.1. If internal site, prior to navigating to the patient demographics page, you will be asked to upload the signed consent form. The Consent form version and Date Signed are required fields on this page. If you are not ready to upload the signed consent, you may select “Cancel.”
  - 9.2. The signed informed consent must be uploaded to the patient’s trial page. If not previously done, select the green “Add new signed consent form” button.

Image 9

Patient Demographic **LCH 14C03 NU 10C03**

Signed Consent Forms are missing for LCH 14C03: LCH 14C03 uses NU IRB and requires signed consent form upload.

Signed Consent Forms are missing for NU 10C03: NU 10C03 uses NU IRB and requires signed consent form upload.

**Demographic Information** Delete This Patient and Protocol Information

|                        |              |
|------------------------|--------------|
| Name                   | Batman Wayne |
| Address                |              |
| City                   | 1            |
| State                  |              |
| Country                |              |
| Zip                    | 10001        |
| Home Phone             |              |
| Mobile Phone           |              |
| Business Phone         |              |
| Sex                    | Male         |
| Medical Record Numbers |              |
| SSN                    |              |
| Date of Birth          | 10/01/2020   |
| Survival Status        | Alive        |
| Diagnosis Date         |              |
| Diagnosis              |              |
| Histology              |              |
| Primary Site           |              |
| Stage                  |              |

Edit Demographics Edit Survival Edit Diagnosis

Image 9.2-10

**Signed Consent Forms** Add new signed consent form

Signed Consent Forms are missing for NU 10C03: NU 10C03 uses NU IRB and requires signed consent form upload.

No signed consent forms have been added yet.

**Screening** Delete This Screening From This Patient

|                      |   |
|----------------------|---|
| Screening Date       | 11/15/2020  |
| Potential Start Date | 11/15/2020  |
| Treating Physician   |   |
| Affiliate            | Northwestern Memorial Hospital                            |
| Result               |   |
| Screening Number     |   |
| Comments             |   |
| Race/Ethnicity       | Race Not Reported/Refused, Ethnicity Not Reported/Refused |
| Case Report Forms    | <a>Start working on eCRFs</a>                             |

Edit Register

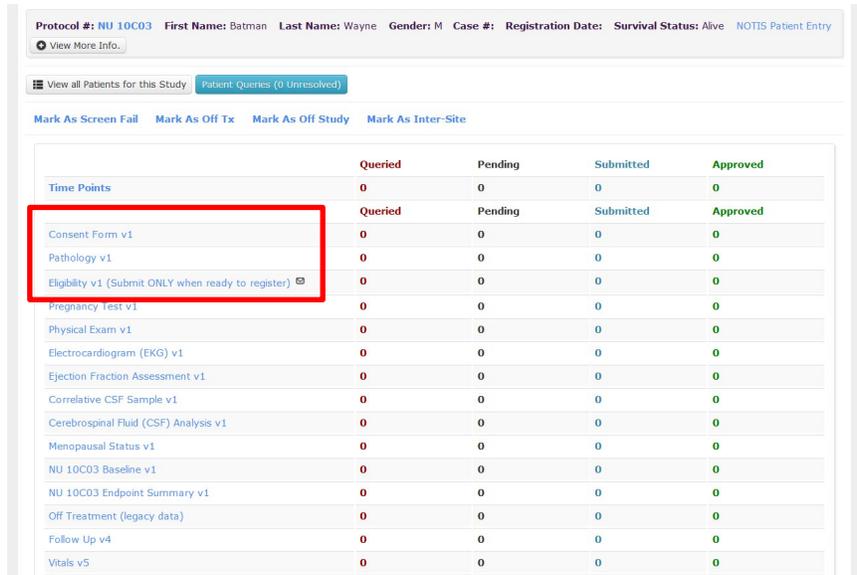
**Registration**

No registration information

10. Under the Screening Section, select the hyperlink to “Start working on eCRFs.”

- This is the patient's eCRF home page. Reference the protocol to determine which forms are required to be submitted to register the patient on the trial. In most cases this will be the following eCRFs: Consent Form, Pathology, and Eligibility.

Image 11



Protocol #: NU 10C03 First Name: Batman Last Name: Wayne Gender: M Case #: Registration Date: Survival Status: Alive NOTIS Patient Entry

View More Info.

View all Patients for this Study (Patient Queries: 0 Unresolved)

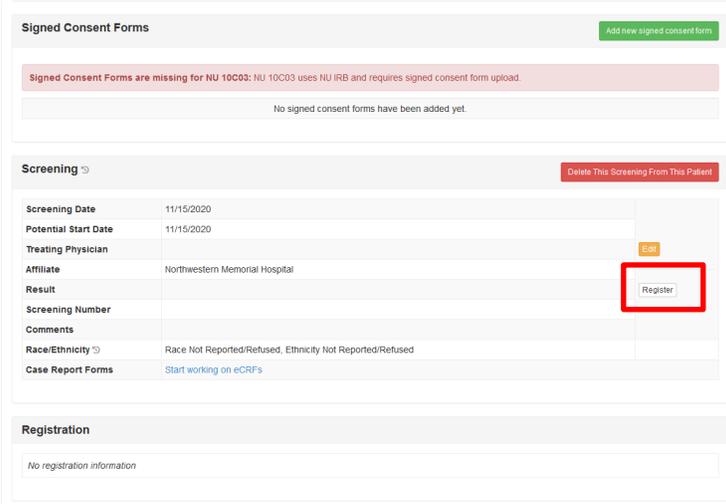
Mark As Screen Fail Mark As Off Tx Mark As Off Study Mark As Inter-Site

|   | Queried | Pending | Submitted | Approved |
|---|---------|---------|-----------|----------|
| <b>Time Points</b>  | 0       | 0       | 0         | 0        |
| Consent Form v1   | 0       | 0       | 0         | 0        |
| Pathology v1  | 0       | 0       | 0         | 0        |
| Eligibility v1 (Submit ONLY when ready to register)  | 0       | 0       | 0         | 0        |
| Pregnancy Test v1   | 0       | 0       | 0         | 0        |
| Physical Exam v1  | 0       | 0       | 0         | 0        |
| Electrocardiogram (EKG) v1  | 0       | 0       | 0         | 0        |
| Ejection Fraction Assessment v1   | 0       | 0       | 0         | 0        |
| Correlative CSF Sample v1   | 0       | 0       | 0         | 0        |
| Cerebrospinal Fluid (CSF) Analysis v1   | 0       | 0       | 0         | 0        |
| Menopausal Status v1  | 0       | 0       | 0         | 0        |
| NU 10C03 Baseline v1  | 0       | 0       | 0         | 0        |
| NU 10C03 Endpoint Summary v1  | 0       | 0       | 0         | 0        |
| Off Treatment (legacy data)   | 0       | 0       | 0         | 0        |
| Follow Up v4  | 0       | 0       | 0         | 0        |
| Vitals v5   | 0       | 0       | 0         | 0        |

- Ensure that these forms are saved and submitted. The eligibility eCRF should be submitted last as it will send an automatic e-mail to the assigned QAM and assigned Clinical Coordinator listed on the Protocol Personnel page in NOTIS. If you did not get an automatic e-mail, ensure the Eligibility eCRF is Submitted and that you are listed on the Protocol Personnel page.
- The QAM will review the submission. If there are any additional questions, the QAM will query the applicable eCRF and/or send an e-mail to the study team. Otherwise, the QAM will approve the eligibility, register the patient, and provide a Confirmation of Registration via e-mail.

110. To the right-hand side of the Screening Section, select the white “Register” button.

Image 110



**Signed Consent Forms** Add new signed consent form.

Signed Consent Forms are missing for NU 10C03: NU 10C03 uses NU IRB and requires signed consent form upload.

No signed consent forms have been added yet.

---

**Screening** Delete This Screening From This Patient

|                      |   |                      |
|----------------------|---|----------------------|
| Screening Date       | 11/15/2020  |                      |
| Potential Start Date | 11/15/2020  |                      |
| Treating Physician   |   | <a href="#">Edit</a> |
| Affiliate            | Northwestern Memorial Hospital                            |                      |
| Result               |   | <b>Register</b>      |
| Screening Number     |   |                      |
| Comments             |   |                      |
| Race/Ethnicity       | Race Not Reported/Refused, Ethnicity Not Reported/Refused |                      |
| Case Report Forms    | <a href="#">Start working on eCRFs</a>                    |                      |

---

**Registration**

No registration information

111. After your selection, you will be taken to the Registration Information page.

Image 111

Registration Information for [Batman Wayne](#) on [NU 10C03](#) at Northwestern Memorial Hospital

\* Required fields

Screening Date 11/15/2020

Potential Start Date 11/15/2020

Screening Result

Screening Comments

Protocol History LCH 14C03: 10/15/2020

Patient's Affiliates Northwestern Memorial Hospital

Registration Date\* 11/15/2020

Randomization Date

Disease Site\* Please select a disease site

Treating Physician\*

Method of Payment

112. Information entered in the Screening Information section will be copied over. If any of this information has changed at time of Registration, you may edit here. Otherwise, the Registration Date, Disease Site, Treating Physician, and Case Number are required fields on this page.

113. Once all information has been entered, click the blue “Submit” button.

## Navigating to eCRFs

There are two methods to get to eCRFs.

### Method 1

Log in to NOTIS and at the top of the page on the toolbar, select “eCRFs.” All studies for which you have access to eCRFs will be displayed here. Click on the study you would like to access.

A pop-up window should appear showing all patients currently screened and with eCRFs started; and patients currently registered at your site. Select the patient you wish to enter data for by clicking the “View” hyperlink. You will be directed to the patient’s eCRF home page.

### Method 2

Log in to NOTIS and go to the protocol page of the study you wish to enter data. Click on the “Patients” tab. Click on the blue “View eCRFs” option on the right-hand side. A pop-up window should appear showing all patients currently screened and with eCRFs started; and patients currently registered at your site. Select the patient you wish to enter data for by clicking the “View” hyperlink. You will be directed to the patient’s eCRF home page.

**Tip:** If the patient you are looking for is not showing up on the pop-up box, navigate to the Patient Demographics page and follow Steps 9 and 10 in Screening and Registration.

## Introduction to eCRFs

- The eCRFs in NOTIS are specific to each trial, with a master set of forms that may be used across multiple trials. They will contain all the data elements required for appropriate monitoring and analysis of the trial.
- NOTIS eCRFs are organized by form type, not by study visit. Use the study procedures table located in the protocol to determine what forms to complete for each visit. In this section we discuss the different types of forms you may see. Most studies will have transitioned to Form Builder forms, but some studies may still utilize legacy forms. The main takeaway is understanding that the form types will look and operate slightly different.

## Form Builder Forms

These are the newer eCRFs in NOTIS. At the top of these forms, there is a “Toggle Data Table” link. When clicked, all entered data will be displayed on the same page for easier searching and sorting.



## Legacy Forms

These are the older eCRFs in NOTIS and there's no “Toggle Data Table” link at the top the forms.

## NOTIS Rails Patient Data

- The Quality Assurance Monitor (QAM) will monitor NOTIS Rails data at each monitoring visit. Data entered here should match NOTIS eCRFs. If the data between these two systems is not consistent, a query will be issued. The query will be placed on the eCRF query message board and will reference the discrepancy.
- A subsequent guidelines document will incorporate data guidelines for NOTIS Rails.
  - One such guideline is the following: NOTIS Rails Treatment Stop Date corresponds to the date that the physician took patient off treatment.

## Disclaimer

*Please note these are general guidelines. There may be situations that require deviation from the guidelines. An example of such a situation may include following a precedent set for a clinical trial to ensure data consistency. If there are any questions, please reach out to the Quality Assurance Department.*



## General Guidelines for eCRFs

- There are always two steps to completing a form. Once data is entered in a form, you must click “Save.” Not doing so will result in losing your work. When data on the form is complete to the best of your knowledge and ready to submit for review and approval, you must click “Submit.” This lets the QAM know that data is ready for their review. Saved work may mean entry was started, but is not yet ready to be reviewed. The QAM can see the saved forms and data, but are only able to approve or query forms that are Submitted.
- Required data fields will be designated by a red asterisk \*. These data fields must be completed on an eCRF to save.
- When a study procedure is not completed per protocol, please follow the appropriate guidance below:
  - If the procedure missed was part of a larger assessment, such as platelets results, where the rest of the CBC panel was completed, add a comment in the comment section that platelets was not done. A deviation should also be submitted if the protocol requires that specific component to be completed at the specified time point.
  - If the procedure missed was an entire assessment, a deviation should be submitted. Data entry will not be required to indicate the procedure as not done.
    - The exception here is that if the procedure missed was a correlative/research sample, data entry will be required to indicate the procedure was not done. The corresponding eCRF should indicate not done at the applicable time point, explaining why it was missed. A deviation should also be submitted if the protocol requires the sample to be completed at the specified time point.

## Entry Guidelines by eCRF Type

### Time Points

- Located at the top of the eCRF list, time points are the dates that each cycle occurred for each patient. The dates entered should be the actual dates that encompassed that cycle and the dates should not overlap. The dates entered in Time Points will now flag data entered on other eCRFs to the corresponding cycle.
- If the cycle length deviates from the protocol specified length, enter a comment in the corresponding time point.
- The start date for the (first, as applicable) Follow-Up time point should correspond with the EOT date. This will now flag data entered for the EOT visit with the Follow-Up period.
- If a study patient was on study longer than the average/anticipated time, reach out to the Quality Assurance Department to add additional time points. For example, a study may be built for 12 cycles of treatment anticipating that most patients will receive no more than 12 cycles. However, some patients may be on treatment for more than what was anticipated and these additional time points need to be added in by the eCRF developer.

### Medical History and Baseline Conditions

New studies have a medical history form to capture all the baseline health conditions. For older studies that don't have this form, any health issues that are active at the time of screening should be entered as adverse events, and marked as Yes, present at baseline on the AE eCRF. It is important to note that even though these baseline health conditions are on the AE eCRF, if they are indicated as present at baseline, they will not be counted as adverse events.

### Menopausal Status

Depending on version used, this may only need to be completed for female patients. In some instances, it may be required to be completed for both female and male patients.

### Pregnancy test

Enter fields as required, form may be repeated as necessary per protocol. Depending on the version used, this may only need to be completed for female patients. In some instances, it may be required to be completed for both female and male patients.

### Vitals

- Enter fields as required, form may be repeated as necessary per protocol (often each study visit). Depending on the version used, the eCRF may include additional data fields not specified in the protocol (e.g. pulse ox (SpO2) or respiration). Unless specified in the protocol, these specific data points do not need to be captured.
- Note the unit in which the data field is asking for measurements (e.g. weight in kg versus lbs.).

### Performance Status (PS)

Depending on what type of PS is required per protocol (e.g. ECOG PS, KPS, LPS), will dictate the version used. Enter fields as required, form may be repeated as necessary per protocol. This eCRF is usually a drop down menu selection. The menu selection is a standard answer set corresponding to the applicable PS.



## Correlative Samples

Depending on what type of samples are required per protocol (i.e. tissue, blood; fresh, archival), will dictate the version used. The form is often protocol specific. Enter fields as required, form may be repeated as necessary per protocol. As indicated in the general guidelines, data entry will be required to indicate the procedure was not done. The corresponding eCRF should indicate not done at the applicable time point, explaining why it was missed. A deviation should also be submitted if the protocol requires the sample to be completed at the specified time point.

## Labs

- Enter fields as required, form may be repeated as necessary per protocol.
- These newer lab forms may appear in a different format than the legacy Lab forms. On the Form Builder lab eCRF, instead of entering the lab range, you will need to answer if the lab value is out of range.
- If patient requires more frequent lab draws than is required per protocol and there are abnormalities on those labs, those abnormal labs constitute adverse events. You must enter the abnormal lab values that correspond to adverse events, even if they are outside the protocol specified time points. You do not need to enter the normal labs drawn on the same day. For example, if the platelet value on a CBC panel was abnormal you only need to enter the platelet value and not the rest of the panel. This serves as secondary source to verify and correspond with the adverse event entered.
- If a patient has multiple lab draws per day, you are only required to record the highest grade AE per day and enter the corresponding lab values on the eCRF for that date.

## Treatment

- Treatment eCRFs will capture the study medications, therapies, or interventions taken while on study.
- **Treatment Dates** – The start date should be the date the patient first received that cycle's/day's treatment, whether given in clinic or taken as oral at home. If the treatment was given in clinic as one-time administration (e.g. an infusion), the end date should be the same as the start date. If the drug was taken continuously over a specified period of time (e.g. daily oral medications), the end date should be the last date of drug taken that cycle or the last date the drug was taken at the starting dose before a modification happened.
- **Prescribed Dose** – should be entered as either the protocol prescribed dose or the dose at which the drug has been modified to for those dates. For example, the flat dose specified in the protocol for all patients (i.e. 200 mg) or the weight-based dose (i.e. 15 mg/kg).
- **Received Dose** – should be entered as the amount of medication the patient received during the dates entered. For example, the administered dose that the patient received based on their weight (i.e. a 15 mg/kg prescribed dose for a patient weighing 80 kg would be a 1200 mg received dose); or the total administered dose the patient took for continuous medications, which is a calculation of each daily dose multiplied by the number of days administered (i.e. a 200 mg/day over 8 days would be a 1600 mg received dose). This field is NOT automatically calculated by NOTIS and must be hand calculated and entered by the study team.
- **Total Received Dose** – On Legacy Treatment forms, NOTIS will auto-calculate all of the received doses entered to carry through to the Total Received Dose. This is not done on Form Build Treatment forms, nor is it a requested data point.
- **Treatment Modification** – Any changes to the protocol specified treatment plan need to be captured as treatment modification entries. This may include any time the drug is held, reduced or discontinued.



Please do include specific comments in the Reason field as to exactly why the modification happened. Some modifications may be planned, while others may be unplanned (e.g. patient noncompliance).

- **Patient Calendars** – Provides a place to upload any oral study drug diaries that the study may require. Please ensure that the patient’s drug diary has all fields completed and is signed and dated appropriately by patient and study team. If oral compliance is documented separately, it should be uploaded with the corresponding calendar.

## Adverse Events (AE)

- The Adverse Event eCRF will capture all adverse events experienced for patients on a clinical trial. As discussed in the Medical History and Baseline Conditions section, it may also house medical history and baseline conditions, depending on the form version. All adverse event forms will have the same format, but some may list out the specific study agents if there are more than one, otherwise it will simply say “study agent.” AE eCRF entry should match source logs. In some instances, the source log may need to be modified to ensure the data entered in the eCRF has a corresponding source. Some examples include whether the event was a Dose Limiting Toxicity (DLT) or whether the event met expedited reporting criteria. There are other instances, with questions on the AE eCRF that are not listed on the logs, such as Outcome, Action taken etc. These questions should be answered based on other sources in the patient’s medical records. In the future, the Adverse Event eCRF will phase out such questions that will be captured elsewhere in the data. Since adverse events can be ongoing for a period of time, in such instances, the event line only needs to be “Saved.” Once all information on the eCRF has been entered and the event ends, or the patient is off study, the line can be submitted for review.
- **Using CTCAE** – Most studies will utilize the CTCAE for grading adverse events. Please check the version specified in the protocol and ensure you are using the correct version to grade events. The terms, categories, and grades are provided as a drop down menu on each adverse event form that is opened. The CTCAE is imported as a standard answer set. Therefore, you will only be able to select options as available in the CTCAE version you are using. If the adverse event is an abnormal lab value that cannot be found in the CTCAE, it most likely should not be included as an AE. For example, the patient’s BUN is elevated. This is not a CTCAE term. If the event is not a medically important event, does not correspond to a diagnosis, or does not meet any other adverse event criteria, it should be not included as an AE.
- **Term** – Use drop down menu to select appropriate term, or start typing to locate.
- **Category** – By selecting the term first, the category will automatically populate. Conversely, if you know the category, but not the term, you may start with the Category drop down first and the terms will be narrowed down.
- **Grade** – Use drop down menu to select correct grade. For grade 5 events, select only Grade 5 for the event that directly caused patient’s death. If the patient was experiencing multiple concurrent AEs at the time of death, only the AE that the PI determined was cause of death should be listed as grade 5.
- **Comments** – If it is necessary to use any term of “Other” within a category, please use the comments box to specify the details. The comments field should not include location of source from AE log. Anything that can and should be documented on a corresponding eCRF should not be included in the AE comments field, such as lab values.
- **Present at baseline** – This question only applies to older AE eCRFs. New studies have a separate form to catch medical history. Only those health issues that are active at the time of screening should be marked as “Yes”, “present at baseline”. If the same health condition changes grade during the study, the

subsequent AEs would be entered as a new line, with the new grade, and should be marked as “No”, “present at baseline”.

- **Start/End Dates** – Start date should be the date that the AE is first noted. It is not necessary to record a start date for any AE’s that are marked as “Yes”, “present at baseline”. End dates will either be the date of resolution of AE, or the date that the AE changes grade. Ongoing AEs at the time the patient is off study can be left without an end date and submitted for approval. AE end dates can be the same as the start date of next event.
- **Outcome** – Use drop down menu to select appropriate outcome. Select an outcome of “Change in Grade” rather than “Resolved” if the AE changes grade on the next day.
- **Relationship to Study Agent** – Use drop down menu to select the appropriate relationship - **Unrelated, Unlikely, Possible, Probably, Definite and Awaiting Physician Assessment**. Be sure that there is an attribution before submitting the form for approval. It is acceptable to use the “Awaiting Physician Assessment” selection as a placeholder until the investigator determines relationship, but do not submit the form for approval with that selected. If the same event changes attribution during the study, the event will be entered as a new line, with the new attribution. The previous entry will have the date of the attribution change in the end date field with an outcome of Not Resolved. This is the only instance where an end date and an outcome of Not Resolved can be used together.
- **Action Taken with Study Agent** – Use drop down menu to select the appropriate action that happened as a result of the AE. If no action was taken, please utilize the “Dose Not Changed” option. “N/A” should only be used for events present at baseline (when treatment administration did not yet begin) or for instances where a specific agent was not assigned to a patient (i.e. randomized trial).
- **Was Event Reported as SAE** – Any event that met the criteria of an SAE per protocol, should be recorded on the AE log and marked as “Yes” on this data field.
- **Off Treatment Due to this AE?** – Select “Yes” on this data field only if the AE directly led to the patient being taken off treatment.
- **Was event a DLT?** – DLT stands for Dose Limiting Toxicity. Phase I dose-finding protocols will define what events meet the criteria for a DLT, and use the collection of DLTs as part of the dose-finding cohort. Refer to the protocol to determine if this is applicable to your study. If not applicable, please select “No” on this data field. The investigator should be making this determination and documenting in source.

## Concomitant Medications

- Report all medications that the patient is taking, starting at the time point referenced in the protocol, usually from the time of signing informed consent. This data may also include concomitant surgeries, radiation, or any other intervention. If the patient is taking a medication for an ongoing/pre-existing health condition, enter the corresponding event on the Medical History or AE eCRF, as described in those sections. Since concomitant medications can be ongoing for a period of time, in such instances, the event line only needs to be “Saved.” Once all information on the eCRF has been entered and the medication ends, or the patient is off study, the line can be submitted for review. ConMed eCRF entry should match source logs.
- **Agent Name** – Medication name - generic or manufacturer name is acceptable
- **Agent Dose** – Enter only a numeric value here
- **Dose Unit** – Select from the drop down list for mg, mcg, IU, gram, inhalations, etc.
- **Agent Frequency** – Select from drop down menu. If the medication is being taken as PRN but also has instructions for how to take when it is needed, please only indicate PRN here.

Reference Material: NOTIS eCRF Guidelines

Version 2

12.11.2020



- **Agent Route** – Select appropriate medication route from drop down menu
- **Start Date** – If the patient is taking a medication at the start of the study and the start date is known, please enter here. If the patient starts a new medication while on the study, complete start date must be entered.
- **Start Date Unknown** – Use this date field if the patient is on a medication at the start of the study and cannot recall the exact date they started taking it. Reference guidance in the FAQ section of this document if an approximate date is known.
- **Reported Date** – Use this date field to enter when the patient reported the ConMed use to the study team/investigator.
- **Stop Date** – Complete this date field when a stop date for the medication is known
- **Indication** – Select from the drop down menu the reason that this medication is being given
  - **Adverse Event** – Use comment box to specify the corresponding AE (i.e. Gr 3 Anemia). A corresponding AE must be logged on the AE eCRF.
  - **Prophylaxis** – Most commonly used as the indication for vitamins or supplements
  - **Supportive Care (Per protocol)** – Select this option for any pre-meds that the study may require before each infusion. (i.e. Benadryl, Tylenol, etc.) It is ok for any meds that are given as supportive care to be left as ongoing. You do not need to enter the start and stop date for each of these meds for every time a patient received a study infusion.
  - **Treatment of Baseline Health Condition** – Use the comment box to indicate the corresponding baseline health condition. A corresponding baseline health condition must be logged on the Medical History or AE eCRF, as applicable.
  - **Other** – Use this selection sparingly, as most indications should be covered under the other selections. Specify in comment box.
- **Ongoing?** – Select “YES” for any ConMeds that are ongoing at the time of study discontinuation.

### Prior/Follow Up Treatment

- Complete one form for each prior or follow up cancer therapy that the patient received before or after the study (if applicable).
- **Cancer type** – Select from drop down menu
- **Treatment type** – Review all options from drop-down menu to select the most appropriate. Radiation, surgery and transplants are included on this list in addition to various drug therapies
- **Start Date** – Enter the start date of the treatment
- **End date** – Enter the end date of the treatment
- **Number of Cycles Completed** – Enter the number of cycles completed
- **Total Dose** – Enter the total dose received
- **Dose unit** – Enter the dose unit

### Follow-Up

- Almost all studies will collect follow-up data as specified by the time points in the study procedures table.
- **Date of Status Update** – Enter the date of the patient’s survival status. For a survival status of alive, the date will correspond to the date last known alive (e.g. the date of an office visit or phone call). For a survival status of deceased, the date will correspond to the date of death.
- **Patient Status** – Select status (**alive, deceased, lost to follow-up**) from drop down menu. A status of lost to follow-up will only be selected as an option once. Refer to the protocol prior to determining if a patient



is lost to follow-up. If no such guidance is indicated in the protocol, local policies may be used to determine if a patient is lost to follow-up. If the protocol nor policies do not exist, reference guidance in the FAQ section of this document to determine if a patient is lost to follow-up. If patient is lost to follow-up, enter the date last known alive.

- **Since Last Follow-Up, Has Patient progressed or relapsed after protocol therapy discontinued** – Only complete this section if progression/relapse was not already documented on a previous follow-up form or was not documented as the reason that the patient stopped study treatment. Unless specified, this form will capture the first progression date.
- **Has Patient Started New Anti-Cancer Therapy** – Enter only if not previously reported. If a new anti-cancer therapy was started, a corresponding follow-up treatment eCRF should be entered.
- **Has patient been diagnosed with a new primary cancer?** – Enter only if not previously reported; new metastases should NOT be entered here
- **Comments** – Provide any additional information that may be relevant to the patient's follow-up status (i.e. patient has progression and will be discharged to hospice).



## Queries

- As part of routine remote monitoring, the QAM will review all data that has been submitted for approval and will issue queries when there are discrepancies with the data or if data is missing that should have been entered.
- Queries are entered by the Quality Assurance Monitor in two (2) places - the queries dashboard and the form itself (form level queries). All queries are manually entered by the QAM. Form level queries can only be entered in existing data points.
- Queries Dashboard** – There is a blue button at the top of each patient’s eCRF page that says “Patient Queries” and lists how many are unresolved. Within this dashboard you will see who issued the query, what form it applies to, and the specifics in the query message about what needs to be addressed, changed, or updated on the form.

**Case Report Forms** Go to  Release No

Protocol #:  First Name:  Last Name:  Gender:  Case #:  Registration Date:  Survival Status: Alive NOTIS Patient Entry

[View More Info.](#)

[View all Patients for this Study](#) **Patient Queries: (13 Unresolved)** 

[Mark As Screen Fail](#)
[Unmark Off Tx](#)
[Unmark Off Study](#)
[Mark As Inter-Site](#)
[Mark As Transfer](#)

|  | Queried | Pending | Submitted | Approved |
|--|---------|---------|-----------|----------|
| <b>Time Points</b> Last Entered: <span style="color: orange;">Follow Up (Date Off Treatment through Date Off Study)</span> 02/11/2020 - 03/05/2020 | 0       | 0       | 2         | 2        |
| Consent Form v1  | 0       | 0       | 0         | 1        |

**Query by** Treatment and  Please upload patient diary from Cycle 2 and complete treatment forms.

06/29/2020 13:12

**Query by** Electrocardiogram (EKG) v2 Was EKG done on C6D1?

06/29/2020 13:09

Responded by  added

07/06/2020 09:55



- You may respond to the query with additional information or to state that the query was addressed by clicking the grey “Respond” button. The corresponding data point needs to be addressed, saved, and re-submitted for review. The query will remain on the dashboard until the QAM confirms that the query has been addressed and manually closes it out.
- There is a “Show/Hide Resolved Queries” link at the top of the queries tab. When clicked, it will toggle between showing and hiding resolved queries. All resolved queries have a green background while unresolved queries have a yellow background.

| Created by             | For Form                               | Message   |
|------------------------|--|---|
| Query by<br>[Redacted] | Adverse Events Nivolumab<br>[Redacted] | Please submit the pending form for approval<br>Delete Respond Mark as resolved Mark as Unread |
| 05/28/2020 13:37       |  |   |
| Query by<br>[Redacted] | Adverse Events Nivolumab<br>[Redacted] | Please enter SAE on 12/4/2017. Thanks!<br>Delete Respond Mark as unresolved Mark as Unread    |
| 02/07/2020 13:36       |  |   |
|                        | Responded by<br>[Redacted]             | Added SAE Mark as Read  |
|                        | 02/18/2020 15:29                       |   |

- On the patient’s main CRF page, you will see four columns to the right: “Queried” in red, “Pending” in black, “Submitted” in blue and “Approved” in green. You can easily see which forms fall under what category.
  - **Queried** forms are forms that have an open query that needs to be resolved.
  - **Pending** forms are forms that have been opened and data entry has been started and saved.
  - **Submitted** forms are forms in which all required data has been entered and is ready for review by the QAM.
  - **Approved** forms are forms that have been reviewed and approved by the QAM.



Mark As Screen Fail   **Unmark Off Tx**   **Unmark Off Study**   Mark As Inter-Site   Mark As Transfer

|   |   | Queried | Pending | Submitted | Approved |
|---|---|---------|---------|-----------|----------|
| <b>Time Points</b>                                  | Last Entered: Follow Up (Date Off Treatment through Date Off Study) 02/11/2020 - 03/05/2020 | 0       | 0       | 2         | 2        |
|   |   | Queried | Pending | Submitted | Approved |
| Consent Form v1                                     |   | 0       | 0       | 0         | 1        |
| Pathology v1  |   | 0       | 0       | 0         | 1        |
| Eligibility v1 (Submit ONLY when ready to register) |   | 0       | 0       | 0         | 1        |
| Prior Treatment v4                                  |   | 0       | 0       | 0         | 5        |
| Vitals v8 w/ ECOG PS                                |   | 0       | 0       | 0         | 4        |
| Physical Exam v2                                    |   | 0       | 0       | 0         | 4        |
| Electrocardiogram (EKG) v1                          |   | 0       | 0       | 0         | 1        |
| CBC with Differential (CBC w diff) v3               |   | 0       | 0       | 0         | 4        |
| Comprehensive Chemistry Panel v3                    |   | 0       | 0       | 0         | 4        |
| PSA v3  |   | 0       | 0       | 0         | 4        |
| Testosterone v1                                     |   | 0       | 0       | 0         | 1        |
| Treatment sEphB4-HSA v1                             |   | 0       | 0       | 0         | 2        |
| Adverse Events sEphB4-HSA v1                        |   | 5       | 0       | 2         | 18       |
| Concomitant Medications (Condensed) v1              |   | 0       | 0       | 13        | 0        |
| RECIST 1.1 Response v2                              |   | 0       | 0       | 0         | 1        |
| Correlative Samples v16                             |   | 0       | 0       | 0         | 2        |
| Follow Up v3  |   | 0       | 0       | 1         | 0        |

- You will see the forms that have been queried by clicking on the links. Please pay close attention to the query and all fields within that form as you amend the data. When you have completed the query request, you will need to click “Save” and then “Submit” for the form to be ready to be re-reviewed.

|            |   |                      |                  |   |     |            |                            |
|------------|---|----------------------|------------------|---|-----|------------|----------------------------|
| 10/15/2019 | <a href="#">Edit</a> <a href="#">Print</a><br>Queried: patient was registered on 10/1/2019, and this event starts 10/15/2019. Please confirm if present at baseline should be marked no. <a href="#">Status history</a><br><a href="#">Delete</a><br><input type="radio"/> Submit | Creatinine increased | Investigations 1 | 1.24mg/dL-10.15.2019<br>1.5mg/dL ???<br>10.26.2019<br>1.34mg/dL ???<br>10.29.2019 | Yes | 10/15/2019 | Not Recovered/Not Resolved |
|------------|---|----------------------|------------------|---|-----|------------|----------------------------|

- You must also then navigate back to the queries tab and respond to the query there.

**Tip:** If you have 2 computer monitor screens, open up the patient’s queries tab on one screen and the main eCRF page on another. This will allow you to easily view the queries within the tab on one screen while you navigate to the specified form on the other.



## FAQ

|  |   |
|--|---|
| <b>QUESTION:</b> Hyperglycemia – if fasting status cannot be confirmed is it documented as an AE for CTC AE version 4? | <b>ANSWER:</b> Assume patients not fasting unless noted, but will utilize current standard by team for studies.   |
| <b>Q:</b> What is the baseline to calculate weight loss?   | <b>A:</b> Vitals used for registration are baseline vitals  |
| <b>Q:</b> When is patient considered Lost to Follow Up?  | <b>A:</b> Unless protocol language states different criteria, patient will be considered lost to follow up after three documented attempts, on patient activity log in research chart (can be done in parallel, i.e. calling patient and also utilizing electronic search)  |
| <b>Q:</b> If physical exam component was not explicitly indicated in EMR – normal or not done?                         | <b>A:</b> If EMR notes “normal unless otherwise noted” can document as normal. If no clear documentation, should put not done.  |
| <b>Q:</b> Should physical exam abnormalities include items noted in the ROS, narrative and diary even if PE is normal? | <b>A:</b> It should match actual PE and ROS, all other abnormalities can be marked on AE log  |
| <b>Q:</b> How to enter the date if it is unknown and partial date is not allowed?                                      | <b>A:</b> If the Month and Year are known but the day is unknown, enter 15 for the Day. If only the Year is known, enter July 1 for Month and Day. Please ask subject to make a best guess/estimate for an unknown Year. If subject is not able to guess, please enter the result of the current year minus 10 years. |