



NINDS Common Data Element (CDE) Project

Traumatic Brain Injury Version 3.0

Internal Review / Public Review

Treatment/Intervention Data Subgroup Materials

Subgroup Summary

Instruments Pending Review

- Pediatric Intensity Level of Therapy (PILOT)
- Therapy Intensity Level (TIL)

Case Report Forms

- Adverse Events
- Discharge Status: Emergency Department, Intensive Care Unit, and Hospital
- Intraoperative Management
- Pre-Hospital and Emergency Department Therapies
- Prior and Concomitant Medications
- Rehabilitation Treatment
- Serious Adverse Events
- Surgical and Therapeutic Procedures



NINDS CDE Project Traumatic Brain Injury Version 3.0 Treatment/Intervention Data Subgroup Summary

The NINDS TBI v3.0 Common Data Element (CDE) Treatment/Intervention Data Subgroup updated CDEs describing evidence-based treatments commonly delivered in the care of traumatic brain injury patients and which are commonly collected to inform neuroscientific clinical research. Relevant venues of care considered included care in the emergency department, operating room, inpatient, rehabilitation and outpatient settings.

The Treatment/Intervention Data Subgroup focused on treatments that are commonly employed and known to affect important neurobehavioral or clinical outcomes, based on research evidence or expert consensus. The intent is to define traumatic brain injury treatments which, because of their efficacy, are likely associated with outcome and which could confound the interpretation of neurologic research. We provide standardized methods for documenting such treatments in ongoing studies along with key characteristics of administration. The subgroup did not attempt to develop CDEs for emerging treatments with an evolving evidence base.

The subgroup assessed data related to transitions of care (discharge status, ER destination) as well as treatment/intervention data (surgeries and other procedures, ER/admission therapeutic procedures, intraoperative management as well as surgical and therapeutic procedures), therapies (post discharge/outpatient treatment and therapeutic intensity level), safety data (AEs, SAEs), and lastly drug therapy (prior and concomitant medications).

Overlap addressed with other subgroups may include the Outcomes and Endpoints Subgroup as admission or discharge location could be considered either a treatment or an outcome. As well, there is potential overlap with the General Activities of Daily Living Subgroup as these are integral to the determination of care needs and patient transfers.



Summary of Recommendations

Subdomain	Instrument/CRF Name	Classification	Population
Discharge Information	Discharge Status: Emergency Department, Intensive Care Unit, and Hospital	Supplemental – Highly Recommended; Supplemental	Adult; Pediatric
Surgeries and Other Procedures	Pre-Hospital and Emergency Department Therapies	Supplemental – Highly Recommended; Supplemental	Adult; Pediatric
	Intraoperative Management	Supplemental	Adult; Pediatric
	Surgical and Therapeutic Procedures	Supplemental	Adult; Pediatric
Therapies	Pediatric Intensity Level of Therapy (PILOT)	Pending Review	Pediatric
	Therapy Intensity Level	Pending Review	Adult
	Rehabilitation Treatment	Supplemental – Highly Recommended; Supplemental	Adult; Pediatric
Drugs	Prior and Concomitant Medications	Supplemental	Adult; Pediatric
Adverse Events	Adverse Events	Supplemental – Highly Recommended	Adult; Pediatric
	Serious Adverse Events	Supplemental – Highly Recommended; Supplemental	Adult; Pediatric

Adverse Events
(New for TBI)

[Study Name/ID pre-filled]

Site Name:
Participant ID:

Visit Date:
Visit Name:

Has the participant had any adverse events during the study? ☐ No ☐ Yes

Table 1 Record diagnoses (if known) or signs/symptoms the participant experienced during the study that qualify as adverse events

Adverse Event	Onset Date and Time	Site AE Awareness Date	Ongoing?	Resolution Date	Severity	Investigator Assessment of Study Intervention Causality	Action Taken with Study Intervention	Other Action Taken	Outcome Attributed to the Event	Serious Adverse Event? ¹	Unexpected Adverse Event? ²	IRB Notified? ³
Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	<input type="checkbox"/> No <input type="checkbox"/> Yes	Data to be filled in by site	<input type="checkbox"/> Mild <input type="checkbox"/> Moderate <input type="checkbox"/> Severe	<input type="checkbox"/> Unrelated <input type="checkbox"/> Unlikely <input type="checkbox"/> Possible <input type="checkbox"/> Probable <input type="checkbox"/> Definite	<input type="checkbox"/> None <input type="checkbox"/> Study Intervention Interrupted <input type="checkbox"/> Study Intervention Discontinued <input type="checkbox"/> Study Intervention Modified <input type="checkbox"/> Other, specify:	<input type="checkbox"/> None <input type="checkbox"/> Non-Study Treatment Required	<input type="checkbox"/> Recovered/Resolved <input type="checkbox"/> Recovered/Resolved with Sequelae <input type="checkbox"/> Recovering/Resolving <input type="checkbox"/> Not Recovered/Not Resolved <input type="checkbox"/> Fatal	<input type="checkbox"/> No <input type="checkbox"/> Yes	<input type="checkbox"/> No <input type="checkbox"/> Yes	<input type="checkbox"/> No <input type="checkbox"/> Yes
Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	<input type="checkbox"/> No <input type="checkbox"/> Yes	Data to be filled in by site	<input type="checkbox"/> Mild <input type="checkbox"/> Moderate <input type="checkbox"/> Severe	<input type="checkbox"/> Unrelated <input type="checkbox"/> Unlikely <input type="checkbox"/> Possible <input type="checkbox"/> Probable <input type="checkbox"/> Definite	<input type="checkbox"/> None <input type="checkbox"/> Study Intervention Interrupted <input type="checkbox"/> Study Intervention Discontinued <input type="checkbox"/> Study Intervention Modified <input type="checkbox"/> Other, specify:	<input type="checkbox"/> None <input type="checkbox"/> Non-Study Treatment Required	<input type="checkbox"/> Recovered/Resolved <input type="checkbox"/> Recovered/Resolved with Sequelae <input type="checkbox"/> Recovering/Resolving <input type="checkbox"/> Not Recovered/Not Resolved <input type="checkbox"/> Fatal	<input type="checkbox"/> No <input type="checkbox"/> Yes	<input type="checkbox"/> No <input type="checkbox"/> Yes	<input type="checkbox"/> No <input type="checkbox"/> Yes

Recorder Signature:

Date:

¹ Serious: Yes should be answered to identify an adverse event defined by the investigator or sponsor as serious because it is life-threatening, results in death, requires in-patient hospitalization, prolongs existing hospitalization, results in persistent or significant disability, is a congenital anomaly/birth defect or is an important medical event.

² Unexpected: Yes should be answered to identify an adverse event that was not expected, based on those described in the Investigator’s Brochure for use of the investigational drug or medical device. An adverse event is categorized by the sponsor as “unexpected” because the adverse event has not been previously described in the Investigator’s Brochure or has increased in frequency or severity compared to what is described by the Investigator’s Brochure.

³ No: Not needed now because was not serious but will be reported at annual review; Yes: Required if serious.

Adverse Events CRF Module Instructions

GENERAL INSTRUCTIONS

Important note: None of the data elements included on this CRF Module are classified as Disease Core (i.e., strongly recommended for all TBI clinical studies). All the data elements are classified as Supplemental – Highly Recommended (i.e., strongly recommended for all study designs and certain disease conditions or study types) as they are critical for studies of an intervention, especially randomized controlled clinical trials of novel treatments. They will not necessarily be relevant to other studies.

The data elements on this CRF Module are part of the NINDS CDE Safety Data Domain.

Additional details regarding classification definitions are available: [Link to be added once available.]

Please see the Data Dictionary for element classifications.

ADVERSE EVENTS

Adverse events (AEs) document any unfavorable or untoward medical occurrence that is observed with use of a drug or medical device in a participant enrolled in a study without regard for cause or relationship. AEs are the construct through which the safety of an intervention is recorded and assessed during a study. Typical AE descriptors include event dates of onset and resolution, severity, causality, outcome, and seriousness.

RECORDING ADVERSE EVENTS

All AEs, both serious and non-serious, regardless of relationship to the study intervention, should be recorded on the AE CRF. AE data should be collected from the time the informed consent form is signed through the duration of the clinical investigation. Standard medical terminology should be used when recording AEs. Furthermore, it is recommended that studies that plan to submit data to regulatory authorities should code their AE data using the Medical Dictionary for Regulatory Activities (MedDRA): <https://www.meddra.org/> or Common Terminology Criteria for Adverse Events (CTCAE): https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm.

SERIOUS ADVERSE EVENTS

A serious adverse event (SAE) is defined as any untoward medical occurrence that: results in death; is a life-threatening medical situation; requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability or incapacity; is a congenital anomaly or birth defect; or is an important medical event.

Important medical events that may not result in death, be life threatening, or require hospitalization may be considered a serious adverse event when, based upon appropriate medical judgment, they may jeopardize the participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsion that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

If an event is documented as serious, then a separate SAE Report form must be completed. For studies under a Food and Drug Administration (FDA) Investigational New Drug (IND) application, a 3500A is completed and submitted as an expedited report, if the event is also unexpected and related to the study intervention. Because the data collected for an SAE are descriptive and beyond the scope of a study, the SAE information is usually kept in a separate file. In addition to the SAE descriptors, it is useful to track when the SAE is sent to the Institutional Review Board (IRB), sponsor, FDA, and Data Safety Monitoring Board (DSMB) and responses are received.

In some neurological studies, there has been confusion over the relationship between a study endpoint (e.g., myocardial infarction) and an SAE. The AE may be heart attack, described as mild. However, since it resulted in a hospitalization, it is coded as “serious” (SAE). The event may also be a study endpoint that is

Adverse Events CRF Module Instructions

captured on the SAE form and sent for adjudication. This process would be tracked but the information collected is generally beyond the study scope and is not captured on study CRFs nor entered into the study data management system.

Further safety reporting requirements for adverse events that occur during clinical trials using investigational medication(s) or device(s) can be found on the U.S. Food and Drug Administration website: [U.S. Food and Drug Administration Investigational New Drug Reporting Requirements](#)

SPECIFIC INSTRUCTIONS

Please see the Data Dictionary for definitions for each of the data elements included in this CRF Module.

- Any Adverse Events During the Study – Choose one. If answered YES, at least one AE must be recorded in Table 1.
- Definition of AE – Any untoward medical occurrence in a study participant that does not necessarily have a causal relationship with the study intervention. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a study intervention or study procedure, whether or not related to the study intervention or procedure. Each AE should be listed on a separate row of the table. Any worsening of a baseline condition or reoccurrence of a baseline condition that had previously ended for a time should be listed as an AE. Events, such as nausea and vomiting are considered two events, and therefore should be listed on separate lines. A participant may experience an unexpected AE. An unexpected adverse reaction has a nature or severity of which is not consistent with the study intervention description (e.g., Investigator's Brochure for an unapproved investigational product or package insert/summary of product characteristics for an approved product). The unexpected AE must be reported, whether related to the study intervention or not, with as much detail as is available. See the Data Dictionary for additional information on coding the adverse events using either the Common Terminology Criteria for Adverse Events (CTCAE) or the Medical Dictionary for Regulatory Activities (MedDRA).
- Onset Date and Time – Record the date and time the adverse event started. Record the date/time according to the [ISO 8601](#), the International Standard for the representation of dates and times. The date/time should be recorded to the level of granularity known (e.g., year, year and month, complete date plus hours and minutes, etc.) and in an unambiguous format acceptable to the study database like DD-MMM-YYYY. When date/time data are prepared for aggregation or sharing, they should be converted to the format specified by [ISO 8601](#); YYYY-MM-DD T:hh:mm:ss. If a previously recorded AE worsens, a new record should be created with a new start date/time. There should be no AE start date prior to the date of the informed consent. Any AE that started prior to the informed consent date belongs instead in the medical history. If an item recorded on the medical history worsens during the study, the date of the worsening is entered as an AE with the start date/time as the date/time the condition worsened.
- Site AE Awareness Date – Record the date and time the site became aware of the adverse event. Record the date/time according to the [ISO 8601](#), the International Standard for the representation of dates and times. The date/time should be recorded to the level of granularity known (e.g., year, year and month, complete date plus hours and minutes, etc.) and in an unambiguous format acceptable to the study database like DD-MMM-YYYY. When date/time data are prepared for aggregation or sharing, they should be converted to the format specified by [ISO 8601](#); YYYY-MM-DD T:hh:mm:ss.
- Ongoing? – Choose No or Yes. If NO, record date of resolution.
- Resolution Date – Record the date (and time) the adverse event stopped or worsened. Record the date/time according to the [ISO 8601](#), the International Standard for the representation of dates and times. The date/time should be recorded to the level of granularity known (e.g., year, year and month, complete date plus hours and minutes, etc.) and in an unambiguous format acceptable to the study database like DD-MMM-YYYY. When date/time data are prepared for aggregation or sharing,

Adverse Events CRF Module Instructions

they should be converted to the format specified by [ISO 8601](#); YYYY-MM-DD T:hh:mm:ss. If an AE worsens, record an end date/time and create a new AE record with a new start date/time and severity.

- Severity – Choose the one severity that best describes the investigator’s assessment of the intensity of the AE. The three severity grades are from the [Clinical Data Interchange Standards Consortium \(CDISC\) terminologies](#). Severe events interrupt the participant’s normal daily activities and generally require systemic drug therapy or other treatment; they are usually incapacitating. Consequently, a change in severity may constitute a new reportable AE. Severity is not synonymous with seriousness. A severe rash is not likely to be an SAE. Likewise, a severe headache is not necessarily an SAE. However, mild chest pain may result in a day’s hospitalization and thus is an SAE. It is helpful to define the severity categories in the protocol or Manual of Operations to obtain consistency in reporting across sites.
- Investigator Assessment of Study Intervention Causality – Choose one. Record the investigator’s assessment as to whether there is at least a reasonable possibility that the AE is related to (or caused by) use of the study intervention. Definitions for each of the relatedness response should be supplied in the protocol. Permissible values included are from [NCI Guidelines: Adverse Event Reporting Requirements](#):
 - Unrelated to investigational agent/intervention
 - Unrelated – The AE *is clearly NOT related* to the intervention
 - Unlikely – The AE *is doubtfully related* to the intervention
 - Related to investigational agent/intervention
 - Possible – The AE *may be related* to the intervention
 - Probably – The AE *is likely related* to the intervention
 - Definite – The AE *is clearly related* to the intervention
- Action Taken with Study Intervention – Choose one. This CDE is only appropriate for clinical trials and should be removed from the CRF if a study does not have an intervention.
- Other Action Taken – Choose one. If non-study medical treatment was required, then the corresponding medication(s) needs to be recorded on the Prior and Concomitant Medications CRF. If non-study interventions other than medications were required, they need to be documented on the appropriate study-specific CRF.
- Outcome Attributed to the Event – Choose one. The outcome of an AE may not be captured at the visit during which it was first reported but must be captured to provide a complete picture of the event. Entering the outcome of an AE may be deferred until the AE is resolved, or the participant completes the study. For AEs that have not resolved at the time of a study visit, the outcome should be marked as “Not recovered/Not resolved” on the AE CRF.
- Serious Adverse Event? – Choose either No or Yes. This question should only be answered YES if the outcome of the AE results in at least one of the following: death; a life-threatening experience; inpatient hospitalization; prolongation of existing hospitalization; a persistent or significant disability or incapacity; a congenital anomaly/birth defect; or an Important Medical Event. If an AE is serious, this provides a trigger that additional information must be provided by the site investigator. The site investigator then completes a Serious Adverse Event (SAE) form. Additionally, the site institution and/or IRB may also have an SAE form and procedures for reporting SAEs.
- Unexpected Adverse Event? – Choose No or Yes. This question should be answered YES if the AE was not previously identified as an adverse event associated with use of the investigational drug or medical device, based on those described in the Investigator’s Brochure. An event may also be identified as unexpected if the adverse event increased in frequency or severity than what is described by the Investigator’s Brochure.

Discharge Status:

Emergency Department, Intensive Care Unit, and Hospital

[Study Name/ID pre-filled]

Site Name:

Participant ID:

Visit Date:

Visit Name:

EMERGENCY DEPARTMENT DISCHARGE STATUS

1. Where was the participant/~~subject~~ discharged to from the Emergency Department ~~ER~~? (Choose one)

- | | |
|---|--|
| <input type="checkbox"/> N/A – participant patient dead on arrival | <input type="checkbox"/> Admission to hospital – intermediate/ high care unit |
| <input type="checkbox"/> N/A – participant patient died in Emergency Room | <input type="checkbox"/> Discharge to nursing home skilled nursing facility (SNF) |
| <input type="checkbox"/> Admission to hospital – ward | <input type="checkbox"/> Discharge to long term acute care hospital (LTACH) |
| <input type="checkbox"/> Admission to hospital – ICU | <input type="checkbox"/> Discharge to street/shelter |
| <input type="checkbox"/> Admission to hospital – other (e.g., observation unit) | <input type="checkbox"/> Left against medical advice |
| <input type="checkbox"/> Discharge to other hospital | <input type="checkbox"/> **Other, specify: |
| <input type="checkbox"/> Discharge to home | <input type="checkbox"/> Unknown |
| <input type="checkbox"/> Independent, lives alone | |
| <input type="checkbox"/> Independent, lives with others (spouse, significant other, adult children, roommate, friend) | |
| <input type="checkbox"/> Home of parents, guardians, relatives | |

~~** Emergency room discharge destination reason~~

- ☐ ~~Medical necessity~~
☐ ~~Social circumstances~~
☐ ~~No ICU beds available~~
☐ ~~Requiring specialized facilities~~
☐ ~~Normal CT~~
☐ ~~Unknown~~
☐ ~~Other, specify:~~

IF ADMITTED TO HOSPITAL COMPLETE: HOSPITAL DISCHARGE STATUS

1. **Vital status on hospital discharge (Choose one):

- ☐ Alive
☐ Dead (Stop here. Complete death form)
☐ Unknown

2. **Hospital discharge date and time:

3. **Where was the participant discharged to from the hospital? ~~Destination upon discharge from hospital~~ (Choose one):

- | | |
|---|---|
| <input type="checkbox"/> Discharge to rehabilitation unit | <input type="checkbox"/> Discharge to street/shelter |
| <input type="checkbox"/> Discharge to other hospital | <input type="checkbox"/> Left against medical advice |
| <input type="checkbox"/> Discharge to nursing home skilled nursing facility (SNF) | <input type="checkbox"/> Emergency Department-Non-trauma Center |
| <input type="checkbox"/> Discharge to long term acute care hospital (LTACH) | <input type="checkbox"/> **Other, specify: |
| <input type="checkbox"/> Discharge to home/ private residence | <input type="checkbox"/> Unknown |
| <input type="checkbox"/> Independent, lives alone | |
| <input type="checkbox"/> Independent, lives with others (spouse, significant other, adult children, roommate, friend) | |
| <input type="checkbox"/> Home of parents, guardians, relatives | |

Discharge Status:

Emergency Department, Intensive Care Unit, and Hospital

[Study Name/ID pre-filled]

Site Name:

Participant ID:

~~** Where was the definitive clinical care received for the participant/subject? (Choose one):~~

- ☐ ~~None~~
- ☐ ~~Outpatient Clinic~~
- ☐ ~~Emergency Department-Trauma Center~~
- ☐ ~~Emergency Department-Non-trauma Center~~
- ☐ ~~**Other, specify:~~

~~Additional Supplemental Elements:~~

~~These elements may be included if relevant to the study. For additional details like permissible values, see the data dictionary associated with this GRF.~~

IF ADMITTED TO THE INTENSIVE CARE UNIT (ICU): COMPLETE ICU DISCHARGE

1. ICU discharge date and time:

2. Where was the participant discharged to from the ICU? (Choose one)

~~ICU discharge destination type:~~

- | | |
|---|---|
| <input type="checkbox"/> N/A – participant patient died | <input type="checkbox"/> Discharge to home |
| <input type="checkbox"/> Discharge to other ICU | <input type="checkbox"/> Independent, lives alone |
| <input type="checkbox"/> Discharge to general ward | <input type="checkbox"/> Independent, lives with others (spouse, significant other, adult children, roommate, friend) |
| <input type="checkbox"/> Discharge to rehabilitation unit | <input type="checkbox"/> Home of parents, guardians, relatives |
| <input type="checkbox"/> Discharge to other hospital | <input type="checkbox"/> Discharge to street/shelter |
| <input type="checkbox"/> Discharge to nursing home skilled nursing facility (SNF) | <input type="checkbox"/> Left against medical advice |
| <input type="checkbox"/> Discharge to long term acute care hospital (LTACH) | <input type="checkbox"/> Other, specify: |
| | <input type="checkbox"/> Unknown |

3. ICU length of stay (days):

Recorder Signature:

Date:

Discharge Status: Emergency Department, Intensive Care Unit, and Hospital CRF Module Instructions

GENERAL INSTRUCTIONS

This case report form (CRF) collects information on the discharge status and destination of participants following treatment for traumatic brain injury in the emergency department, hospital ward, and intensive care unit. Complete the form at the time of final discharge from the facility, using only the predefined response options to ensure consistency across cases. All efforts should be made to minimize missing data and confirm the information before completion.

Important note: None of the data elements included on this CRF Module are classified as Disease Core (i.e., strongly recommended for all TBI clinical studies). Some of the data elements are classified as Supplemental – Highly Recommended (i.e., strongly recommended for all study designs and certain disease conditions or study types), as indicated by asterisks below, and should be collected in studies where discharge status and destination provide important information on patient outcomes, care transitions, and healthcare utilization.

****Element is classified as Supplemental – Highly Recommended**

The remaining data elements are classified as Supplemental and should only be collected if the research team considers them appropriate for their study design and type(s).

The Supplemental CDEs are applicable to the following study designs and types:

In all study designs involving TBI patients, such as clinical trials and observational cohorts, where discharge status and destination provide important information on patient outcomes, care transitions, and healthcare utilization.

The data elements on this CRF Module are part of the NINDS CDE Treatment/Intervention Data Domain.

Additional details regarding classification definitions are available: [Link to be added once available.]

Please see the Data Dictionary for element classifications.

~~Some of the data elements are classified as Basic (i.e., essential information for specified conditions, study types, or designs), as indicated by asterisks below, for at least one study type.~~

~~**Element is classified as Basic~~

~~Additional classification information is provided below:~~

- ~~● Emergency department room discharge destination type other text — Classified as Basic for Acute Hospitalized and Epidemiology studies~~
- ~~● Emergency room discharge destination reason — Classified as Basic for Acute Hospitalized and Epidemiology studies~~
- ~~● Vital status — Classified as Basic for Acute Hospitalized studies~~
- ~~● Hospital discharge date and time — Classified as Basic for Acute Hospitalized and Moderate/Severe TBI: Rehabilitation studies~~
- ~~● Hospital discharge destination type — Classified as Basic for Acute Hospitalized, Epidemiology, and Moderate/Severe TBI: Rehabilitation studies~~
- ~~● Hospital discharge destination other text — Classified as Basic for Acute Hospitalized, Epidemiology, and Moderate/Severe TBI: Rehabilitation studies~~
- ~~● Definitive clinical care post trauma location type — Classified as Basic for Concussion/Mild TBI and Epidemiology studies~~
- ~~● Definitive clinical care post trauma location other text — Classified as Basic for Concussion/Mild TBI and Epidemiology studies~~

Discharge Status: Emergency Department, Intensive Care Unit, and Hospital CRF Module Instructions

~~The remaining data elements are classified as Supplemental (i.e., non-Core) and should only be collected if the research team considers them appropriate for their study.~~

SPECIFIC INSTRUCTIONS

Please see the Data Dictionary for definitions for each of the data elements included in this CRF Module.

- Where was the participant discharged to from the Emergency Department? – Choose one. Response obtained ~~prospectively or retrospectively~~ from the source documents.
 - Where was the participant discharged to from the Emergency Department? Other, specify – Response is obtained ~~prospectively or retrospectively~~ from the source documents. The destination on discharge from the emergency department room is generally related to the severity of injuries and indicates the intensity of care considered appropriate.
If Discharged from the Emergency Department to:
Admission to hospital – ward
Admission to hospital – ICU
Admission to hospital – other (e.g., observation unit)
Complete the remaining items on the form, as appropriate for the participant's clinical course
 - ~~• Emergency room discharge destination reason – Choose one. Response is obtained prospectively or retrospectively from the source documents. The destination on discharge from the emergency room is generally related to the severity of injuries and indicates the intensity of care considered appropriate.~~
 - ~~• Emergency room discharge destination reason other text – Choose one. Response obtained prospectively or retrospectively from the source documents.~~
 - Vital status on hospital discharge – Choose one. Response is obtained retrospectively from the source documents.
 - Hospital discharge date and time – Date/time should be recorded to the level of granularity known (e.g., year, year and month, complete date plus hours and minutes, etc.) and in an unambiguous format acceptable to the study database like DD-MMM-YYYY. When date/time data are prepared for aggregation or sharing, they should be converted to the format specified by [ISO 8601](#); YYYY-MM-DD T:hh:mm:ss. Response is obtained retrospectively from the source documents.
 - Where was the participant discharged to from the hospital? – Choose one. Response is obtained retrospectively from the source documents.
 - Where was the participant discharged to from the hospital? Other, specify – Response is obtained retrospectively from the source documents.
 - ~~• Definitive clinical care post trauma location type – Choose one.~~
 - ~~• Definitive clinical care post trauma location other text – Choose one.~~
- If the participant spent time in the ICU complete the remaining questions on the form.
- ICU discharge date time – Date/time should be recorded to the level of granularity known (e.g., year, year and month, complete date plus hours and minutes, etc.) and in an unambiguous format acceptable to the study database like DD-MMM-YYYY. When date/time data are prepared for aggregation or sharing, they should be converted to the format specified by [ISO 8601](#); YYYY-MM-DD T:hh:mm:ss. Response is obtained retrospectively from the source documents.
 - Where was the participant discharged to from the ICU? – Choose one. Response is obtained retrospectively from the source documents.
 - Where was the participant discharged to from the ICU? Other, specify – Response is obtained retrospectively from the source documents.
 - ICU stay duration – Record the duration of the participant's stay in the ICU in days. Response is obtained retrospectively from the source documents.

Ex) If the participant's clinical course is from the ED, to the ICU, to the hospital wards, all sections of the form should be completed

Discharge Status: Emergency Department, Intensive Care Unit, and Hospital CRF Module Instructions

REFERENCES

Reid LD (AHRQ), Fingar KR (IBM Watson Health). Inpatient Stays and Emergency Department Visits Involving Traumatic Brain Injury, 2017. HCUP Statistical Brief #255. March 2020. Agency for Healthcare Research and Quality, Rockville, MD. <https://hcup-us.ahrq.gov/reports/statbriefs/sb255-Traumatic-Brain-Injury-Hospitalizations-ED-Visits-2017.jsp>.

Yue JK, Krishnan N, Chyall L, Haddad AF, Vega P, Caldwell DJ, Umbach G, Tantry E, Tarapore PE, Huang MC, Manley GT, DiGiorgio AM. Predictors of Extreme Hospital Length of Stay After Traumatic Brain Injury. World Neurosurg. 2022 Nov;167:e998-e1005. Epub 2022 Sep 1.

Intraoperative Management

[Study Name/ID pre-filled]

Site Name:
Participant ID:

Visit Date:

Visit Name:

1. American Society of Anesthesiologists (ASA) monitor type (Choose all that apply):

- ☐ BP
- ☐ ECG
- ☐ SaO2
- ☐ End-tidal CO2

~~Advanced neuromonitoring in place?~~

- ☐ ~~Yes~~
- ☐ ~~No~~
- ☐ ~~Unknown~~

2. Intraoperative neuromonitoring in place? Choose all that apply.

- ☐ Intracranial pressure (external ventricular drain)
Most abnormal intraoperative value recorded:
- ☐ Intracranial pressure (parenchymal monitor)
Most abnormal intraoperative value recorded:
- ☐ PbtO2 monitoring
Most abnormal intraoperative value recorded:
- ☐ SjVO2 monitoring
Most abnormal intraoperative value recorded:
- ☐ Electrode for EEG monitoring
Most abnormal finding and number/frequency:
- ☐ Microdialysis
Most abnormal intraoperative value recorded for each metabolite:
- ☐ Other, specify:
Most abnormal intraoperative value recorded:
- ☐ Unknown

3. Temperature measurement (Celsius):

a. Means of measuring temperature?

- ☐ Oral
- ☐ Rectal
- ☐ Tympanic
- ☐ Axillary
- ☐ Forehead Cutaneous Infrared
- ☐ Bladder
- ☐ Esophageal
- ☐ Brain
- ☐ Other, specify:
- ☐ Unknown

~~Partial pressure oxygen brain tissue measurement (mmHg)~~

4. Hypocapnia measured during surgery? ~~Inadvertent hypocapnia indicated?~~

- ☐ Yes, intentional
- ☐ Yes, unintentional
- ☐ Yes, unknown intention

Intraoperative Management

[Study Name/ID pre-filled]

Site Name:
Participant ID:

- ☐ No
- ☐ Suspected
- ☐ Unknown

5. Hypotension (SBP<100mmHg) measured during surgery?

- ☐ Yes
- ☐ No
- ☐ Suspected
- ☐ Unknown
- b. If Yes, duration:
- c. If Yes, lowest recorded value:

6. Hypoxia (SpO2<90% or pO2 < 60mmHg) measured during surgery?

- ☐ Yes
- ☐ No
- ☐ Suspected
- ☐ Unknown
- d. If Yes, duration:
- e. If Yes, lowest recorded value:

~~Volatile intravenous anesthesia given?~~

- ☐ ~~Yes~~
- ☐ ~~No~~
- ☐ ~~Unknown~~

7. Type of anesthesia administered? (Choose all that apply) (Please enter medications in Prior and Concomitant Medications CRF)

- ☐ Volatile
- ☐ Intravenous
- ☐ Unknown
- ☐ Other, specify:

8. Arterial line used?

- ☐ Yes
- ☐ No
- ☐ Unknown

9. Foley catheter used?

- ☐ Yes
- ☐ No
- ☐ Unknown

10. Blood transfusion performed?

- ☐ Yes
- ☐ No
- ☐ Unknown

If Yes, volume of blood transfusion:

11. Other blood product transfusion type performed (Choose all that apply):

- ☐ FFP
- ☐ Platelet
- ☐ Cryoppt

Intraoperative Management

[Study Name/ID pre-filled]

Site Name:
Participant ID:

☐ ~~pRBC~~

If Yes, volume of product transfusion:

12. Were any pharmacologic treatments administered to reverse coagulopathy just before or during surgery (e.g., factor VII, vitamin K, prothrombin complex concentrates (PCC), fresh frozen plasma (FFP), adexanet alfa, desmopressin (DDAVP), tranexamic acid (TXA), aminocaproic acid)?

☐ Yes (if Yes, please enter medications in Prior and Concomitant Medications CRF)

☐ No

☐ Unknown

13. Duration of surgery: (minutes)

14. Extubated at end of case?

☐ Yes

☐ No

☐ Unknown

~~Microdialysis glutamate value~~

~~Microdialysis lactate to pyruvate ratio value~~

15. Cerebral spinal fluid drainage ~~indicated~~ performed during surgery?

☐ Yes

☐ No

☐ Unknown

16. Pre op hemoglobin:

17. Post-op hemoglobin:

18. Estimated intraoperative blood loss:

19. Use of intraoperative vasopressors?

☐ Yes (if Yes, please enter medications in Prior and Concomitant Medications CRF)

☐ No

☐ Unknown

20. Use of induction agents (e.g., ketamine, etomidate)?

☐ Yes (if Yes, please enter medications in Prior and Concomitant Medications CRF)

☐ No

☐ Unknown

21. Maximum peak airway pressure during case:

22. Any intraoperative airway pressure concerns?

☐ Yes

☐ No

☐ Unknown

23. Hyperglycemia measured during procedure?

☐ Yes

☐ No

☐ Unknown

Intraoperative Management

[Study Name/ID pre-filled]

Site Name:
Participant ID:

24. Hypoglycemia measured during procedure?

- ☐ Yes
☐ No
☐ Unknown

Recorder Signature:

Date:

Intraoperative Management CRF Module Instructions

GENERAL INSTRUCTIONS

This case report form (CRF) contains data elements that collect information related to intraoperative management during procedures for traumatic brain injury treatment.

Important note: None of the data elements included on this CRF Module are classified as Disease Core (i.e., strongly recommended for all TBI clinical studies).

All the data elements are classified as Supplemental and should only be collected if the research team considers them appropriate for their study design and type(s).

The Supplemental CDEs may be applicable to the following study designs and type: Clinical Trials, Observational Studies, Comparative Effectiveness Studies, and/or Epidemiologic Studies and of utility in select studies where intraoperative treatment must be considered in an overall treatment effect.

The data elements on this CRF Module are part of the NINDS CDE Treatment/Intervention Data Domain.

Additional details regarding classification definitions are available: [Link to be added once available.]

Please see the Data Dictionary for element classifications.

SPECIFIC INSTRUCTIONS

Please see the Data Dictionary for definitions for each of the data elements included in this CRF Module.

Note that gathered data specifically refers to intraoperative findings or events defined as those occurring while the patient is physically within an operating theater or equivalent room of a care facility. The exception is anticoagulation reversal where we are interested not only in products administered intraoperatively but also those administered just prior to the procedure often in a different care environment. Throughout we have aimed to capture and characterize events and treatments which may be associated with the outcome of the patient. Particular attention is paid to secondary insults which may be associated with additional neurologic injury and poorer prognosis. Many types of second insults may occur in the in-hospital situation, both systemic and intracranial. Systemic second insults may also include, for example, episodes of hypoglycemia, hyponatremia, hypernatremia, hyperthermia and many more.

We recommend documenting the clinically most relevant and frequently occurring second insults: hypoxia, hypotension, inadvertent hypocapnia and seizure activity. Hypoxia, hypotension and inadvertent hypocapnia are the most frequent causes of jugular desaturations, and periods of low brain tissue oxygen tension. The depth and duration of systemic second insults during the clinical course is related to poorer outcome. Accurate detection of the number and duration of episodes of second insults should be possible in modern care environments. An effort to document the depth and duration of such insults is desirable. Pediatric-specific notes: Second insults are commonly defined by threshold values but these values are not well established in pediatrics. Based on the available data for pediatric TBI, thresholds of 80-180 mg/dL for glucose are recommended. A threshold for hemoglobin is more difficult to define given emerging data on the lower limit of hemoglobin safely tolerated by critically ill children in general and the variable effect of blood transfusion in children with severe TBI specifically.

- ASA (American Society of Anesthesiologists) monitor type – Choose all that apply.
<https://www.asahq.org/standards-and-practice-parameters/standards-for-basic-anesthetic-monitoring#:~:text=2.3.2%20Methods%20%E2%80%93any%20interruption%20at%20any%20time.%E2%80%9D>
- ~~Advanced neuromonitoring in place? — Choose one.~~

Intraoperative Management CRF Module Instructions

- Intraoperative neuromonitoring in place? - Choose all that apply. Refers only to monitors in place during another surgical procedure, and not to placement of the devices.
- Most abnormal intraoperative value recorded – Enter the most abnormal value recorded from the selected intraoperative neuromonitoring modality. The recorded value should be confident they are recording a valid reading and not an artifact.
- Temperature measurement – Record the participant's temperature in degrees Celsius.
- Means of measuring temperature? – Choose one. If Other, specify is selected, record the location where the temperature was measured.
- ~~Partial pressure oxygen brain tissue measurement – Capture in millimeters of mercury (mmHg).~~
- Hypocapnia measured during surgery? – Choose one. Response obtained from medical charts and/or patient data management system. Add date stamp for when assessed. Hypocapnia reduces cerebral blood flow and volume; it can result from inadvertent or intentional hyperventilation. It can be used as a treatment for intracranial hypertension but can result in cerebral ischemia.
- Hypotension (SBP<100mmHg) measured during surgery? – Choose one. Note that across multiple published guidelines higher blood pressure targets are now recommended than in the past. Given this we have selected the 100mmHg as a contemporary adult systolic blood pressure threshold for hypotension, recognizing that some sources recommend age-specific values.
- Hypotension duration – If hypotension is measured during surgery, record duration in minutes.
- Hypotension lowest recorded value – If hypotension is measured during surgery, enter lowest recorded value.
- Hypoxia (SpO2<90% or pO2 < 60mmHg) measured during surgery? – Choose one. We recognize that different sources recognize different threshold definitions for hypoxia, with some higher than 90%.
- Hypoxia duration – If hypoxia is measured during surgery, record duration in minutes.
- Hypoxia lowest recorded value – If hypoxia is measured during surgery, enter lowest recorded value.
- ~~Volatile or intravenous anesthesia indicator – Choose one.~~
- Type of anesthesia administered? – Choose all that apply. Please enter medications in Prior and Concomitant Medications CRF.
- Arterial line used? – Choose one.
- Foley catheter used? – Choose one.
- Blood transfusion performed? – Choose one.
- Volume of blood transfusion – If blood transfusion is performed, record volume in units.
- Other blood product transfusion performed – Choose all that apply.
- Volume of product transfusion – If other blood product transfusion is performed, record volume in units, packs or mLs.
- Were any pharmacologic treatments administered to reverse coagulopathy just before or during surgery? – Choose one. If Yes, please enter medications in Prior and Concomitant Medications CRF. Examples include factor VII, vitamin K, prothrombin complex concentrates (PCC), fresh frozen plasma (FFP), adexanet alfa, desmopressin (DDAVP), tranexamic acid (TXA), aminocaproic acid.
- Duration of surgery – Record duration of surgery in minutes.
- Extubated at end of case? – Choose one.
- Cerebral spinal fluid drainage performed during surgery? – Choose one.
- Pre op hemoglobin – Record preoperative hemoglobin measurement in g/dL.
- Post op hemoglobin – Record postoperative hemoglobin measurement in g/dL.
- Estimated intraoperative blood loss – Record estimated volume of intraoperative blood loss in mL/cc.
- Use of intraoperative vasopressors? – Choose one. If Yes, please enter medications in Prior and Concomitant Medications CRF.
- Use of induction agents (e.g., ketamine, etomidate)? – Choose one. If Yes, please enter medications in Prior and Concomitant Medications CRF.
- Maximum peak airway pressure during case – Record maximum peak pressure measurement from ventilator.
- Any intraoperative airway pressure concerns? – Choose one.
- Hyperglycemia measured during procedure? – Choose one.

Intraoperative Management CRF Module Instructions

- Hypoglycemia measured during procedure?– Choose one.

REFERENCES

Adelson PD, Bratton SL, Carney NA, Chesnut RM, du Coudray HE, Goldstein B, Kochanek PM, Miller HC, Partington MD, Selden NR, Warden CR, Wright DW; American Association for Surgery of Trauma; Child Neurology Society; International Society for Pediatric Neurosurgery; International Trauma Anesthesia and Critical Care Society; Society of Critical Care Medicine; World Federation of Pediatric Intensive and Critical Care Societies. Guidelines for the acute medical management of severe traumatic brain injury in infants, children, and adolescents. Chapter 6. Threshold for treatment of intracranial hypertension. *Pediatr Crit Care Med*. 2003 Jul;4(3 Suppl):S25-7.

McHugh GS, Engel DC, Butcher I, Steyerberg EW, Lu J, Mushkudiani N, Hernández AV, Marmarou A, Maas AI, Murray GD. Prognostic value of secondary insults in traumatic brain injury: results from the IMPACT study. *J Neurotrauma*. 2007 Feb;24(2):287-93.

Signorini DF, Andrews PJ, Jones PA, Wardlaw JM, Miller JD. Adding insult to injury: the prognostic value of early secondary insults for survival after traumatic brain injury. *J Neurol Neurosurg Psychiatry*. 1999 Jan;66(1):26-31.

~~ER/Admission Therapeutic Procedures~~ Pre-hospital and Emergency Department Therapies

[Study Name/ID pre-filled]

Site Name:
Participant ID:

Visit Date:
Visit Name:

1. Were any treatments performed to support airway/breathing? (Choose one)
☐ Yes
☐ No
☐ Unknown
2. If Yes, type(s) of airway/breathing treatment? (Choose all that apply)
☐ Supplemental oxygen
☐ Adjunctive airway
☐ Temporary support with bag, valve, mask
☐ ~~Intubation~~
☐ Endotracheal intubation
☐ Nasal intubation
☐ Mechanical ventilation
☐ Unknown
☐ ~~No specific treatment~~
☐ Other, specify:
3. Were any pharmacologic treatments administered for sedation and/or paralysis? (Choose one)
☐ Yes (if Yes, please enter medications in Prior and Concomitant Medications CRF)
☐ No
☐ Unknown
4. Were any pharmacologic treatments administered to reverse coagulopathy? (Choose one)
☐ Yes (if Yes, please enter medications in Prior and Concomitant Medications CRF)
☐ No
☐ Unknown
5. Were any pharmacologic treatments (vasoactive medications) administered to raise or lower blood pressure? (Choose one)
☐ Yes (if Yes, please enter medications in Prior and Concomitant Medications CRF)
☐ No
☐ Unknown
6. Were any pharmacologic treatments administered to reduce cerebral edema and/or intracranial pressure? (Choose one)
☐ Yes (if Yes, please enter medications in Prior and Concomitant Medications CRF)
☐ No
☐ Unknown
7. Were any pharmacologic treatments administered to prevent or treat seizures? (Choose one)
☐ Yes (if Yes, please enter medications in Prior and Concomitant Medications CRF)
☐ No
☐ Unknown
8. ******Were any intracranial procedures performed ~~on participant/subject~~? (Choose one)
☐ Yes
☐ No
☐ Unknown

~~ER/Admission Therapeutic Procedures~~ **Pre-Hospital and Emergency Department Therapies**

[Study Name/ID pre-filled]

Site Name:
Participant ID:

9. If Yes, type(s) of intracranial procedure? (Choose all that apply)

- ☐ External ventricular drain
- ☐ Intracranial pressure monitor
- ☐ Brain tissue oxygenation monitor
- ☐ Local debridement and closure
- ☐ Unknown
- ☐ Other, specify:
- ☐ ~~Lobectomy~~
- ☐ ~~Evacuate SDH Subdural~~
- ☐ ~~Evacuate EH Epidural~~
- ☐ ~~Evacuate IH Intracranial~~
- ☐ ~~Abscess drainage~~
- ☐ ~~VP shunt programmable~~
- ☐ ~~VP shunt Non-programmable~~
- ☐ ~~Shunt revision~~
- ☐ ~~Cranioplasty~~
- ☐ ~~Decompression Craniectomy~~
- ☐ ~~Craniotomy~~
- ☐ ~~Brain debridement~~
- ☐ ~~None~~

Recorder Signature:

Date:

~~ER/Admission Therapeutic Procedures~~ **Pre-Hospital and Emergency Department Therapies CRF Module Instructions**

GENERAL INSTRUCTIONS

This case report form (CRF) contains data elements that collect information related to therapeutic procedures the participant received pre-hospital or in the emergency department for traumatic brain injury treatment. Details on pharmacologic treatments should be recorded in the Prior and Concomitant Medications CRF.

Important note: None of the data elements included on this CRF Module are classified as Disease Core (i.e., strongly recommended for all TBI clinical studies). One data element is classified as ~~Basic (i.e., essential information for specified conditions, study types, or designs)~~ Supplemental – Highly Recommended (i.e., strongly recommended for all study designs and certain disease conditions or study types), as indicated by the asterisks below, and should be collected if acute or early outcome studies in which participants receive pre-hospital or Emergency Department care are performed.

****Element is classified as Supplemental – Highly Recommended**

The remaining data elements are classified as Supplemental and should only be collected if the research team considers them appropriate for their study design and type(s).

The Supplemental CDEs are applicable to the following study designs and types: All study designs and domains; recommended for acute or early outcome studies in which participants receive pre-hospital or Emergency Department care.

The data elements on this CRF Module are part of the NINDS CDE Treatment/Intervention Data Domain.

Additional details regarding classification definitions are available: [Link to be added once available.]

Please see the Data Dictionary for element classifications.

SPECIFIC INSTRUCTIONS

Please see the Data Dictionary for definitions for each of the data elements included in this CRF Module.

- Were any treatments performed to support airway/breathing? – Choose one.
- If Yes, type(s) of airway/breathing treatment? – Choose all that apply.
- Were any pharmacologic treatments administered for sedation and/or paralysis? – Choose one. If Yes, please enter medications in Prior and Concomitant Medications CRF.
- Were any pharmacologic treatments administered to reverse coagulopathy? – Choose one. If Yes, please enter medications in Prior and Concomitant Medications CRF.
- Were any pharmacologic treatments (vasoactive medications) administered to raise or lower blood pressure? – Choose one. If Yes, please enter medications in Prior and Concomitant Medications CRF.
- Were any pharmacologic treatments administered to reduce cerebral edema and/or intracranial pressure? – Choose one. If Yes, please enter medications in Prior and Concomitant Medications CRF.
- Were any pharmacologic treatments administered to prevent or treat seizures? – Choose one. If Yes, please enter medications in Prior and Concomitant Medications CRF.
- Were any intracranial procedures performed? – Choose one.
- If Yes, type(s) of intracranial procedure – Choose all that apply.

REFERENCES

Lulla A, Lumba-Brown A, Totten AM, Maher PJ, Badjatia N, Bell R, Donayri CTJ, Fallat ME, Hawryluk GWJ, Goldberg SA, Hennes HMA, Ignell SP, Ghajar J, Krzyzaniak BP, Lerner EB, Nishijima D, Schleien C,

~~ER/Admission Therapeutic Procedures~~

Pre-Hospital and Emergency Department Therapies CRF Module Instructions

Shackelford S, Swartz E, Wright DW, Zhang R, Jagoda A, Bobrow BJ. Prehospital Guidelines for the Management of Traumatic Brain Injury - 3rd Edition. Prehosp Emerg Care. 2023;27(5):507-538.

~~Brain Trauma Foundation; American Association of Neurological Surgeons; Congress of Neurological Surgeons; Joint Section on Neurotrauma and Critical Care, AANS/CNS; Bratton SL, Chestnut RM, Ghajar J, McConnell Hammond FF, Harris OA, Hartl R, Manley GT, Nemecek A, Newell DW, Rosenthal G, Schouten J, Shutter L, Timmons SD, Ullman JS, Videtta W, Wilberger JE, Wright DW. Guidelines for the management of severe traumatic brain injury. I. Blood pressure and oxygenation. J Neurotrauma. 2007;24 Suppl 1:S7-13.~~

~~Chesnut RM, Marshall LF, Klauber MR, Blunt BA, Baldwin N, Eisenberg HM, Jane JA, Marmarou A, Foulkes MA. The role of secondary brain injury in determining outcome from severe head injury. J Trauma. 1993 Feb;34(2):216-22.~~

~~Davis DP. Early ventilation in traumatic brain injury. Resuscitation. 2008 Mar;76(3):333-40.~~

~~Murray GD, Butcher I, McHugh GS, Lu J, Mushkudiani NA, Maas AI, Marmarou A, Steyerberg EW. Multivariable prognostic analysis in traumatic brain injury: results from the IMPACT study. J Neurotrauma. 2007 Feb;24(2):329-37.~~

Site Name:
Participant ID:

[Study Name/ID pre-filled]

Visit Name:

Visit Date:

1. ~~Indicates reported~~ Medication use during the time period relevant to the study protocol?

☐ Yes ☐ No ☐ Unknown

If Yes, please complete the tables below for each prior, concomitant scheduled, or continuous infusion medication.
Include all prescription, over the counter (OTC), herbal, and dietary supplements.

Table 1 Record Medications Prior to Admission Taken by the Participant

Medication Name (Generic Name)	Medication Code	Reason for Administration	Dose per Administration	¹ Dosage Unit and Code	² Frequency	³ Route for Administration	Start Date and Time	⁴ Administration Start Location	End Date and Time	Ongoing?
1.	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown
2.	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown
3.	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown

[Study Name/ID pre-filled]

Site Name:
Participant ID:

Table 2 Record Concomitant Scheduled Medications Taken by the Participant

Medication Name (Generic Name)	Medication Code	Reason for Administration	Dose per Administration	¹ Dosage Unit and Code	² Frequency	³ Route for Administration	Start Date and Time	⁴ Administration Start Location	End Date and Time	Ongoing?
1.	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown
2.	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown
3.	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown

[Study Name/ID pre-filled]

Site Name:
Participant ID:

Table 3 Record Concomitant Continuous Infusion Medications Administered to the Participant

Medication Name (Generic Name)	Medication Code	Reason for Administration	Dose per Administration	¹ Dosage Unit and Code	² Frequency	³ Route for Administration	Start Date and Time	⁴ Administration Start Location	End Date and Time	Ongoing?
1.	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown
2.	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown
3.	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown

Prior and Concomitant Medications

[Study Name/ID pre-filled]

Site Name:
Participant ID:

Code list: Please choose the applicable code(s) and enter under the appropriate corresponding cell

¹Units of Dose

g = gram
gr = grain
gtt = drop
mcg = microgram
mcg/h = microgram per hour
mcg/kg/h = microgram per kilogram per hour
mcg/kg/min = microgram per kilogram per minute
mcL = microliter
mg = milligram
mg/kg/h = milligram per kilogram per hour
mg/kg/min = milligram per kilogram per minute
mL = milliliter
oz = ounce
tbsp = tablespoon
tsp = teaspoon
U = unit
U/min = units per minute
UNK = Unknown
OTH = Other, specify:
NA = Not applicable

²Frequency

BID = Twice daily
TID = Three times a day
QID = Four times a day
QAM = One dose in morning
QPM = One dose in evening
QD = Once daily
QOD = Every other day
~~AD =~~
PC = after meals
AC = before meals
HS = At bedtime
PRN = As needed
Q2H = Every 2 hours
Q4H = Every 4 hours
Q6H = Every 6 hours
Q8H = Every 8 hours
Q12H = Every 12 hours
Continuous infusion
UNK = Unknown
OTH = Other
NA = Not applicable

³Route

~~By ear~~
AU= Both ears (AD = right ear, AS = left ear)
BUC = Buccal (towards back of mouth)
ID= Intradermal
IM = Intramuscular
INH = Inhaled (Respiratory)
IV = Intravenous
NS = Nasal
OU = Both eyes (OD = right eye, OS = left eye)
PO = Oral (swallow)
PR= Rectal
RD= Rapid Dissolve
SC = Subcutaneous
SL = Sublingual (taken under tongue)
SPY = Spray/squirt
SUPP = Suppository, specify:
 R (rectal suppository)
 V (vaginal suppository)
 U (urethral suppository)
TD = Transdermal
TOP = Topical
UNK = Unknown
OTH = Other, specify:

⁴Administration Start Location

ED = Emergency Department
Home
ICU = Intensive care unit (ICU)
OR = Operating Room
Pre-hospital
Regular floor
UNK = Unknown
OTH = Other, specify:

Recorder Signature:

TBI CDE Version 3.1

Date:

Initials:

Prior and Concomitant Medications CRF Module Instructions

GENERAL INSTRUCTIONS

Collecting medications taken prior to the study in a defined time window (e.g., 30 days) is important when there may be potential interactions with the study intervention. The purpose of this form is to collect all medications besides study medications, including medications used to treat the head injury within the time window. Thus, a potential participant may need to stop a medication prior to starting the study intervention (washout period). Furthermore, the study exclusion criteria may identify drugs that cannot be taken during the study and so prior medications are identified to determine whether an individual may be eligible for the study.

Collecting prior and concomitant medications (including intravenous infusions) taken during a study is also important for safety reasons. Some drugs may interact with the study intervention and must not be taken during the study. Additionally, there may be some drugs that are not known to interact with the study intervention and may be identified through an adverse event. It may be helpful to ask study participants or their caregivers to bring prescription and over-the-counter medications to follow-up visits so that the medications can be more easily and accurately recorded on the CRF.

The Prior and Concomitant Medications forms should be filled out at the baseline visit and every study visit/time point thereafter. It is important to be very explicit and detailed when completing these forms to ensure the relevant and accurate data is collected.

Studies that plan to submit their data to regulatory authorities are recommended to code their medication data using a standard terminology such as the RXNorm, MedDRA, WHODrug dictionary, and UCUM.

Important note: None of the data elements included on this CRF Module are classified as Disease Core (i.e., strongly recommended for all TBI clinical studies).

All the data elements are classified as Supplemental and should only be collected if the research team considers them appropriate for their study design and type(s).

The Supplemental CDEs are applicable to the following study design(s) and type(s): Clinical Trials, Observational Studies, Comparative Effectiveness Studies, and/or Epidemiologic Studies focused on drug treatment interventions.

The data elements on this CRF Module are part of the NINDS CDE Treatment/Intervention Data Domain.

Additional details regarding classification definitions are available: [\[Link to be added once available.\]](#)

Please see the Data Dictionary for element classifications.

SPECIFIC INSTRUCTIONS

Please see the Data Dictionary for definitions for each of the data elements included in this CRF Module.

- Medication use during the time period relevant to the study protocol indicator – Choose one. If this question is answered Yes then at least one prior/concomitant medication record needs to be recorded. Do NOT record study medications taken (if study has a drug intervention) on this form. Add date stamp for when assessed. Recommend collection at least on date of TBI. Refer to the Study Drug Dosing form instructions to record study medications.
- Table 1 – Please complete this table for medications taken by the participant prior to admission.
- Table 2 – Please complete this table for concomitant scheduled medications taken by the participant.
- Table 3 – Please complete this table for continuous infusion medications administered to the participant.

Prior and Concomitant Medications CRF Module Instructions

- Medication prior or concomitant name – Verbatim name (generic or trade name) of the medication, including all prescription, over the counter (OTC), herbal, and dietary supplements the participant reports taking. Add date stamp for when assessed. Recommend collection at least on date of TBI. See the data dictionary for additional information on coding the medication name using RXNorm.
- ~~Medication prior or concomitant RXNorm code – Code for the medication the participant reports taking. Add date stamp for when assessed. Recommend collection at least on date of TBI.~~
- Medication prior or concomitant indication text – Response is obtained from report by participant. If given for an AE, enter exact term from AE CRF.
- Medication prior or concomitant dose – Record the strength of the medication the participant is taking. The code list displays the most popular dose unit options.
- Medication prior or concomitant dose unit of measure – Record the units of the medication the participant is taking. See the data dictionary for additional information on coding the dosage unit of measure using Unified Code for Units of Measure (UCUM).
- Medication prior or concomitant dose unit of measure other text – Record the units of the medication the participant is taking.
- ~~Medication prior or concomitant dose unit of measure UCUM code – Code the units of the medication the participant is taking using Unified Code for Units of Measure (UCUM).~~
- Medication prior or concomitant dose frequency – Choose all that apply. Record how often the medication is being taken. The code list displays the most popular options.
- Medication prior or concomitant route type – Choose one route of administration. The code list displays the most popular options.
- Medication prior or concomitant route type other text – Complete with appropriate code.
- Medication prior or concomitant start date and time – Date/time should be recorded to the level of granularity known (e.g., year, year and month, complete date plus hours and minutes, etc.) and in an unambiguous format acceptable to the study database like DD-MMM-YYYY. When date/time data are prepared for aggregation or sharing, they should be converted to the format specified by [ISO 8601](#); YYYY-MM-DD T:hh:mm:ss.
- Medication administration start location – Choose the applicable code for the medication start location.
- Medication prior or concomitant end date and time – Date/time should be recorded to the level of granularity known (e.g., year, year and month, complete date plus hours and minutes, etc.) and in an unambiguous format acceptable to the study database like DD-MMM-YYYY. When date/time data are prepared for aggregation or sharing, they should be converted to the format specified by [ISO 8601](#); YYYY-MM-DD T:hh:mm:ss. Stop Date should be recorded if “Ongoing?” is answered No. Conversely, Stop Date should remain blank if “Ongoing?” is answered Yes.
- Medication prior or concomitant ongoing indicator – Choose one. Answer Yes if the participant is still taking the medication or No if the participant has discontinued taking the medication.

REFERENCES

CDISC SDTM Frequency Terminology (Code C71113)

[\(http://www.cancer.gov/cancertopics/cancerlibrary/terminologyresources/cdisc/\)](http://www.cancer.gov/cancertopics/cancerlibrary/terminologyresources/cdisc/)
<https://datascience.cancer.gov/resources/cancer-vocabulary/cdisc-terminology>
<https://evs.nci.nih.gov/ftp1/CDISC/SDTM/>

MedDRA: <https://www.meddra.org/>

RXNorm for the medication codes (<https://www.nlm.nih.gov/research/umls/rxnorm/index.html>; use the atom unique identifier or RXAUI code)

Unified Code for Units of Measure (UCUM): <https://ucum.org/>

WHODrug: <https://who-umc.org/whodrug/whodrug-global/>

Rehabilitation Treatment (New for TBI)

[Study Name/ID pre-filled]

Site Name:
Participant ID:

Visit Date:
Visit Name:

Name of intervention:
Intervention components:
Quantity:
Rationale:
Relevant citations for this intervention:

****Complete this section for every participant****

Required items

1. Delivered: <input type="checkbox"/> Yes <input type="checkbox"/> No (→skip to #12) <input type="checkbox"/> Unknown (→skip to end)	2. How researcher determined intervention was delivered: <input type="checkbox"/> Extracted from medical record <input type="checkbox"/> Reported by participant <input type="checkbox"/> Reported by caregiver/family member(s) <input type="checkbox"/> Action performed by research team
3. Start date: (mm/dd/yyyy) Or <input type="checkbox"/> Unknown	4. End date: (mm/dd/yyyy) Or <input type="checkbox"/> Unknown <i>Instruction: Same as start date if only one encounter/visit</i>

Optional items

5. Number of completed sessions:	6. Average duration of sessions: minutes
7. Provider type: (See dictionary for codes)	
8. Recipient(s): <input type="checkbox"/> Participant <input type="checkbox"/> Caregiver/family member(s) <input type="checkbox"/> Unknown	
9. Format: <input type="checkbox"/> Individual <input type="checkbox"/> Group <input type="checkbox"/> Unknown	
10. Modality: <input type="checkbox"/> In-person <input type="checkbox"/> Videoconference <input type="checkbox"/> Telephone <input type="checkbox"/> Unknown	
11. In-person location: <input type="checkbox"/> Acute hospital <input type="checkbox"/> Inpatient rehabilitation <input type="checkbox"/> Outpatient <input type="checkbox"/> School <input type="checkbox"/> Workplace <input type="checkbox"/> Participant's home/residence <input type="checkbox"/> N/A (remote-delivered)	
12. Reason not delivered: <input type="checkbox"/> N/A (was delivered) <input type="checkbox"/> No indication <input type="checkbox"/> Contraindication <input type="checkbox"/> Insurance coverage/financial <input type="checkbox"/> Offered but participant/family declined <input type="checkbox"/> Other known: <input type="checkbox"/> Unknown	

Recorder Signature:

Date:

Rehabilitation Treatment CRF Module Instructions

GENERAL INSTRUCTIONS

Purpose: The Rehabilitation Treatment CRF documents receipt of potentially confounding background (non-study) care. This CRF is for non-pharmacological treatments; the Prior and Concomitant Medications CRF should be used for non-study pharmacological treatments. A rehabilitation treatment is considered potentially confounding when (1) it is likely to affect the primary outcome chosen for a given observational or treatment study, and (2) is delivered variably as part of standard clinical care – some patients will get it and others will not. This CRF may also be used for the researcher-delivered experimental and/or comparison interventions if they are non-pharmacological, however, researchers will generally have more detailed information about interventions they deliver and may favor a study-specific CRF.

Instructions: The Rehabilitation Treatment CRF is a template. Before starting a study, customize the template by completing the top portion (intervention name, components, quantity, and rationale) for each non-pharmacological intervention relevant to the study (i.e., potentially confounding). One study will require multiple Rehabilitation Treatment CRFs if multiple potentially confounding background (non-study) interventions are anticipated. Minor variations of the same treatment, to the extent their essential components are shared, can be captured using one version of this CRF. For “complex interventions” (Skivington et al., 2021), the CRF can be limited to those components (i.e., procedures, activities, and/or processes) expected to affect the primary outcome (directly or indirectly) or interact with the active components of the study intervention. After a participant completes the study, fill out all Rehabilitation Treatment CRFs for that participant – one for each potentially confounding intervention.

Important note: Items #1-4 are classified as Supplemental – Highly Recommended (i.e., strongly recommended for Clinical Trials, Observational Studies, Comparative Effectiveness Studies focused on any TBI outcome subdomain). The remaining items are classified as Supplemental for the same study designs and TBI subdomains.

The data elements on this CRF Module are part of the NINDS CDE Treatment/Intervention Data Domain.

Additional details regarding classification definitions are available: [\[Link to be added once available.\]](#)

Please see the Data Dictionary for element classifications.

SPECIFIC INSTRUCTIONS

Please see the Data Dictionary for definitions for each of the data elements included in this CRF Module.

- Name of intervention – Input a unique name for the potentially confounding intervention.
- Intervention components – Describe the procedures, activities, and/or processes used in the intervention, explaining who (provider type) does what, where (location), and how (mode of delivery). Include any equipment and informational materials, as relevant. Include only those aspects of intervention considered essential to the hypothesized mechanism of action.
- Quantity – Describe the quantity of the intervention components in units relevant to their hypothesized mechanisms of action. Specify the minimum amount of the intervention (e.g., number and duration of sessions, number of repetitions or trials, or other measure of dose) considered sufficient to affect the primary outcome of the study (i.e., when at least this much of the intervention is delivered, it is expected to influence the study’s primary outcome). This amount may be more or less than the minimum effective dose for the intervention on its intended target(s).
- Rationale – State why this intervention could theoretically affect the study’s primary outcome. For example, it may be hypothesized, or have been shown in prior studies, to affect the same outcome measure or a more distal/global outcome (e.g., quality of life); or the intervention could affect an outcome that in turn could impact the study’s primary outcome (e.g., total symptom severity or functional disability rating), i.e., have an indirect effect.

Rehabilitation Treatment CRF Module Instructions

- Relevant citations for this intervention – Reference prior studies that support the stated rationale for why the non-study intervention is potentially confounding.
- Delivered – Select ‘Yes’ if the participant received the minimum amount of the intervention considered to be confounding, as defined in ‘Quantity’ above. If a participant received the potentially confounding non-study treatment, but the quantity cannot be reliably determined because of missing or incomplete information, select ‘Yes.’ Select ‘No’ when there is an absence of evidence that a participant received the potentially confounding non-study treatment (e.g., there is no mention of it in the medical record and the participant/family report having not received it). Select ‘unknown’ when a participant’s treatment history cannot be accessed (e.g., medical records are unavailable and the participant/family cannot be interviewed).
- How researcher determined intervention was delivered – Select more than one source if relevant. If there is contradictory information across sources, favor administrative records over participant/family report (Hart et al., 2019)
- Start date – Date/time should be recorded to the level of granularity known (e.g., year, year and month) and in an unambiguous format acceptable to the study database like DD-MMM-YYYY. When date/time data are prepared for aggregation or sharing, they should be converted to the format specified by [ISO 8601](#); YYYY-MM-DD.
- End date – Same as start date if only one encounter/visit. Date/time should be recorded to the level of granularity known (e.g., year, year and month) and in an unambiguous format acceptable to the study database like DD-MMM-YYYY. When date/time data are prepared for aggregation or sharing, they should be converted to the format specified by [ISO 8601](#); YYYY-MM-DD. If one course of treatment was completed, and another course of the same treatment is initiated (typically in a new setting, with a new provider), extend the timeframe to include both.
- Number of completed sessions – Enter the number of treatment sessions (visits with a provider), regardless of their duration or modality (in-person vs. teleconference). Min=1, max=999. Whereas the “Intervention component quantity description text” field is used to specify the minimum amount of the intervention considered sufficient to affect the primary outcome (for any participant), in number of sessions and/or a more relevant unit of dose, this field is intended to capture the number of sessions an individual participant actually received. If a minimum number of sessions is specified in the “Intervention component quantity description text” item and the “Intervention delivery indicator” item is coded as “yes”, the number of sessions recorded here should be equal or greater to the minimum specified in “Intervention component quantity description text.”
- Average duration of sessions – Enter the average or modal (typical) treatment session duration, in minutes. Min=1, max=999.
- Provider type – See dictionary for codes. If more than one provider was involved in the delivery of the potentially confounding non-study treatment, select the code for the most-involved provider.
- Recipient(s) – If the potentially confounding non-study treatment was primarily delivered to one recipient (participant or family/caregiver), select that one recipient. If the treatment involved extensive participation from both the participant and their family/caregiver, select both.
- Format – If the same potentially confounding non-study treatment was delivered in multiple formats, or the format changed during its delivery, select both formats.
- Modality – If the same potentially confounding non-study treatment was delivered in multiple modalities, or the modality changed during its delivery, select all relevant modalities.
- In-person location – If the same potentially confounding non-study treatment was delivered in multiple locations, or the location changed during its delivery, select all relevant locations.
- Reason not delivered – If known, select a reason or reasons why the participant did not receive the potentially confounding non-study treatment. When unclear if the participant *should* have received it, select ‘unknown.’

Rehabilitation Treatment CRF Module Instructions

REFERENCES

Hart T, Whyte J, Vaccaro M, Rabinowitz AR. Self-Report of Outpatient Therapy Dose at 6 and 12 Months After Severe Traumatic Brain Injury. Arch Phys Med Rehabil. 2019;100(5):987-989.

Negrini S, Arienti C, Armijo-Olivo S, Côté P, Heinemann AW, Kiekens C, Kumbhare D, Levack WMM, Meyer-Feil T, Whyte J. RCTrack Executive Committee, GUIDE-Rehab Advisory Committee, Rehabilitation Journals Chief Editors, and PREPARE Project Clinical Partners. The reporting Guideline for Intervention Description in Rehabilitation (GUIDE-Rehab): a tool to open the “black box” of rehabilitation complex interventions. BMJ Evid Based Med. Forthcoming 2025.

Skivington K, Matthews L, Simpson SA, Craig P, Baird J, Blazeby JM, Boyd KA, Craig N, French DP, McIntosh E, Petticrew M, Rycroft-Malone J, White M, Moore L. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. BMJ. 2021 Sep 30;374:n2061.

Serious Adverse Event Report Form (New for TBI)

[Study Name/ID pre-filled]

Site Name:
Participant ID:

Visit Date:
Visit Name:

1. **Is the adverse event serious?¹
- ☐ No (Leave rest of form blank)
- ☐ Yes (Complete rest of the form)
- a. If YES, serious adverse event onset date?

Serious Adverse Event (SAE) Information

2. Site SAE awareness date:
3. Ongoing? ☐ No ☐ Yes
- a. If NO, resolution date:
4. Adverse Event:
5. Outcomes attributed to event
- a. Did the adverse event result in death?
☐ No ☐ Yes
- b. Is the adverse event life threatening?
☐ No ☐ Yes
- c. Did the adverse event result in initial or prolonged hospitalization for the participant?
☐ No ☐ Yes
- d. Did the adverse event require intervention to prevent permanent impairment or damage?
☐ No ☐ Yes
- e. Did the adverse event result in persistent or significant disability or incapacity?
☐ No ☐ Yes
- f. Is the adverse event associated with a congenital anomaly or birth defect?
☐ No ☐ Yes
- g. Is the adverse event a medically important event not covered by other "serious" criteria?
☐ No ☐ Yes
- i. If YES, specify:

6. **Record treatment for event or attach appropriate documentation:

Table 1 Treatment for Event

Record treatment for event
Data to be filled in by site

7. Record relevant tests or laboratory data, including dates or attach the appropriate documentation:

Table 2 Relevant Tests or Laboratory Data

Record relevant tests or laboratory data
Data to be filled in by site

8. **Record concomitant medications or attach the appropriate Case Report Form (CRF) page(s):

Table 3 Concomitant Medications

Record concomitant medications
Data to be filled in by site

9. Record relevant history including pre-existing medical conditions or attach appropriate CRF page(s):

¹Serious: An adverse event is defined by the investigator or sponsor as "serious" because it is life-threatening, results in death, requires in-patient hospitalization, prolongs existing hospitalization, results in persistent or significant disability, is a congenital anomaly/birth defect, or is an important medical event.

Serious Adverse Event Report Form

[Study Name/ID pre-filled]

Site Name:

Participant ID:

Table 4 Relevant History

Record relevant history including pre-existing medical conditions
Data to be filled in by site

Study Intervention Information

10. Name of study intervention:
11. Describe administration of study intervention (e.g., dose, frequency and route used for a drug):
12. Was study intervention discontinued due to the event?
☐ No ☐ Yes
13. Was the seriousness of the event abated after discontinuation of the study intervention?
☐ No ☐ Yes
14. Did event reappear after reintroduction of the study intervention?
☐ No ☐ Yes ☐ N/A
15. Was study blind broken?
☐ No ☐ Yes
16. Did the adverse event cause the participant to be discontinued from the study?
☐ No ☐ Yes

Principal Investigator's Assessment

17. Principal Investigator's opinion of what caused the event:
☐ Study intervention
☐ Concomitant medication, specify:
☐ Concurrent disorder, specify:
☐ Withdrawal of study intervention, specify:
☐ Other, specify:
18. Was this type of event anticipated in the protocol and consent form?
☐ No ☐ Yes

Reporter Information

19. Principal Investigator's name and address: (please specify)
20. Reporter name and telephone number: (please specify)
21. Type of report:
☐ Initial report ☐ Follow-up report ☐ Final report
22. Date report completed:

Sponsor's Assessment

23. Does this adverse event meet the definition to be a serious adverse event?²
☐ No ☐ Yes
24. Does this adverse event meet the definition to be an unexpected event?³
☐ No ☐ Yes
25. Based on the sponsor's assessment, is there at least a reasonable possibility that the adverse event was caused by use of the study intervention?
☐ No ☐ Yes

26. Comments:
Recorder Signature:

Date:

²Serious: An adverse event is defined by the investigator or sponsor as "serious" because it is life-threatening, results in death, requires in-patient hospitalization, prolongs existing hospitalization, results in persistent or significant disability, is a congenital anomaly/birth defect, or is an important medical event.

³Unexpected: An adverse event is categorized by the sponsor as "unexpected" because the adverse event has not been previously described in the Investigator's Brochure or has increased in frequency or severity compared to what is described by the Investigator's Brochure.

Serious Adverse Event Report Form CRF Module Instructions

GENERAL INSTRUCTIONS

Important note: None of the data elements included on this CRF are classified as Core (i.e., strongly recommended for all TBI clinical studies).

Some of the data elements are classified as Supplemental – Highly Recommended (i.e., strongly recommended for all study designs and certain disease conditions or study types) as they are critical for studies of an intervention, especially randomized controlled clinical trials of novel treatments, as indicated by asterisk below. Concomitant medications are most important when trying to determine probable cause. These data elements will not necessarily be relevant to other studies.

****Element is classified as Supplemental – Highly Recommended**

The remaining data elements are classified as Supplemental and should only be collected if the research team considers them appropriate for their study design and type(s).

The Supplemental CDEs are applicable to studies of an intervention, especially randomized controlled clinical trials of novel treatments.

The data elements on this CRF Module are part of the NINDS CDE Safety Data Domain.

Additional details regarding classification definitions are available: [Link to be added once available.]

Please see the Data Dictionary for element classifications.

ADVERSE EVENTS

Adverse events (AEs) document any unfavorable or untoward medical occurrence that is observed with use of a drug or medical device in a participant enrolled in a study without regard for cause or relationship. Adverse events should be recorded using a standard medical terminology, such as the Medical Dictionary for Regulatory Activities (MedDRA) or Common Terminology Criteria for Adverse Events (CTCAE).

SERIOUS ADVERSE EVENT DEFINITION

Serious Adverse Event (SAE) - Any untoward medical occurrence that:

- Results in death,
- Is life-threatening,
- Requires inpatient hospitalization or prolongation of existing hospitalization,
- Results in persistent or significant disability or incapacity,
- Is a congenital anomaly or birth defect, or
- Is an Important Medical Event (IME)

[Glossary of Clinical Research Terms](#)

[Clinical Data Interchange Standards Consortium \(CDISC\) Terminologies](#)

SAE REPORTING

The Serious Adverse Event Report is used to provide detailed information about each SAE that occurs during the study. It contains the information that MedWatch (the FDA Safety Information and Adverse Event Reporting Program) requires for reporting SAEs.

The study protocol should outline who should receive SAE Reports and in what time frame. Depending on the study, SAE Reports may have to be sent to the study coordinating center, Data Safety Monitoring Board (DSMB), the Institutional Review Board (IRB), and the NINDS.

REPORTING OF SAFETY REPORTS FOR STUDIES UNDER AN IND OR IDE

Serious Adverse Event Report Form CRF Module Instructions

For studies conducted under an Investigational New Drug (IND) or Investigational Device Exemption (IDE), the U.S. Food and Drug Administration describes guidelines for sponsors to report events related to use of an investigational agent or medical device.

The sponsor must assess the adverse event and prepare an IND Safety Report when the event meets all of the definitions to be categorized as (1) suspected (at least a reasonable possibility for causality), (2) serious and (3) unexpected.

Safety reporting requirements can be found on the U.S. Food and Drug Administration website: [U.S. Food and Drug Administration Investigational New Drug Reporting Requirements](#)

SPECIFIC INSTRUCTIONS

See [Food and Drug Administration Serious Adverse Event Report Form Instructions](#) for instructions on how to fill out the SAE Report.

Please see the Data Dictionary for definitions for each of the data elements included in this CRF Module.

- Is the adverse event serious? – Choose either No or Yes. This question should only be answered YES if the outcome of the AE results in at least one of the following: death; a life-threatening experience; inpatient hospitalization; prolongation of existing hospitalization; a persistent or significant disability or incapacity; a congenital anomaly/birth defect; or an Important Medical Event. If an AE is serious, this provides a trigger that additional information must be provided by the site investigator. The site investigator then completes the SAE form. Additionally, the site institution and/or IRB may also have an SAE form and procedures for reporting SAEs. If NO, do not complete the rest of the form.
- SAE onset date – Record the date/time according to the [ISO 8601](#), the International Standard for the representation of dates and times. The date/time should be recorded to the level of granularity known (e.g., year, year and month, complete date plus hours and minutes, etc.) and in an unambiguous format acceptable to the study database like DD-MMM-YYYY. When date/time data are prepared for aggregation or sharing, they should be converted to the format specified by [ISO 8601](#); YYYY-MM-DD T:hh:mm:ss.
- Site SAE awareness date – Record the date and time the site became aware of the serious adverse event. Record the date/time according to the [ISO 8601](#), the International Standard for the representation of dates and times. The date/time should be recorded to the level of granularity known (e.g., year, year and month, complete date plus hours and minutes, etc.) and in an unambiguous format acceptable to the study database like DD-MMM-YYYY. When date/time data are prepared for aggregation or sharing, they should be converted to the format specified by [ISO 8601](#); YYYY-MM-DD T:hh:mm:ss.
- Resolution date – Record the date/time according to the [ISO 8601](#), the International Standard for the representation of dates and times. The date/time should be recorded to the level of granularity known (e.g., year, year and month, complete date plus hours and minutes, etc.) and in an unambiguous format acceptable to the study database like DD-MMM-YYYY. When date/time data are prepared for aggregation or sharing, they should be converted to the format specified by [ISO 8601](#); YYYY-MM-DD T:hh:mm:ss.
- Adverse event – Text may be prepopulated from Adverse Events CRF.
- Relevant tests or laboratory data – See General CDE Data Standards [Laboratory Tests and Tracking](#) CRF Module
- Concomitant medications – See General CDE Data Standards [Prior and Concomitant Medications](#) CRF Module
- Relevant history – See General CDE Data Standards [Medical History](#) CRF Module
- Date report completed – Record the date/time according to the [ISO 8601](#), the International Standard for the representation of dates and times. The date should be recorded to the level of granularity known (e.g., year, year and month, complete date) and in an unambiguous format acceptable to the study

Serious Adverse Event Report Form CRF Module Instructions

database like DD-MMM-YYYY. When date/time data are prepared for aggregation or sharing, they should be converted to the format specified by [ISO 8601](#); YYYY-MM-DD T:hh:mm:ss.

Surgical and Therapeutic Procedures

[Study Name/ID pre-filled]

Site Name:
Participant ID:

Visit Date:
Visit Name:

1. Surgical or therapeutic procedure type (some examples below):

- | | | |
|--|--|---|
| <ul style="list-style-type: none">● Appendectomy● Cholecystectomy● Colostomy● Ileostomy● Feeding tube placement● Fundoplication● Scoliosis surgery● Tendon release● Tympanostomy tubes● Tracheostomy● Airway surgery● Unknown● Diagnostic<input type="checkbox"/> Decompressive hemicraniectomy<input type="checkbox"/> Cisternostomy<input type="checkbox"/> External ventricular drain<input type="checkbox"/> Elevation of depressed skull fracture<input type="checkbox"/> Intracranial pressure monitor<input type="checkbox"/> Diagnostic cerebral angiogram<input type="checkbox"/> Angiogram with no other intervention<input type="checkbox"/> Angiogram with coiling of traumatic aneurysm<input type="checkbox"/> Angiogram with stent placement<input type="checkbox"/> Craniotomy and hematoma evacuation<input type="checkbox"/> Unilateral decompressive craniectomy<input type="checkbox"/> Bilateral decompressive craniectomy<input type="checkbox"/> Frontal sinus cranialization | <ul style="list-style-type: none">● Anterior temporal lobectomy (ATL)● Anterior temporal lobectomy plus (ATL+)● Amygdalohippocampectomy● Lesionectomy● Lesionectomy plus (Lesionectomy+)● Extratemporal resection (Topectomy)● Multi-lobar resection● Hemispherectomy | <ul style="list-style-type: none">● Vagus nerve stimulation (VNS) surgery● Corpus callosotomy● Multiple subpial transaction● radiosurgery● Therapeutic brain stimulation● Other, specify● Appendicostomy● Appendectomy● Neurological surgery● Bony orthopedic surgery |
|--|--|---|

2. ICD-10-CM code (Code from the International Classification of Diseases, ~~Tenth Ninth~~ Revision, Clinical Modification (ICD-10-CM) for the selected surgical procedure):

3. Inpatient or Outpatient:

☐ Inpatient ☐ Outpatient ☐ Home health

4. Surgical or therapeutic procedure start date and time:

5. Surgical or therapeutic procedure end date and time:

6. Was surgical procedure performed on admission or in a delayed fashion?

☐ On admission ☐ Delayed

7. Was surgical procedure performed for intractable ICP?

☐ Yes ☐ No ☐ Unknown

Recorder Signature:

Date:

Surgical and Therapeutic Procedures CRF Module Instructions

GENERAL INSTRUCTIONS

This case report form (CRF) contains data elements that collect information related to surgical and other therapeutic procedures the participant is treated with during acute hospital care for traumatic brain injury.

Important note: None of the data elements included on this CRF Module are classified as Disease Core (i.e., strongly recommended for all TBI clinical studies).

All the data elements are classified as Supplemental and should only be collected if the research team considers them appropriate for their study design and type(s).

The Supplemental CDEs may be applicable to the following study designs and type: Clinical Trials, Observational Studies, Comparative Effectiveness Studies, and/or Epidemiologic Studies, and apply to studies of patients who received surgical intervention as treatment of their TBI.

The data elements on this CRF Module are part of the NINDS CDE Treatment/Intervention Data Domain.

Additional details regarding classification definitions are available: [Link to be added once available.]

Please see the Data Dictionary for element classifications.

SPECIFIC INSTRUCTIONS

Please see the Data Dictionary for definitions for each of the data elements included in this CRF Module.

- Surgical or therapeutic procedure type – Choose all that apply. Recommend collection during acute hospital care. Document information on a continuing basis and check/update on discharge/death from review of medical charts. Add date stamp for when assessed. In previous trials and studies, information on surgical procedures has typically been documented in free text format, thus often precluding any meaningful analysis. Therefore the use of ICD-910 coding is proposed.
- Surgical or therapeutic procedure Other, specify – Document other procedures like tracheostomy, percutaneous endoscopic gastrostomy (PEG), inferior vena cava (IVC) filter. Also record any other surgical procedures performed due to polytrauma. Recommend collection during acute hospital care. Document information on a continuing basis and check/update on discharge/death from review of medical charts. Add date stamp for when assessed. In previous trials and studies, information on surgical procedures has typically been documented in free text format, thus often precluding any meaningful analysis. Therefore the use of ICD-910 coding is proposed.
- Surgical therapeutic procedure ICD-10-CM code– Recommend collection during acute hospital care. Document information on a continuing basis and check/update on discharge/death from review of medical charts. Add date stamp for when assessed. In previous trials and studies, information on surgical procedures has typically been documented in free text format, thus often precluding any meaningful analysis. Therefore the use of ICD-910 coding is proposed.
- Inpatient or Outpatient – Choose one.
- Surgical therapeutic procedure start date and time – Date/time should be recorded to the level of granularity known (e.g., year, year and month, complete date plus hours and minutes, etc.) and in an unambiguous format acceptable to the study database like DD-MMM-YYYY. When date/time data are prepared for aggregation or sharing, they should be converted to the format specified by [ISO 8601](#); YYYY-MM-DD T:hh:mm:ss.
- Surgical or therapeutic procedure end date and time – Date/time should be recorded to the level of granularity known (e.g., year, year and month, complete date plus hours and minutes, etc.) and in an unambiguous format acceptable to the study database like DD-MMM-YYYY. When date/time data are prepared for aggregation or sharing, they should be converted to the format specified by [ISO 8601](#); YYYY-MM-DD T:hh:mm:ss.
- Was surgical procedure performed on admission or in a delayed fashion? – Choose one.
- Was surgical procedure performed for intractable ICP? – Choose one.

Surgical and Therapeutic Procedures CRF Module Instructions

REFERENCES

International Classification of Diseases, Tenth ~~Ninth~~ Revision, Clinical Modification (ICD-~~9~~10-CM):

~~<http://www.cdc.gov/nchs/icd/icd9cm.htm>~~

<https://www.cdc.gov/nchs/icd/icd-10-cm/index.html>