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EpiCARE – a network for rare and complex epilepsies

HP-ERN-2016 European Reference Networks / Framework Partnership Agreement

D 16.1. Report on e-CRF Development and Utilization
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1. Version log

Version	Date	Released by	Nature of Change
Version 1	6 Jan 2018	E. Perucca (Fondazione Istituto Neurologico, Pavia, Italy) and R.Nabbout (Hopital Enfant Malade, Necker, Paris, France)	First version

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2. Definition and acronyms

Acronyms	Definitions
AED(s)	Antiepileptic drug(s)
CDE(s)	Common Data Element(s)
EEG	Electroencephalogram
EMA	European Medicines Agency
EU	European Union
FDA	Food and Drug Administration (U.S.)
ILAE	International League against Epilepsy
MRI	Magnetic resonance imaging
NINDS	National Institute for Neurological Diseases and Stroke
PEACE	Pediatric Epilepsy Academic Consortium for Extrapolation
PMDA	Pharmaceuticals and Medical Devices Agency (Japan)
TF	Task Force

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3. Introduction

As part of WP V (clinical trials) it is essential to develop an electronic Case Report Form (CRF) for the collection and recording of patient data relevant to clinical research, and clinical trials in particular, to be used across the network of EpiCARE members. Use of a common core CRF is important to ensure that all members use not only a standardized and consistent terminology, but also a standardized set of clinical information which can permit comparability of data across trials and, whenever applicable, optimal conditions for data pooling and metanalysis.
The present deliverable (D 16.1 Report on e-CRF Development and Utilization) describes activities that were implemented in the first year of existence the EpiCARE network in order to establish an e-CRF to be used for clinical implementation.

4. Activities carried out and results

The present work was developed by an ad hoc Task Force (WP V TF) assembled in consultation with the EPICARE coordinator and with EpiCARE centres. The WP V TF includes the following members: Rima Nabbout (Paris, France) and Emilio Perucca (Pavia, Italy) as TF Chairs, Helen Cross (London, UK as EpiCARE coordinator), Geraldine Boylan (Cork, Ireland), Lieven Lagae (Leuven, Belgium), Sylvain Rheims (Lyon, France), Vicente Villanueva (Valencia, Spain). In addition, each EpiCARE center nominated a representative to act as liaison with the WP-V TF. The working group met regularly by teleconference and a face to face meeting was held on September 4, 2017, in conjunction with the International Congress of Epileptology in Barcelona, Spain.

The WP V TF recognized the need for an e-CRF to be used for clinical trials, particularly trials to be conducted on a multicentre basis within the EpiCARE network. In order to achieve this objective, it was considered important to develop an e-CRF based the latest on International League against Epilepsy (ILAE)-approved terminology and containing all the key elements which may be relevant to the conduction of clinical trials, e.g. demographic data (including social status), results of physical and neurological examination, etiology of epilepsy, syndromic diagnosis (when known), seizure types, results of laboratory tests, results of special investigations (including EEG, MRI and functional MRI), antiepileptic drug (AED) therapy data (including information on plasma concentrations of AEDs), treatment emerging adverse events, and information about use of devices (if applicable). It was also considered important that the core elements of the CRF be accepted and shared in the broadest possible manner with the epilepsy community at large.

Based on the above considerations, it was decided that the best approach was to construct the e-CRF by using the Epilepsy Common Data Elements (CDEs) being developed in collaboration by the ILAE and the U.S. National Institute for Neurological Disorders and Stroke (NINDS) (NINDS, 2017), taking advantage of the fact that the committee in charge of the Epilepsy CDEs development includes members of the EpiCARE WP-V TF. The CRF presented as part of the present deliverable includes 18 different modules covering all the above mentioned elements of demographics, diagnosis, disease-related parameters and treatment-related outcomes (see Annex). For information about epilepsy and seizure type, the CDEs have been updated in order to align them with the 2017 ILAE classification of epilepsy (Scheffer et al, 2017) and seizures (Fisher et al, 2017).

A feature of the e-CRF modules which are part of CDEs is that they overlap across study types, which allows for comparisons and meta-analysis across studies. Consistency of the data elements and these modules is kept in order to ensure the ability to transfer critical medical information electronically from one centre to another. Their use is expected

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to increase the efficiency and effectiveness of clinical research studies and clinical treatment, increase data quality, facilitate data sharing, and help educate new clinical investigators (Grinnon et al., 2012).

Although the CDE-based CRF presented includes basically all the key items of relevance for the areas described, but it is understood that simplification and adaptation will be needed depending on the objectives and specificities of clinical trials for which it will be used.

At present, we have no data yet on the utilization of the proposed e-CRF within the EpiCARE network, but its modules have been already validated as part of the NINDs program and are widely used by researchers worldwide. Actual implementation of clinical trials as part of WP-V activities, and related e-CRF utilization, will be dependent on the availability of funds. It is envisaged that individual EpiCARE centers will take the lead in developing application to funding agencies and organizations for trials of relevant clinical trials. It is also hoped that EU authorities will also clarify the possibility of ERN networks partnering with industry in developing orphan medications for conditions where there are high unmet needs.

5 Conclusions

An e-CRF has been constructed based on the NINDS Epilepsy CDEs, updated to incorporate the latest ILAE classification of seizures and epilepsy. The proposed e-CRF contains the key aspects of information which are relevant to clinical trials in rare and complex epilepsy diseases including demographic and social status data, results of physical and neurological examination, etiology of epilepsy, syndromic diagnosis, seizure types, results of laboratory tests and special investigations, AED and devices therapy data and treatment emerging adverse events. Application of the e-CRF remains dependent on future availability of funds to initiate high-priority clinical trials. The proposed e-CRF can be found in the Annex.

6 Bibliography / References

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7 ANNEX

1 General Core

[Study Name/ID pre-filled]

Site Name:

Subject ID:

1. Date of birth:

2. Gender:
   - ☐ Male
   - ☐ Female
   - ☐ Unknown
   - ☐ Unspecified
   - ☐ Not reported

3. Ethnicity("X" ONLY one with which you MOST CLOSELY identify):
   - ☐ Hispanic or Latino
   - ☐ Not Hispanic or Latino
   - ☐ Unknown
   - ☐ Not Reported

4. Race category (choose all that apply):
   - ☐ American Indian or Alaska Native
   - ☐ Asian
   - ☐ Black or African American
   - ☐ Native Hawaiian or Other Pacific Islander
   - ☐ White
   - ☐ Unknown
   - ☐ Not Reported

5. Number of years of education[1]: years:

6. SNOMED CT Code:

7. Medical History Term:

[1] Years of education is Supplemental – Highly Recommended

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2 General Core CRF Module Instructions

2.1 General Instructions

Most of the data elements on this form are known as General Core CDEs and will be collected for every study population. The data element “Number of years of education” is classified as a Supplemental – Highly Recommended CDE (highly recommended and commonly collected in clinical research studies but whose relevance depends on the study design or type of research involved). These items will be used to compare baseline characteristics among study groups and to identify confounding variables.

As stated in the NIH Guidelines on Inclusion of Women and Minorities as participants/subjects in Clinical Research: The Office of Management and Budget (OMB) Directive No. 15 defines the minimum standard of basic racial and ethnic categories, which are used below. NIH has chosen to continue the use of these definitions because they allow comparisons across many national databases, especially national health databases. Therefore, the racial and ethnic categories described below should be used as basic guidance, cognizant of the distinction based on cultural heritage. (NIH Guideline on the Inclusion of Women and Minorities)

Responses to categories are obtained from self-report when possible or obtained from parent/legal guardian interview.

As stated above, all of the elements included on this CRF are considered Core (i.e., strongly recommended for all studies to collect), with the exception of Years of Education, which is Supplemental – Highly Recommended (i.e., strongly encouraged to collect based on the type of study).

For pediatric studies, the data elements on this CRF reflect child characteristics, not caregiver characteristics.

2.2 Specific Instructions

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

- Date and Time of Birth – 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 the format acceptable to the study database. Recording date of birth will give the most detailed information required for calculation of age and is recommended as first choice. However, in some studies recording date of birth may elicit discussions on a potential violation of privacy legislation and specifically HIPAA regulations. In these cases, the calculated age should be recorded.
- Gender – Choose one. Response is obtained by report of the participant/subject or caretaker. Gender is the socially constructed identity of sex. Gender is equated with phenotypic sex. Gender may differ from the sex of an individual determined genetically. The NIH Guidelines on Inclusion of Women and Minorities as Subjects in Clinical Research: The Office of Management and Budget Directive No. 15 (NIH Guideline on The Inclusion of Women and Minorities)
    - Unspecified is defined as Undifferentiated/Indeterminant/Intersex
- Ethnicity – Choose one. Response is obtained by report of the participant/subject or caretaker. If more detailed characterizations of ethnicity are collected to enhance data quality and consistency, it is recommended that they be "collapsible" up to the two categories for reportable ethnicity, as needed for reporting to FDA under its guidance. Other regulatory bodies may expect the reporting of ethnicity values which more appropriately reflect the population of their areas (e.g., Japanese ancestry for MHLW reporting to Japan). These may be collected as an extension to the suggested code list.
- Race – Choose all that apply. Response is obtained by report of the participant/subject or caretaker. Collecting information on race may not be allowed in some countries for concerns related to discrimination. In other countries, however, these concerns are considered a reason for recording race in order to guarantee equal access to care. Investigators receiving funding from the US National Institutes of Health (NIH) are required to report the number of subjects enrolled on an annual basis using the racial categories listed.

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- Years of education – For years completed, after the age of 5, code the number of years attained (0–30 years), normed to someone moving full time at the usual pace, i.e., a year that was repeated counts as only 1 year and the usual single-year full-time load completed over several years counts as 1 year. Certificate and technical programs do NOT count no matter how specialized. The number of years of typical completion of the relevant program is counted. If the subject obtained their education outside the United States, ask about their educational system to estimate the correct coding – Internship, Residency, and Fellowship years are experiential training and do not count.
- Condition/Disease SNOMED CT Code **–** Code each of the medical history conditions using SNOMED CT.
- Medical History Term – Record one Medical History term per line. See the data dictionary for additional information on coding the condition using SNOMED CT.

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3 Social Status

[Study Name/ID pre-filled] Site Name:

Subject ID:

1) Employment:
   a. Employment status:

☐Working now (Answer 6b below)
☐Student
☐Looking for work, unemployed
☐Only temporarily laid off
☐Sick leave or maternity leave
☐Retired
☐Disabled, permanently or temporarily
☐Keeping house (Regardless of marital status)
☐Other, specify:
☐Unknown

   b. If working now, do you work 35 hours or more per week?

☐Yes
☐No
☐Hours vary
☐Unknown
☐Not reported

2) Education Level (select the highest level attained)[1]:

☐Never attended/ Kindergarten only
☐1st Grade
☐2nd Grade
☐3rd Grade
☐4th Grade
☐5th Grade
☐6th Grade
☐7th Grade
☐8th Grade
☐9th Grade
☐10th Grade
☐11th Grade
☐12th Grade, no diploma
☐High school graduate
☐GED or equivalent
☐Some college, no degree
☐Associate degree: occupational, technical, or vocational program
☐Associate degree: academic program
☐Bachelor's degree (e.g., BA, AB, BS, BBA)
☐Master's degree (e.g., MA, MS, MEng, MEd, MBA)
☐Professional school degree (e.g., MD, DDS, DVM, JD)
☐Doctoral degree (e.g., PhD, EdD)
☐Unknown

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3) If pediatric participant/subject (<18 yo), Mother's Education Level (select the highest level attained)[1]:

- ☐ Never attended/ Kindergarten only
- ☐ 1st Grade
- ☐ 2nd Grade
- ☐ 3rd Grade
- ☐ 4th Grade
- ☐ 5th Grade
- ☐ 6th Grade
- ☐ 7th Grade
- ☐ 8th Grade
- ☐ 9th Grade
- ☐ 10th Grade
- ☐ 11th Grade
- ☐ 12th Grade, no diploma
- ☐ High school graduate
- ☐ GED or equivalent
- ☐ Some college, no degree
- ☐ Associate degree: occupational, technical, or vocational program
- ☐ Associate degree: academic program
- ☐ Bachelor's degree (e.g., BA, AB, BS, BBA)
- ☐ Master's degree (e.g., MA, MS, MEng, MEd, MBA)
- ☐ Professional school degree (e.g., MD, DDS, DVM, JD)
- ☐ Doctoral degree (e.g., PhD, EdD)
- ☐ Unknown

3.1 GENERAL INSTRUCTIONS

This form contains data elements that are collected to describe the social status of the study population. The items are used to compare baseline characteristics among study groups and to identify confounding variables.
Responses to categories are obtained from self-report when possible or obtained from parent/legal guardian interview.

3.2 SPECIFIC INSTRUCTIONS

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

- Education Level – Choose the highest level attained by the participant/subject.

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4 Physical Exam CRF Module Instructions

1. Date of Exam: //20 mm dd yyyy
2. If follow-up exam, change from prior exam: ☐No change ☐Improved ☐Worse ☐Unknown ☐Other, specify:
3. **Tanner Stage: ☐I ☐II ☐III ☐IV ☐V
4. Handedness: ☐Left hand ☐Right hand ☐Both hands ☐Unknown

Results of Physical Exam Table

Body System	Result	Describe Abnormality or Comment if Body System is Not Examined
Constitutional symptoms (e.g., fever, weight loss)	☐Normal☐Abnormal ☐Not examined	Data to be entered by site
Eyes	☐Normal☐Abnormal ☐Not examined	Data to be entered by site
Ears, Nose, Mouth, and Throat	☐Normal☐Abnormal ☐Not examined	Data to be entered by site
Cardiovascular	☐Normal☐Abnormal ☐Not examined	Data to be entered by site
Respiratory	☐Normal☐Abnormal ☐Not examined	Data to be entered by site
Gastrointestinal	☐Normal☐Abnormal ☐Not examined	Data to be entered by site
Genitourinary	☐Normal☐Abnormal ☐Not examined	Data to be entered by site
Musculoskeletal	☐Normal☐Abnormal ☐Not examined	Data to be entered by site
Integumentary (skin and/or breast)	☐Normal☐Abnormal ☐Not examined	Data to be entered by site
Neurological	☐Normal☐Abnormal ☐Not examined	Data to be entered by site
Psychiatric	☐Normal☐Abnormal ☐Not examined	Data to be entered by site

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Body System	Result	Describe Abnormality or Comment if Body System is Not Examined
Endocrine	☐Normal☐Abnormal ☐Not examined	Data to be entered by site
Hematologic/Lymphatic	☐Normal☐Abnormal ☐Not examined	Data to be entered by site
Allergic/Immunologic	☐Normal☐Abnormal ☐Not examined	Data to be entered by site

4.1 General Instructions

The Physical Exam is generally administered at screening and/or baseline to determine study eligibility. It may also be administered at follow-up visits to track a participant's/subject's physical status. This CRF is Supplemental for certain types of clinical research, but is not intended for all studies. If the study is going to conduct a physical exam, investigators should consider these elements, but there may be some studies where a physical exam is not appropriate or could be abbreviated.

Special attention should be given to recording dysmorphic features, neurocutaneous stigmata, and carotid bruits.

Tanner Stage Definitions

Pubic hair (both male and female)

- Tanner I
    - no pubic hair at all (prepubertal Dominic state) [typically age 10 and younger]
- Tanner II
    - small amount of long, downy hair with slight pigmentation at the base of the penis and scrotum (males) or on the labia majora (females) [10–11.5]
- Tanner III
    - hair becomes more coarse and curly, and begins to extend laterally [11.5–13]
- Tanner IV
    - adult-like hair quality, extending across pubis but sparing medial thighs [13–15]
- Tanner V
    - hair extends to medial surface of the thighs [15+]

Genitals (male)

- Tanner I
    - prepubescent (testicular volume less than 1.5 ml; small penis of 3 cm or less) [typically age 9 and younger]
- Tanner II
    - testicular volume between 1.6 and 6 ml; skin on scrotum thins, reddens and enlarges; penis length unchanged [9-11]
- Tanner III

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- testicular volume between 6 and 12 ml; scrotum enlarges further; penis begins to lengthen to about 6 cm [11-12.5]

- Tanner IV
  - testicular volume between 12 and 20 ml; scrotum enlarges further and darkens; penis increases in length to 10 cm and circumference [12.5-14]
- Tanner V
  - testicular volume greater than 20 ml; adult scrotum and penis of 15 cm in length [14+]

Breasts (female)

- Tanner I
  - no glandular tissue: areola follows the skin contours of the chest (prepubertal) [typically age 10 and younger
- Tanner II
  - breast bud forms, with small area of surrounding glandular tissue; areola begins to widen [10-11.5]
- Tanner III
  - breast begins to become more elevated, and extends beyond the borders of the areola, which continues to widen but remains in contour with surrounding breast [11.5-13]
- Tanner IV
  - increased breast size and elevation; areola and papilla form a secondary mound projecting from the contour of the surrounding breast [13-15]
- Tanner V
  - breast reaches final adult size; areola returns to contour of the surrounding breast, with a projecting central papilla. [15+]

Pictoral representation may be found at:Pictoral representation shown here

**Recommended for pediatric studies ONLY

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5 Vital Signs

[Study Name/ID pre-filled]

Site Name:
Subject ID:

1. Date and Time: // 20 mm dd yyyy : ☐am ☐pm
   ☐24-hour clock
2. Heart Rate/Pulse: /beats per minute
3. Respiratory Rate: /breaths per minute
4. Blood Pressure: / mmHg (systolic/diastolic)

   Participant's/Subject's Position: ☐Sitting ☐Standing ☐Supine
5. Temperature:☐°F ☐°C

   Temperature Method:
   - ☐Oral
   - ☐Rectal
   - ☐Axillary
   - ☐Tympanic

   ☐Bladder
   ☐Esophageal
   ☐Brain
   ☐Other, specify:
6. Weight: ☐pounds ☐kilograms
7. Height/Length: ☐inches ☐centimeters

5.1 Additional Pediatric-specific Elements

These elements are recommended for pediatric studies.

8. Head Circumference: ☐inches ☐centimeters

5.2 General Instructions

Vital signs are likely to be captured at study visits to help monitor the health of study participants/subjects and possibly to assess the safety of the intervention.
Height and weight are commonly collected at the baseline visit. Depending on the study population and study intervention it may be appropriate to collect height and weight at subsequent study visits.

5.3 Specific Instructions

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

- Date and time–Record the date vital signs are taken. 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 the format acceptable to the study database. Not every study will need to collect time and this field should be removed if not applicable.

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- Pulse–Record the pulse of the participant/subject in beats per minute.
- Respiratory rate–Record the respiratory rate of the participant/subject in breaths per minute.
- Blood pressure systolic measurement–Record the systolic blood pressure of the participant/ subject. The standard unit for measuring blood pressure is mmHg, which is approximately equivalent to Torr.
- Blood pressure diastolic measurement–Record the diastolic blood pressure of the participant/ subject. The standard unit for measuring blood pressure is mmHg, which is approximately equivalent to Torr.
- Blood pressure position–Record the position the participant/subject was in when blood pressure was measured.
- Temperature–Record the temperature of the participant/subject. Also indicate the scale used to capture temperature.
- Temperature unit of measure-Choose either F (degrees Fahrenheit) or C (degrees Celsius).
- Temperature method–Choose one. Record the location where the temperature was measured. This element is most relevant to pediatric clinical studies.
- Weight–Record the weight of the participant/subject. To be collected at the visit, not self-reported. Also, indicate whether weight was measured in pounds (lbs) or kilograms (kg).
- Weight unit of measure–Choose either pounds (lb) or kilograms (kg).
- Height/Length–Record the height (or length for the very young) of the participant/subject. To be collected at the visit, not self-reported. Also, indicate whether height was measured in inches (in) or centimeters (cm).
- Height/Length unit of measure–Choose either inches (in) or centimeters (cm).
- Head circumference measurement–Record the head circumference of the participant/ subject as well as the units for the measurement.
- Head circumference unit of measure–Choose only one unit.

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6 Neurological Exam

[Study Name/ID pre-filled]

Site Name:
Subject ID:

Date of Exam: //20 (m m dd yyyy)
If follow-up exam, change from prior exam:
☐No change
☐Improved
☐Worse
☐Unknown
☐Other, specify:

6.1 Mental Status

Table for Mental Assessments

Mental assessments	Abnormality Present?	Explain Abnormality
Attention	☐Yes ☐No ☐Unknown	Data to be entered by site
1. Memory: a. Working Memory	☐Yes ☐No ☐Unknown	Data to be entered by site
b. Recent (Episodic) Memory	☐Yes ☐No ☐Unknown	Data to be entered by site
c. Remote (Semantic) Memory	☐Yes ☐No ☐Unknown	Data to be entered by site
2. Language: a. Spontaneous speech	☐Yes ☐No ☐Unknown	Data to be entered by site
b. Comprehension	☐Yes ☐No ☐Unknown	Data to be entered by site
c. Naming	☐Yes ☐No ☐Unknown	Data to be entered by site
d. Repetition	☐Yes ☐No ☐Unknown	Data to be entered by site
e. Reading	☐Yes ☐No ☐Unknown	Data to be entered by site
3. Affect	☐Yes ☐No ☐Unknown	Data to be entered by site

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6.2 Cranial Nerves

4. Cranial Nerves–global assessment:

☐Normal ☐Cannot Assess, explain:
☐Abnormal (explain further in questions 5a through 5k below) ☐Other, specify:

Table for Recording Which of the Following Cranial Nerves are Abnormal

Cranial Nerve Number	Laterality	Explain Abnormality
CN II	☐Left ☐Right ☐Bilateral	Data to be entered by site
CN III	☐Left ☐Right ☐Bilateral	Data to be entered by site
CN IV	☐Left ☐Right ☐Bilateral	Data to be entered by site
CN V	☐Left ☐Right ☐Bilateral	Data to be entered by site
CN VI	☐Left ☐Right ☐Bilateral	Data to be entered by site
CN VII	☐Left ☐Right ☐Bilateral	Data to be entered by site
CN VIII	☐Left ☐Right ☐Bilateral	Data to be entered by site
CN IX	☐Left ☐Right ☐Bilateral	Data to be entered by site
CN X	☐Left ☐Right ☐Bilateral	Data to be entered by site
CN XI	☐Left ☐Right ☐Bilateral	Data to be entered by site
CN XII	☐Left ☐Right ☐Bilateral	Data to be entered by site

5. Nystagmus:

☐Yes (Specify type below) ☐No ☐Cannot Assess, explain:

a. Type of Nystagmus:

☐Physiologic ☐Abnormal ☐Other, specify:

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6.3 Motor

Table for Recording Motor Assessments

Motor assesments	Abnormality Present?	If Abnormal, indicate type:
7. Muscle Bulk–global assessment:	☐Yes ☐No (If 'No" skip to question 8) ☐Cannot assess, explain:	☐Abnormal and symmetric ☐Abnormal and asymmetric
a. Right upper extremity (RUE)	☐Yes ☐No ☐Cannot assess, explain:	☐Abnormal–Decreased ☐Other, specify:
b. Left upper extremity (LUE):	☐Yes ☐No ☐Cannot assess, explain:	☐Abnormal–Decreased ☐Other, specify:
c. Right lower extremity (RLE):	☐Yes ☐No ☐Cannot assess, explain:	☐Abnormal–Decreased ☐Other, specify:
d. Left lower extremity (LLE):	☐Yes ☐No ☐Cannot assess, explain:	☐Abnormal–Decreased ☐Other, specify:
8. Muscle Tone–global assessment:	☐Yes ☐No (If 'No" skip to question 9) ☐Cannot assess, explain:	☐Abnormal and symmetric ☐Abnormal and asymmetric
a. Right upper extremity (RUE)	☐Yes ☐No ☐Cannot assess, explain:	☐Abnormal–Increased ☐Other, specify:
b. Left upper extremity (LUE):	☐Yes ☐No ☐Cannot assess, explain:	☐Abnormal–Increased ☐Other, specify:
c. Right lower extremity (RLE):	☐Yes ☐No ☐Cannot assess, explain:	☐Abnormal–Increased ☐Other, specify:
d. Left lower extremity| (LLE):	☐Yes ☐No ☐Cannot assess, explain:	☐Abnormal–Increased ☐Other, specify:
e. Truncal tone:**	☐Yes ☐No ☐Cannot assess, explain:	☐Abnormal–Increased ☐Abnormal–Decreased ☐Other, specify:
9. Muscle Strength–global assessment:	☐Yes ☐No (If 'No" skip to question 10) ☐Cannot assess, explain:	☐Abnormal and symmetric ☐Abnormal and asymmetric

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Motor assesments	Abnormality Present?	If Abnormal, indicate type:
a. Right upper extremity (RUE)	☐Yes ☐No ☐Cannot assess, explain:	☐Abnormal–Decreased ☐Other, specify:
b. Left upper extremity (LUE):	☐Yes ☐No ☐Cannot assess, explain:	☐Abnormal–Decreased ☐Other, specify:
c. Right lower extremity (RLE):	☐Yes ☐No ☐Cannot assess, explain:	☐Abnormal–Decreased ☐Other, specify:
d. Left lower extremity (LLE):	☐Yes ☐No ☐Cannot assess, explain:	☐Abnormal–Decreased ☐Other, specify:

10. Weakness? ☐Yes (answer questions 10a and 10b) ☐No

a. Does the weakness suggest one of the following patterns?

☐Right Hemiparesis
☐Left Hemiparesis
☐Diplegia/Paraparesis
☐Quadriplegia/Quadraparesis
☐Peripheral Nerve Lesion(s), describe:
☐Neuropathic Weakness, describe:
☐Myopathic Weakness, describe:
☐Other, specify:

b. Specify the neurological location of the weakness:

☐Brain
☐Spinal Cord
☐Peripheral Nervous System
☐Other, specify:

11. Tremor?

☐Yes (Specify type below)
☐No
☐Cannot Assess, explain:
☐Other, specify:

a. Type of Tremor:

☐Postural
☐Rest
☐Intention
☐Other, specify:

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6.4 Cerebellar/Coordination

Table for Recording Cerebellar/Coordination Assessments

Cerebellar/Coordination assesments	Abnormality Present?	If Abnormal, explain: (Select all that apply)
12. inger-to-Nose	☐Yes ☐No ☐Cannot Assess ☐Other specify:	☐RUE ☐LUE ☐Dysmetria ☐Slowness ☐Cannot Assess due to Weakness ☐Other, specify:
13. apid Alternating Movements	☐Yes ☐No ☐Cannot Assess ☐Other specify:	☐RUE ☐LUE ☐Dysmetria ☐Slowness ☐Cannot Assess due to Weakness ☐Other, specify:
14. eel-to-Shin	☐Yes ☐No ☐Cannot Assess ☐Other specify:	☐RUE ☐LUE ☐Dysmetria ☐Slowness ☐Cannot Assess due to Weakness ☐Other, specify:

6.5 Reflexes

15. Reflexes–global assessment:

☐Normal ☐Cannot Assess

☐Abnormal (Continue to 15a and 15b) ☐Other, specify:

a. Assessment of Limbs

i. Right Arm:

☐Increased with clonus ☐Hypoactive

☐Increased without clonus ☐Absent

ii. Left Arm:

☐Increased with clonus ☐Hypoactive

☐Increased without clonus ☐Absent

iii. Right Leg:

☐Increased with clonus ☐Hypoactive

☐Increased without clonus ☐Absent

Left Leg:

☐Increased with clonus ☐Hypoactive

☐Increased without clonus ☐Absent

b. Plantar Response

i. Right:

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☐Flexor
☐Extensor
☐Equivocal
☐Cannot Assess
☐Other, specify:

ii. Left:

☐Flexor
☐Extensor
☐Equivocal
☐Cannot Assess
☐Other, specify:

6.6 Gait

16. Gait–global assessment: ☐ Normal ☐ Abnormal (Indicate type below) ☐Cannot Assess ☐Other, specify:

a. Type of Abnormal Gait:

☐Ataxic Gait
☐Hemiparetic Gait–Left side
☐Hemiparetic Gait–Right side
☐Diplegic Gait
☐Parkinsonian Gait
☐Other Gait Abnormalities, specify:

6.7 Sensory/Sensation

17. Sensory System–global assessment:

☐Normal
☐Abnormal (Continue to 17a–17d)
☐Cannot Assess
☐Other, specify:

a. Symmetry of Abnormality:

☐Symmetric ☐Asymmetric

b. Location of Abnormality (Select all that apply):

☐Stocking, explain:
☐Stocking/Glove, explain:
☐Dermatome, explain:
☐Sensory Nerve, explain:
☐Other, specify:

c. Patient Description of abnormal symptoms:

d. Sensory Modalities Affected (Select all that apply):

☐Light Touch
☐Pain and Temperature
☐Vibration
☐Proprioception
☐Other, specify:

** Recommended for pediatric studies ONLY

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6.8 General Instructions

The Neurological Exam is generally administered at screening and/or baseline to determine study eligibility. It may also be administered at follow-up visits to track a participant's/subject's physical status. This CRF is Supplemental for certain types of clinical research, but is not intended to be used in all studies. If the study is going to conduct a neurological exam, investigators should consider these elements, but there may be some studies where a physical exam is not appropriate or could be abbreviated.

The data elements collected on this form may need to be modified for study-specific research hypotheses. Some, but not all epilepsy studies, will include Neuropsychological testing. For these studies, the mental status section of the Neurological Exam can and should be modified, and the Recommended Neuropsychology Instruments should be consulted. Every CDE contained in this CRF Module may not be appropriate for every epilepsy study, e.g. pediatric versus adult populations. The CDEs are dependent on the age of the patients, the research question(s) being investigated, and other data being collected. However please note that if a study chooses not to collect the information contained on this CRF Module, the researchers should be prepared to justify why if study section asks.

6.9 Suggested Screening Tools

Attention–forward digit span–6 is normal in adults
Working Memory–reverse digit span–4 is normal in adults
Recent (Episodic) Memory–recall of 3 objects after 5 minute delay–3/3 is normal in adults
Remote (Semantic) Memory–listing of verifiable historical or personal events

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7 Syndromes by Age of Onset

[Study Name/ID pre-filled] Site Name:

Subject ID:

7.1 Syndromes by Age of Onset: (check all that apply)

Neonatal Period Table

Neonatal Period	Present?
Benign familial neonatal epilepsy (BFNE)	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Early myoclonic encephalopathy (EME)	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Ohtahara syndrome	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A

Infancy Table

Infancy	Present?
Epilepsy of infancy with migrating focal seizures	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
West syndromes	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Myoclonic epilepsy in infancy (MEI)	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A

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Infancy	Present?
Benign infantile epilepsy	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Benign familial infantile epilepsy	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Dravet syndrome	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Myoclonic encephalopathy in nonprogressive disorders	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A

Childhood Table

Childhood	Present?
Febrile seizures plus (FS+; can start in infancy)	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Early onset benign childhood occipital epilepsy (Panayiotopoulos type)	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Epilepsy with myoclonic atonic seizures	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Benign childhood epilepsy with centrotemporal spikes (BCECTS)	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A

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Childhood	Present?
Autosomal-dominant nocturnal frontal lobe epilepsy (ADNFLE)	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Late onset childhood occipital epilepsy (Gastaut type)	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Epilepsy with myoclonic absences	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Lennox-Gastaut syndrome	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Epileptic encephalopathy with continuous spike-and-wave during sleep (CSWS)	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Landau-Kleffner syndrome (LKS)	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Childhood absence epilepsy (CAE)	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A

Adolescence – Adult Table

Adolescence – Adult	Present?
Juvenile absence epilepsy (JAE)	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A

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Adolescence – Adult	Present?
Other familial temporal lobe epilepsies	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Juvenile myoclonic epilepsy (JME)	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Progressive myoclonus epilepsies (PME)	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Autosomal Dominant Epilepsy with Auditory Features (ADEAF)	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Epilepsy with generalized tonic-clonic seizures alone	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A

Less Specific Age Relationship Table

Less Specific Age Relationship	Present?
Familial focal epilepsy with variable foci (childhood to adult)	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Reflex epilepsies	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A

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Distinctive Constellations Table

Distinctive Constellations	Present?
Mesial temporal lobe epilepsy	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Rasmussen syndrome	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Gelastic seizures with hypothalamic hamartoma	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A

Other Localization Related Epilepsies Table

Other Localization Related Epilepsies	Present?
Temporal lobe epilepsy	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Frontal lobe epilepsy	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Occipital lobe epilepsy	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
Parietal lobe epilepsy	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A

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Other Localization Related Epilepsies	Present?
Focal epilepsy (specific localization unknown)	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A

Other Table

Other	Present?
The epilepsy does not fit into one of these specific electro-clinical or distinctive constellations categories	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A

7.2 Additional Information

If two or more epilepsy syndromes were selected as present, rate the confidence level that these are distinct syndromes:

☐ No Confidence
☐ Possible
☐ Probable
☐ Definite
☐ Unknown
☐ N/A

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7.3 GENERAL INSTRUCTIONS

Based on the current International League Against Epilepsy (ILAE) guidelines, this CRF Module is recommended to classify syndromes for all epilepsy studies. Only one syndrome should be checked for a given time point, however *it is possible to have had a syndrome in infancy that develops into another syndrome during childhood. Therefore, if the form is used more than once during follow-up, the possible evolution of syndromes can be codified.*

The following definitions should be used when completing this form:

- Not Present/None = The summary of evidence suggests no possibility
- Possible = The summary of evidence suggests less than 50% confidence level
- Probable = The summary of evidence suggests greater than 50% confidence level
- Definite = The summary of evidence suggests 100% confidence level
- Unknown = The summary of evidence is not sufficient to support a finding
- N/A = Not Applicable; to be used at the discretion of the Principal Investigator based on study design

7.4 REFERENCES

Berg AT, Berkovic SF, Brodie MJ, Buchhalter J, Cross JH, van Emde Boas W, Engel J, French J, Glauser TA, Mathern GW, Moshé SL, Nordli D, Plouin P, Scheffer IE. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005-2009. Epilepsia. 2010 Apr; 51(4):676-85. Epub 2010 Feb 26.
Freely available online at: Classifications and Terminology Report

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8 Classification of Etiology

[Study Name/ID pre-filled] Site Name:

Subject ID:

Etiology Classification Table

Etiology Classification (choose only one)	Present
☐ Genetic or presumed genetic OR epilepsy of unknown cause	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A
☐ Structural or metabolic	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A

Specific Etiologies Table

Specific Etiologies* (answer all)	Present?	Primary Cause (only 1)	Secondary Cause (only 1)	If more than one specific etiology is selected, specify:
Viral, bacterial and parasitic infections	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A	☐ Primary Cause	☐ Secondary Cause	Data to be entered by site
Traumatic brain injury	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A	☐ Primary Cause	☐ Secondary Cause	Data to be entered by site
Stroke	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A	☐ Primary Cause	☐ Secondary Cause	Data to be entered by site

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Specific Etiologies* (answer all)	Present?	Primary Cause (only 1)	Secondary Cause (only 1)	If more than one specific etiology is selected, specify:
Intraventricular hemorrhage	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A	☐ Primary Cause	☐ Secondary Cause	Data to be entered by site
Hypoxic-ischemic encephalopathy	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A	☐ Primary Cause	☐ Secondary Cause	Data to be entered by site
Other metabolic or toxic insults	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A	☐ Primary Cause	☐ Secondary Cause	Data to be entered by site
Neurocutaneous syndromes	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A	☐ Primary Cause	☐ Secondary Cause	Data to be entered by site
Inborn errors of metabolism	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A	☐ Primary Cause	☐ Secondary Cause	Data to be entered by site
Genetic and chromosomal development encephalopathies	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A	☐ Primary Cause	☐ Secondary Cause	Data to be entered by site
Developmental encephalopathy of unknown cause as evidenced by the presence of mental retardation, cerebral palsy, or autism with no evidence of a specific insult of disorder to which cause can be attributed preceding the onset of epilepsy	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A	☐ Primary Cause	☐ Secondary Cause	Data to be entered by site

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Specific Etiologies* (answer all)	Present?	Primary Cause (only 1)	Secondary Cause (only 1)	If more than one specific etiology is selected, specify:
Malformations of cortical or other brain development with or without known genetic determinants	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A	☐ Primary Cause	☐ Secondary Cause	Data to be entered by site
Neoplasia	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A	☐ Primary Cause	☐ Secondary Cause	Data to be entered by site
Mesial temporal sclerosis	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A	☐ Primary Cause	☐ Secondary Cause	Data to be entered by site
Dementia	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A	☐ Primary Cause	☐ Secondary Cause	Data to be entered by site
Other degenerative neurologic diseases	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A	☐ Primary Cause	☐ Secondary Cause	Data to be entered by site
Genetic or presumed genetic, if known specify:	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A	☐ Primary Cause	☐ Secondary Cause	Data to be entered by site
Epilepsy of unknown cause, without relevant abnormalities on examination, cognition, history, or imaging	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A	☐ Primary Cause	☐ Secondary Cause	Data to be entered by site

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Specific Etiologies* (answer all)	Present?	Primary Cause (only 1)	Secondary Cause (only 1)	If more than one specific etiology is selected, specify:
Other, specify:	☐ No ☐ Possible ☐ Probable ☐ Definite ☐ Unknown ☐ N/A	☐ Primary Cause	☐ Secondary Cause	Data to be entered by site

*Element is classified as Core.

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8.1 GENERAL INSTRUCTIONS

The Classification of Etiology is generally administered at screening or baseline to determine study eligibility. It may also be administered at a later timepoint in the study to track changes in etiology that result from obtaining new information that would reclassify the participant/subject. If the study captures etiology at more than one timepoint during the study, data should clearly identify etiology at baseline from etiology at another timepoint(s).

Based on the current International League Against Epilepsy (ILAE) guidelines, this CRF Module is recommended to classify etiology for epilepsy studies. The classification of etiology included on the CRF are based on the current International League Against Epilepsy (ILAE) guidelines, which outline the concepts, terminology, and approaches for classifying the etiology of epilepsy[2].

The following definitions should be used when completing this form:

- No = Not present
- Possible = The summary of evidence suggests less than 50% confidence level
- Probable = The summary of evidence suggests greater than 50% confidence level
- Definite = The summary of evidence suggests 100% confidence level
- Unknown = The summary of evidence is not sufficient to support a finding
- N/A = Not Applicable; to be used at the discretion of the Principal Investigator based on study design

8.2 REFERNCES

Berg AT, Berkovic SF, Brodie MJ, Buchhalter J, Cross JH, van Emde Boas W, Engel J, French J, Glauser TA, Mathern GW, Moshé SL, Nordli D, Plouin P, Scheffer IE. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005-2009. Epilepsia. 2010 Apr;51(4):676-85. Epub 2010 Feb 26.

Freely available online at Report of the Commission on Classification and Terminology.

[2] Berg AT, Berkovic SF, Brodie MJ, Buchhalter J, Cross JH, van Emde Boas W, Engel J, French J, Glauser TA, Mathern GW, Moshé SL, Nordli D, Plouin P, Scheffer IE. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005-2009. Epilepsia. 2010 Apr; 51(4):676-85. Epub 2010 Feb 26.

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9 Classification of Seizures

[Study Name/ID pre-filled] Site Name:

Subject ID:

1) Classification of Seizures (check all that apply)*

☐ Focal – complete questions for focal seizure subtypes** (see question **2** below)
☐ Generalized - complete questions for Generalized seizure subtypes** (see question **3** below)
☐ Unknown if generalized or focal
☐ Unclassified - complete questions for Unclassified seizure type** (see question **4** below)

2) Focal Seizure Subtypes (according to degree of impairment)

a) ☐ Focal aware (Without impairment of awareness):
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A

i) ☐ Focal aware-motor/observable (With observable motor or autonomic components):
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A

ii) ☐ Focal Aware-non-motor (Involving subjective sensory or psychic phenomena only):
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A

b) ☐Focal Impaired Awareness (with impairment of awareness (roughly corresponds to the concept of "complex partial seizure")):
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A

i) ☐Focal impaired awareness-motor/observable (With observable motor or autonomic components):
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A

ii) ☐Focal impaired awareness-non-motor (without observable motor components):
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A

c) ☐ Focal to bilateral, tonic clonic seizure (involving tonic, followed by clonic movements, replaces the term "secondarily generalized seizure"):
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A

d) ☐ Focal, unknown awareness:

i) With observable motor:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A

ii) ☐ Without observable motor:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A

e) ☐ Clonic:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A

f) ☐ Tonic:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A

g) ☐ Atonic:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A

h) ☐ Epileptic spasm:

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☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A

3) Generalized Seizure Subtypes**[i]
(answer all)
a) ☐ Motor: ☐ Yes ☐ No
i) ☐ Myoclonic: ☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A
(1) ☐ Myoclonic atonic:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A
ii) ☐ Clonic:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A
iii) ☐ Tonic:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A
iv) ☐ Atonic:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A
v) ☐ Generalized tonic-clonic:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A
vi) ☐ Epileptic spasms:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A
vii) ☐ Not otherwise specified:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A

b) ☐ Non-motor (absence) (specify type below): ☐ Yes ☐ No
i) ☐ Absence NOS:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A
ii) ☐ Typical absence:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A
iii) ☐ Atypical absence:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A
iv) ☐ Myoclonic absence:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A
v) ☐ Absence with eyelid myoclonia:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A

4) ☐ Seizure subtypes of Unknown onset (unknown if focal or generalized):
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A

a) ☐ Generalized tonic-clonic:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A
i) ☐ Myoclonic-tonic-clonic:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A
b) ☐ Motor not otherwise specified:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A
c) ☐ Clonic:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A
d) ☐ Tonic:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A
e) ☐ Myoclonic:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A
f) ☐ Atonic:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A
g) ☐ Epileptic spasms:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A
h) ☐ Motor not otherwise specified:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A

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i) ☐ Non-motor not otherwise specified:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A

5) ☐ Unclassified - Complete below for Unclassified seizure type**
a) ☐ Seizure type is unclassified:
☐ No ☐ Possible ☐ Probably ☐ Definite ☐ Unknown ☐ N/A

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9.1 GENERAL INSTRUCTIONS

This CRF Module is recommended to classify seizures for epilepsy studies. The seizure classifications included on the CRF are based on the current International League Against Epilepsy (ILAE) guidelines, which outline the concepts, terminology, and approaches for classifying seizures.[ii]
Elements on this form are classified as Supplemental, unless specified by an asterisk as described below:
* Element is classified as Core
**Element is classified as Supplemental – Highly Recommended

9.2 SPECIFIC INSTRUCTIONS

- The following definitions should be used when completing this form:
  No = Not present
  Possible = The summary of evidence suggests less than 50% confidence level
  Probable = The summary of evidence suggests greater than 50% confidence level
  Definite = The summary of evidence suggests 100% confidence level
  Unknown = The summary of evidence is not sufficient to support a finding
  N/A = Not Applicable; to be used at the discretion of the Principal Investigator based on study design
- Focal Unknown Awareness: If a seizure is definitely focal, but awareness is unknown, please use the Focal Unknown Awareness categorization.
- Tonic, clonic, atonic and epileptic spasm: When these seizure types occur in patients with combined focal and generalized epilepsy, it is often difficult to determine whether their onset is focal or generalized. Please use the Unknown Onset box in these cases. (e.g. Lennox Gastaut Syndrome).
- In a combined focal and generalized epilepsy (e.g. Lennox Gastaut Syndrome), the tonic, atonic or tonic-clonic seizure should be considered to be of unknown onset unless captured on EEG with a clear focal or generalized onset.
- Focal Impaired Awareness: This categorization should be used if a subject has focal seizure and they have confusion or difficulty understanding their environment or difficulty remembering what has occurred even in the absence of an altered level of consciousness.
- A seizure should only be considered “definite” tonic-clonic if there is a description of tonic activity followed by clonic activity with fall to the ground and post-ictal stupor. If one of those elements have not been witnessed, then it should be labeled “possible” or “probable.” There needs to be a witnessed event. If there is a tonic-clonic seizure and other evidence of focality, it should be identified as focal to bilateral.
- Individuals will be presumed to have a single epilepsy seizure type (focal or generalized) unless they have evidence to the contrary or they have a syndrome that is typically associated with both focal and generalized seizures.
- If a seizure cannot be adequately classified, it should not be fit into a category to which it does not belong.

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10 Magnetic Resonance Imaging (MRI)

[Study Name/ID pre-filled] Site Name:

Subject ID:

1. Imaging Parameters:
   a. Epilepsy-specific Protocol: *(Check only one)* ☐ Yes ☐ No
   b. Sequences Obtained:
   c. Date Scan Performed: / / m m dd yyyy
2. Imaging Normality: *(Check only one)*
   ☐ Normal
   ☐ Abnormal
   ☐ Incidental (not relevant for epilepsy evaluation)
      a. If Abnormal, number of abnormality types:
      b. If Abnormal, describe type(s):
3. Lateralization: (Check only one) ☐ Left ☐ Right ☐ Bilateral
4. Distribution: (Check only one) ☐ Unifocal ☐ Multilobar ☐ Hemispheric
   ☐ Multifocal ☐ Diffuse / generalized
5. Location:

Table for Recording Locations - Cortical

Cortical (Check only one)	Side (Check only one)
☐ Basal occipital (BO)	☐ Left ☐ Right
☐ Dorsal lateral frontal (DLF)	☐ Left ☐ Right
☐ Dorsal lateral parietal (DLP)	☐ Left ☐ Right
☐ Frontal Polar (FP)	☐ Left ☐ Right
☐ Insula (INS)	☐ Left ☐ Right
☐ Lateral occipital (LO)	☐ Left ☐ Right
☐ Lateral temporal (LT)	☐ Left ☐ Right
☐ Mesial frontal (MF)	☐ Left ☐ Right
☐ Mesial occipital (MO)	☐ Left ☐ Right
☐ Mesial parietal (MP)	☐ Left ☐ Right
☐ Mesial temporal (MT)	☐ Left ☐ Right
☐ Orbital frontal (OF)	☐ Left ☐ Right
☐ Temporal polar (TP)	☐ Left ☐ Right

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Table for Recording Locations - Subcortical

Subcortical (Check only one)	Side (Check only one)
☐ Basal ganglia	☐ Left ☐ Right
☐ Callosum	☐ Left ☐ Right
☐ Grey-white matter junction	☐ Left ☐ Right
☐ Periventricular	☐ Left ☐ Right
☐ Thalamus	☐ Left ☐ Right
☐ White matter-other	☐ Left ☐ Right

6. Features (Check all that apply):

☐ Agenesis
☐ Atrophy
☐ Cortical thinning
☐ Cystic (including multicystic)
☐ Decreased grey-white matter distinction
☐ Dysgenesis (includes dysmorphology of cortical mantle)
☐ Heterotopic tissue versus migration abnormality
☐ Hypertrophy
☐ Hyperplasia (grey or white matter)
☐ Hypoplasia (grey or white matter)
☐ Loss of architecture (specific to hippocampus)
☐ Malformation related white matter signal abnormality

7. Contrast enhancement (Check only one): ☐ Yes ☐ No

8. Impression of Specific Abnormalities (Check all that apply):

   a. ☐ Mesial Temporal Sclerosis

      If applicable, specify:
      ☐ Hippocampal sclerosis
      ☐ Hippocampal sclerosis plus inter-lateral temporal dysplasia/atrophy
      ☐ Hippocampal sclerosis with remote dual pathology (i.e., remote lesion)

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b. ☐Malformation of cortical development (MCD)

If applicable, specify:

☐ Band heterotopias
☐ Development tumor-like lesion
☐ Focal cortical dysplasia
☐ Hemimegalencephaly
☐ Heterotopia / heterotopion (other)
☐ Hypothalamic hamartoma
☐ Lissencephaly
☐ Microcephaly
☐ Pachygyria
☐ Partial Hemimegalencephaly
☐ Periventricular nodular heterotopias
☐ Polymicrogyria
☐ Schizencephaly (malformation related only)
☐ Transmantle focal cortical dysplasia
☐ Tuberous sclerosis

Comments:

9. ☐Vascular

If applicable, specify:

☐ Arterial stroke
☐ Arterial vascular malformation
☐ Cavernoma
☐ Hemorrhage (including post hemorrhage evidence, e.g. periventricular)
☐ Venous stroke
☐ Vascular malformation (other)

10. ☐Neoplasm[3]

If applicable, specify:

☐ Primary ☐ Secondary

11. ☐Inflamatory/infectious

If applicable, specify:

[3] If Developmental tumor-like lesion, see MCD to classify

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☐ Abcess
☐ Cysticercosis
☐ Encephalitis (other)
☐ Limbic encephalitis
☐ Sarcoidosis
☐ Vasculitis

12. ☐Atrophy or tissue loss

If applicable, specify:

☐ Encephalomalacia (related to surgery, abscess, radiation, trauma)
☐ Focal or lobar atrophy (other)
☐ Trauma related
☐ Vascular related (If caused by Stroke, see Vascular to classify)

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10.1 GENERAL INSTRUCTIONS

Provided below are the minimum requirements for MRI epilepsy evaluation to evaluate cause for seizures and confirm or direct investigations to the seizure focus. They are directed at identifying the most common causes of focal epilepsy: Malformations of cortical development, MTS, tumor, vascular, and inflammatory causes. As malformations of cortical development are the most common causes of epilepsy in children emphasis should be on T2 (including FSE) images; FLAIR imaging gains in importance in adolescence and adulthood when mesial temporal sclerosis and gliosis are of greater concern.

If the 1st MRI scan is performed between ages 8 and 18 months is normal, then the MRI study should be repeated at age 24-30 months if seizures persist (the cerebral cortex is difficult to evaluate in children imaged 8-18 months due to on-going myelination and relatively poor of contrast between cortex and white matter).

General sequences are listed, but not specific imaging parameters as they depend on make of scanner and magnetic field strength. Suggestions are provided for adult, children and infants (<1 years age).

In addition to these basic imaging protocols, consideration should be given to:

- Axial magnetization transfer T1 weighted images in children <14 y.o.
- High resolution coronal turbo/fast spin echo T2 weighted images of the hippocampal formations (orthogonal to the long axis), 3 mm skip 0.
- Contrast need not be routinely used unless characterization of vascular, tumor or inflammatory lesion is considered necessary.
- Perfusion, diffusion sequences are optional.
- Turbo / fast spin echo proton density sequences (4-5 mm thick) can be useful in detection of subtle transmantle dysplasias.

10.2 Adults (14 and older)

- Axial turbo / fast spin echo T2-weighted images (2 mm skip 0), whole brain
- Coronal turbo / fast spin echo T2 weighted high resolution coronal oblique sequence (512 x 512, maximum slice thickness of 4 mm), whole brain
- Coronal fast FLAIR T2 weighted (and axial for children if possible)
- Sagittal or coronal 3D T1 weighted gradient echo volume sequence (256 x 256, maximum slice thickness of 1.5 mm, preferably 1.0 mm for isotropic voxels). Sagittal preferred, coronal acceptable, axial is not advised. The quality of this sequence is critical since it is relied upon for post-processing–reformatting for evaluation of cortical thickness, image registration and segmentation, including volumetry.
- Standard sagittal T1-weighted sequence images (if gradient echo volume sequence is not acquired in the sagittal plane)

All coronal sequences should be acquired in an oblique plane orthogonal to the long axis of the hippocampus.

10.3 Children for 1-14 years:

- Axial turbo / fast spin echo T2-weighted images (2 mm skip 0), whole brain
- Coronal turbo / fast spin echo T2 weighted high resolution coronal oblique sequence (512 x 512, maximum slice thickness of 4 mm), whole brain
- Axial fast FLAIR T2 weighted (and coronal if possible)
- Sagittal or coronal 3D T1 weighted gradient echo volume sequence (256 x 256, maximum slice thickness of 1.5 mm, preferably 1.0 mm for isotropic voxels). Sagittal preferred, coronal acceptable, axial is not advised. The

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quality of this sequence is critical since it is relied upon for post-processing– reformatting for evaluation of cortical thickness, image registration and segmentation, including volumetry.

- Standard sagittal T1-weighted sequence images (if gradient echo volume sequence is not acquired in the sagittal plane)

All coronal sequences should be acquired in an oblique plane orthogonal to the long axis of the hippocampus.

10.4 Infants (< one year)

- Children younger than one year require special sequences as immature myelination affects the ability to identify common causes of epilepsy. MR imaging (especially high resolution T2 images) performed early in the first year of life in infants with epilepsy is important to identify areas of cortical or subcortical dysplasia,.
- Axial turbo / fast spin echo T2-weighted images (2 mm skip 0), whole brain
- Coronal turbo / fast spin echo T2 weighted high resolution coronal oblique sequence (512 x 512, maximum slice thickness of 4 mm), whole brain
- Axial fast FLAIR T2 weighted
- Sagittal turbo / fast spin echo T2-weighted images (2 mm skip 0), whole brain
- Standard sagittal T1-weighted sequence images (if gradient echo volume sequence is not acquired in the sagittal plane)
- (Volumetric T1 weighted sequences are less useful prior to age one year due to incomplete myelination on T1 sequences)

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11 Functional Magnetic Resonance Imaging (fMRI)

[Study Name/ID pre-filled] Site Name:

Subject ID:

1. Date of Study: //20 mm dd yyyy
2. Last seizure occurrence in relation to study: //20 mm dd yyyy : (HH:MM) ☐AM ☐PM ☐24-hr clock
3. Scanner: (Check only one) ☐1.5T ☐ 3.0T ☐Other
   a. If Other, specify:
4. Technique: (Check only one) ☐BOLD ☐ASL ☐Other
   a. If Other, specify:
5. Complicating Factors: (Check all that apply)
   ☐Postictal ☐Vascular malformation
   ☐Mass ☐Carotid stenosis
6. Paradigm Task Design: (Check all that apply) ☐Block Design ☐Event Related
7. Behavioral Monitoring: (Check only one) ☐Yes ☐No
8. Domain Tested: (Check all that apply)
   ☐Motor
   ☐Somatosensory
   ☐Visual
   a. ☐***Language:***
   ☐Expressive ☐Receptive ☐Both
   b. ☐Memory:
   ☐Explicit
   ☐Implicit
   ☐Recall
   ☐Encoding
   ☐Verbal
   ☐Visual spatial
   ☐Both

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9. Analysis: ☐Native space ☐Standard space (Talairach, MNI, other)
    a. If Standard space, specify:

Analysis software: (Check all that apply)

☐SPM ☐AFNI ☐FSL ☐MEDX ☐Other

Analysis:

☐Visual blinded ☐Visual unblinded

Analysis:

☐ROI ☐Mask ☐VBM

    b. If ROI, specify hemisphere:
    c. If ROI, specify region:
    d. If ROI, specify activation mean:

10. Language: (Check only one)
    a. ☐Frontal Laterality:

        ☐Right ☐Left ☐Bilateral ☐Unknown

    b. ☐Temporal Laterality:

        ☐Right ☐Left ☐Bilateral ☐Unknown

    c. ☐Hemisphere Laterality:

        ☐Right ☐Left ☐Bilateral ☐Unknown

11. Memory: (Check only one)
    a. Hemisphere Laterality:

        ☐Right ☐Left ☐Bilateral ☐Unknown

12. Description of Language and Memory Paradigms (TBD-list if Visual or Auditory)

11.1 General Instructions

fMRI should be performed in the awake conscious state. There is some evidence that information can be obtained from the sleep or the sedated state. The deeper the anesthesia the less reliable data is the data obtained. When possible it is helpful to monitor response. When there is an issue when activation maps are peculiar it is

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helpful to know how well the task was performed. However, there are times when effort is more important than performance success. Also unmonitored cognitive paradigms may be robust and reliable. It is important that the patient can perform the task. Simple tasks often give robust activation of the expensive network. Fancy control conditions may remove desired responses. If a patient is visually impaired, has a field cut, or is illiterate then auditory tasks may be preferred. Null datasets are not informative; they should either not be used, the study should be repeated, or other (invasive means) used.

Task paradigms may be block designs or event related designs. Most language and sensory/motor fMRI employ block design. Memory paradigms usually employ event related designs as data may be analyzed based on successful encoding of test items. Hemicycles should be 20-40 seconds, must be divisible by TR, and usually are 3-5 cycles, 3 is the minimum and used for more robust tasks (motor), 4 is usually adequate. If compliance is an issue it is better to use many short runs and combine, then one long run. For event related designs one needs 30 successfully answered/encoded items and similar number of controls.

Image data may be processed by any number of software programs. Data may be analyzed in native (individual) space or in a standard anatomical atlas. The former is more helpful for individual surgical planning, the later makes it easier to compare results across a group of patients. Image ratings may be visual or they may be semi-quantitative. If visual then, for research purposes, it is best if the rater is blinded to patient identity and circumstances. There are several methods for regional of analysis approaches. Hemispheric and regional indices have been used but it is helpful to recall that crossed dominance can be found and it is helpful to target task and rating to intended surgical field. Some use anatomical regions (e.g. Broca's, Wernicke's), some sue functional regions based on normal volunteers' data. Methods include those based on voxel counts that exceed a particular threshold, t-scores for region, or bootstrap methods that adjust thresholds on an individual basis that are data driven. To gain signal by minimizing multiple comparisons and degrees of freedom a Mask approach analysis is sometimes used (where the primary analysis is constrained to the regions selected).

There are four circumstances when BOLD fMRI signal may be attenuated and thus result in spurious interpretation; they are 1) post ictal state 2) mass lesion with edema 3) vascular steal 4) critical carotid stenosis (usually elderly). It is thus important to know when previous seizure occurred, and how severe, e.g. cluster or prolonged.

- Motor tasks include tapping fingers, wiggling tongue (motor cortex), or foot.
- Sensory tasks include brushing face, hand or foot (somatossensory cortex); tones (auditory cortex), or flashing/alternating checkerboard (visual cortex).
- Memory tasks have material specificity (verbal, visual spatial), and may use novel or familiar items, may involve implicit or explicit memory, and may image encoding or retrieval (hippocampal formation and mesial temporal structures).
- Language/Speech tasks take several forms. Fluency tasks (may be semantic or phonemic) generally target anterior "expressive" areas (IFG), and are usually free fluency (generate words to letters (CLFPRW, a phonemic task; generate words to categories (animals, food), or may be paced (generate a noun to a presented verb; or generate a rhyme, or antonym; or stem completion. For these tasks it helps to have an outside scanner measure of ability, it is hard to generate signal if the patient cannot generate 3 words over 30 seconds to any one stimuli.

Other tasks involve a decision which allow for in scanner monitoring, but change the activation maps. This indicate (push button, raised finger) if a presented word matches a pre-specified category (e.g. animals). Tasks may also decide whether presented items match in some way, or whether a sentence is grammatically or syntactically correct. Tasks that employ phrases, sentences, or paragraphs are more likely to "activate" temporal "receptive cortex" also superior temporal sulcus. They may be passive (listening to stories) or require some action on the item(s) presented (is this sentence grammatically correct, is this definition of a word correct).

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12 Laboratory Tests and Tracking

[Study Name/ID pre-filled]

Site Name:
Subject ID:

Table 1: Lab Panel

Lab Panel: (Choose one)	Date Collected and Time Collected:	Accession Number:
☐ CHEMISTRY (Blood) ☐ HEMATOLOGY (Blood) ☐ URINALYSIS ☐ Other:	(mm /d d /y y y y): (h h: m m) ☐ AM ☐ PM ☐ (24-hr clock)	Data to be filled in by site

Indicate the appropriate result for each test.

Table 2: Test Results

Test Name	Test performed?	Result	Units for Result	Was test result abnormal?	If abnormal, clinically significant?
Urea	☐Yes ☐No	Data to be entered by site	Data to be entered by site	☐ Normal ☐ Abnormal	☐ Clinically significant ☐ Not clinically
Creatinine	☐Yes ☐No	Data to be entered by site	Data to be entered by site	☐ Normal ☐ Abnormal	☐ Clinically significant ☐ Not clinically
Aspartate Aminotransferase (ASAT/SGOT)	☐Yes ☐No	Data to be entered by site	Data to be entered by site	☐ Normal ☐ Abnormal	☐ Clinically significant ☐ Not clinically
Alanine Aminotransferase (ALAT/SGPT)	☐Yes ☐No	Data to be entered by site	Data to be entered by site	☐ Normal ☐ Abnormal	☐ Clinically significant ☐ Not clinically
Total Bilirubin	☐Yes ☐No	Data to be entered by site	Data to be entered by site	☐ Normal ☐ Abnormal	☐ Clinically significant ☐ Not clinically
Sodium	☐Yes ☐No	Data to be entered by site	Data to be entered by site	☐ Normal ☐ Abnormal	☐ Clinically significant ☐ Not clinically
Potassium	☐Yes ☐No	Data to be entered by site	Data to be entered by site	☐ Normal ☐ Abnormal	☐ Clinically significant ☐ Not clinically
Hemoglobin	☐Yes ☐No	Data to be entered by site	Data to be entered by site	☐ Normal ☐ Abnormal	☐ Clinically significant ☐ Not clinically
Hematocrit	☐Yes ☐No	Data to be entered by site	Data to be entered by site	☐ Normal ☐ Abnormal	☐ Clinically significant ☐ Not clinically
White blood cell	☐Yes ☐No	Data to be entered by site	Data to be entered by site	☐ Normal ☐ Abnormal	☐ Clinically significant ☐ Not clinically

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Test Name	Test performed?	Result	Units for Result	Was test result abnormal?	If abnormal, clinically significant?
Neutrophils	☐Yes ☐No	Data to be entered by site	Data to be entered by site	☐ Normal ☐ Abnormal	☐ Clinically significant ☐ Not clinically
Lymphocytes	☐Yes ☐No	Data to be entered by site	Data to be entered by site	☐ Normal ☐ Abnormal	☐ Clinically significant ☐ Not clinically
Eosinophils	☐Yes ☐No	Data to be entered by site	Data to be entered by site	☐ Normal ☐ Abnormal	☐ Clinically significant ☐ Not clinically
Platelet	☐Yes ☐No	Data to be entered by site	Data to be entered by site	☐ Normal ☐ Abnormal	☐ Clinically significant ☐ Not clinically
Other, specify:	☐Yes ☐No	Data to be entered by site	Data to be entered by site	☐ Normal ☐ Abnormal	☐ Clinically significant ☐ Not clinically

12.1 General Instructions

Laboratory tests are routinely administered in clinical trials of pharmacological interventions to assess participant/subject safety.

Laboratory tests may also be used to determine an individual's eligibility for a study.

Laboratory results may be received via electronic files directly from central study laboratories or recorded manually on case report forms if the study is using a local lab. In either scenario, it is recommended that the Laboratory Test Tracking form be used to record when samples were collected (date and time) so that the laboratory tests results can be matched with the samples collected for each participant/subject.

Important note: None of the data elements included on this CRF are considered Core (i.e., strongly recommended for all studies to collect). These data elements are supplemental, frequently used on clinical trials and should be collected if the research team considers them appropriate for their study.

12.2 Specific Instructions

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

- Lab Panel – Choose the lab panel that was performed.
- Date and Time Collected –Record the date (and time) the specimen was collected. 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 the format acceptable to the study database.
- Accession Number – Provide the accession number or bar code number that is assigned to the specimen.
- Test – Indicate the name of each laboratory test that is run on the specimen. See the data dictionary for additional information on coding the test name using Logical Observation Identifiers Names and Codes (LOINC).
- Test Performed – Choose one. Indicate whether or not the test was performed on the specimen.

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- Result – Record the numeric or alpha-numeric results for each laboratory test.
- Unit for Result – Record the units the numeric results for each laboratory test are measured in. See the data dictionary for additional information on coding the unit of measure using Unified Code for Units of Measure (UCUM).
- Abnormal Result – Choose one. Indicate if the laboratory test result is abnormal. Abnormal means the test result falls outside the normal range. Clinical Significance – Choose one. If the laboratory test result is abnormal, indicate if the physician considers the result clinically significant.

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13 Anti Epileptic Drug (AED) Resistance Log

[Study Name/ID pre-filled]

Site Name:
Subject ID:

Please write in the information below for each AED that was taken by the subject in the past, including current AEDs. This form is intended for chronic AED therapies only. Do not list PRN and rescue medications.

Table for Recording AED Resistant Data Details

Line #	AED Name	AED Formulation Known? (e.g., IR, ER, liquid)	AED Schedule Known? (e.g., TID, BID)	Reason for discontinuation known?	Was AED appropriate for the epilepsy syndrome? (Check only one)	Was 3 months of therapy achieved without discontinuation due to adverse events?	Were attempts made to adjust dose? (not titration)	Did the subject continue to have seizures on this AED despite dose adjustment? (Check only one)	Are the answers to all the previous questions known? (Check only one)	Are the answers to all the previous questions "Yes"? (Check only one)
#	Data to be entered.	☐ Yes ☐ No If Known, specify:	☐ Yes ☐ No If Known, specify:	☐ Side effects - idiosyncratic, specify ☐ Side effects - dose related, specify ☐ Lack of efficacy ☐ Side effects - chronic ☐ Other, specify:	☐ Yes ☐ No	☐ Yes ☐ No ☐ Unknown	☐ Yes ☐ No ☐ Unknown	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No

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Line #	AED Name	AED Formulation Known? (e.g., IR, ER, liquid)	AED Schedule Known? (e.g., TID, BID)	Reason for discontinuation known?	Was AED appropriate for the epilepsy syndrome? (Check only one)	Was 3 months of therapy achieved without discontinuation due to adverse events?	Were attempts made to adjust dose? (not titration)	Did the subject continue to have seizures on this AED despite dose adjustment? (Check only one)	Are the answers to all the previous questions known? (Check only one)	Are the answers to all the previous questions "Yes"? (Check only one)
#	Data to be entered.	☐ Yes ☐ No If Known, specify:	☐ Yes ☐ No If Known, specify:	☐ Side effects - idiosyncratic, specify ☐ Side effects - dose related, specify ☐ Lack of efficacy ☐ Side effects - chronic ☐ Other, specify:	☐ Yes ☐ No	☐ Yes ☐ No ☐ Unknown	☐ Yes ☐ No ☐ Unknown	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
#	Data to be entered.	☐ Yes ☐ No If Known, specify:	☐ Yes ☐ No If Known, specify:	☐ Side effects - idiosyncratic, specify ☐ Side effects - dose related, specify ☐ Lack of efficacy ☐ Side effects - chronic ☐ Other, specify:	☐ Yes ☐ No	☐ Yes ☐ No ☐ Unknown	☐ Yes ☐ No ☐ Unknown	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No

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13.1 General Instructions

The AED resistance log tracks drugs received prior to enrollment, to determine whether the patient meets the International League Against Epilepsy definition of treatment resistance. In some cases, only treatment resistant epilepsy patients will be candidates for a study, and this form may be used for screening. The form may be modified so that a separate CRF is filled out at each study visit, rather than maintaining a running log.

The purpose of the form is to determine whether there is sufficient information available about each prior drug exposure, to be able to determine whether the drug was successful. The amount of information that is necessary to determine whether a prior treatment trial is informative, has been determined by the ILAE, as part of their definition of treatment resistant epilepsy, to include drug formulation, drug schedule, appropriateness of the drug to the syndrome, reason for discontinuation, and duration of therapy. For each drug the patient has received prior to enrollment, record the following: AED Name; whether the AED Formulation was known, and if so, what was the formulation (e.g. liquid, controlled release, immediate release); If the AED schedule is known, and if so what it was (e.g. TID, BID); If the reason for discontinuation was known, and if so, what it was (e.g. continued seizures, rash, sleepiness); whether the AED was appropriate for the patient's Epilepsy Syndrome (e.g., if the patient had juvenile myoclonic epilepsy, a narrow spectrum drug such as carbamazepine was NOT used); whether the duration of therapy was >3 months; whether any attempts were made to adjust the dose if seizures were not controlled (that is, was the drug titrated after the initial target dose was achieved); and whether the patient continued to experience seizures despite dose adjustment.

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14 Anti Epileptic Drug (AED) Log

[*Study Name/ID pre-filled*] Site Name:

Subject ID:

Did the subject take any non-study AEDs during the study? ☐ Yes *(Follow instructions below)* ☐ No

Please record all non-study AEDs the participant/subject took while participating in the study. Enter each dose change on a new line.[4]

Table for Recording Anti Epileptic Drug Log Data Details

Name of AED	Generic or Brand Used?	Formulation (e.x., extended release, liquid, sprinkle, etc.)	Dosing Schedule - Times of Administration (00:00-24:00; 99:99=Unknown, 88:88=N/A)	Dose and Units	Route	Start Date (m m/dd/yyyy) Stop Date (m m/dd/yyyy)	Ongoing?	If Applicable, Reason for Discontinuation (Check all that apply)	Comments
Data to be entered	☐ Generic ☐ Brand ☐ Unknown	Data to be entered by site	: : : : ☐ N/A - taken PRN: Average frequency = times per month	Data to be entered by site	Data to be entered by site	Start: // Stop: //	☐ Yes ☐ No	☐ Idiosyncratic Side Effect(s), specify: ☐ Dose Related Side Effect(s), specify: ☐ Chronic Side Effects ☐ Inadequate Seizure Control ☐ Other, specify:	Data to be entered by site

[4] All other medications (i.e., non AEDs) should be recorded on the Non Anti Epileptic Medication Log.

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Name of AED	Generic or Brand Used?	Formulation (e.x., extended release, liquid, sprinkle, etc.)	Dosing Schedule - Times of Administration (00:00-24:00; 99:99=Unknown, 88:88=N/A)	Dose and Units	Route	Start Date (mm/dd/yyyy) Stop Date (mm/dd/yyyy)	Ongoing?	If Applicable, Reason for Discontinuation (Check all that apply)	Comments
Data to be entered	☐ Generic ☐ Brand ☐ Unknown	Data to be entered by site	: : : : ☐ N/A - taken PRN: Average frequency = times per month	Data to be entered by site	Data to be entered by site	Start: // Stop: //	☐ Yes ☐ No	☐ Idiosyncratic Side Effect(s), specify: ☐ Dose Related Side Effect(s), specify: ☐ Chronic Side Effects ☐ Inadequate Seizure Control ☐ Other, specify:	Data to be entered by site

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14.1 General Instructions

Changes to Non study AEDs should be captured during the study period. In some cases, the protocol may request that tracking of non-study AEDs begin prior to initiation of study medication. Collecting Anti Epileptic medications taken prior to the study in a defined time window (e.g. 30 days) may be important when there may be potential interactions with the study intervention.

Collecting AEDs taken during a study is important for safety reasons, and to determine whether outcome was altered by changes to medication. Some AEDs may interact with the study intervention and must not be taken during the study. If taken, it should be indicated as a protocol deviation. Some studies may prohibit changes to background AEDs during active intervention. Participants/Subjects or their caregivers should be asked to bring prescription and over-the-counter medications to follow-up visits so that the medications can be recorded on the case report form.

The Anti Epileptic Drug Log should be filled out at the baseline visit and every study visit/time point thereafter. The form may be modified so that a separate CRF is filled out at each study visit, rather than maintaining a running log. The following abbreviations are recommended to capture dose units:

- g = gram
- gr =grain
- gtt = drop
- mcg =microgram
- mcL = microliter
- mg = milligram
- mL = milliliter
- oz = ounce
- SPY = spray/squirt
- supp = suppository
- TBSP = tablespoon
- Sp = teaspoon
- OTH = other, specify
- UNK= Unknown

Studies that plan to submit their data to regulatory authorities are recommended to code their medication data using a standard terminology such as the WHO Drug dictionary.

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15 Anti Epileptic Drug (AED) Plasma Concentration Log

[Study Name/ID pre-filled]

Site Name:
Subject ID:

Please record all plasma concentrations over the course of the study.[5]

Table for Concentrations Data Details

Line #	Generic Name of AED	[6]Line # on AED Log	Date and Time of Blood Draw (mm/dd/yyyy hh:mm)	Amount of Last Dose Before Blood Draw (Specify Units)	Date and Time of Last Dose Before Blood Draw (mm/dd/yyyy hh:mm)	Plasma Concentration Result (Specify Units) (ND = Not Done)	Clinically Significant Non Adherence Expected/ Confirmed?	Comments
#	Data to be entered by site.	#	// :	Data to be entered by site.	// :	☐ ND	☐ No ☐ Yes	Data to be entered by site.
#	Data to be entered by site.	#	// :	Data to be entered by site.	// :	☐ ND	☐ No ☐ Yes	Data to be entered by site.
#	Data to be entered by site.	#	// :	Data to be entered by site.	// :	☐ ND	☐ No ☐ Yes	Data to be entered by site.
#	Data to be entered by site.	#	// :	Data to be entered by site.	// :	☐ ND	☐ No ☐ Yes	Data to be entered by site.
#	Data to be entered by site.	#	// :	Data to be entered by site.	// :	☐ ND	☐ No ☐ Yes	Data to be entered by site.
#	Data to be entered by site.	#	// :	Data to be entered by site.	// :	☐ ND	☐ No ☐ Yes	Data to be entered by site.
#	Data to be entered by site.	#	// :	Data to be entered by site.	// :	☐ ND	☐ No ☐ Yes	Data to be entered by site.
#	Data to be entered by site.	#	// :	Data to be entered by site.	// :	☐ ND	☐ No ☐ Yes	Data to be entered by site.
#	Data to be entered by site.	#	// :	Data to be entered by site.	// :	☐ ND	☐ No ☐ Yes	Data to be entered by site.
#	Data to be entered by site.	#	// :	Data to be entered by site.	// :	☐ ND	☐ No ☐ Yes	Data to be entered by site.
#	Data to be entered by site.	#	// :	Data to be entered by site.	// :	☐ ND	☐ No ☐ Yes	Data to be entered by site.

[5] This form is designed to be used in conjunction with the Anti Epileptic Drug Log.
[6] Corresponding line number on the Anti Epileptic Drug Log

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Line #	Generic Name of AED	[6]Line # on AED Log	Date and Time of Blood Draw (mm/dd/yyyy hh:mm)	Amount of Last Dose Before Blood Draw (Specify Units)	Date and Time of Last Dose Before Blood Draw (mm/dd/yyyy hh:mm)	Plasma Concentration Result (Specify Units) (ND = Not Done)	Clinically Significant Non Adherence Expected/ Confirmed?	Comments
#	Data to be entered by site.	#	// :	Data to be entered by site.	// :	☐ ND	☐ No ☐ Yes	Data to be entered by site.
#	Data to be entered by site.	#	// :	Data to be entered by site.	// :	☐ ND	☐ No ☐ Yes	Data to be entered by site.
#	Data to be entered by site.	#	// :	Data to be entered by site.	// :	☐ ND	☐ No ☐ Yes	Data to be entered by site.

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15.1 General Instructions

The Plasma Concentration Anti Epileptic Drug (AEDs) Log tracks the study blood draw regimen for an individual study participant/subject across the duration of the study, in a log format. Additional pages may be required to capture the number of blood draws included in each study. For this reason, page numbers should be recorded. The form may also be modified so that a separate CRF is filled out at each study visit, rather than maintaining a running log.

For each blood draw record the Generic Name of AED, Date and Time of Blood Draw, Amount of Last Dose Before Blood Draw, Date and Time of Last Dose Before Blood Draw, Plasma Concentration Result, Clinically Significant Non Adherence, and Comments. The following abbreviations are recommended to capture dose units:

- g = gram
- gr =grain
- gtt = drop
- mcg =microgram
- mcL = microliter
- mg = milligram
- mL = milliliter
- oz = ounce
- SPY = spray/squirt
- supp = suppository
- TBSP = tablespoon
- Sp = teaspoon
- OTH = other, specify
- UNK= Unknown

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16 Adverse Event Tracking Log

[Study Name/ID pre-filled]

Site Name:

Subject ID:

Has the participant/subject had any adverse events during the study?
☐ Yes
☐ No
Record diagnoses (if known) or signs/symptoms the participant/subject experienced during the study that qualify as adverse events.

Table for Recording diagnoses

Adverse Event (Please use medical terminology)	Start Date	End Date-OR-Continuing	Severity	Relatedness	Action Taken with Study Intervention	Action Taken with AED	Outcome	Serious Adverse Event
Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	☐Mild ☐Moderate ☐Severe ☐Life-threatening/ Disabling ☐Death	☐Unrelated ☐Unlikely ☐Probable ☐Possible ☐Definite	☐None ☐Study Intervention Interrupted ☐Study Intervention Discontinued ☐Study Intervention Modified	☐None ☐AED therapy temporarily interrupted ☐AED therapy permanently stopped ☐AED therapy modified	☐Recovered/Resolved ☐Recovered/Resolved With Sequelae ☐Recovering/Resolving ☐Not Recovered/Not Resolved ☐Fatal ☐Unknown	☐ Yes[7] ☐ No
Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	☐Mild ☐Moderate ☐Severe ☐Life-threatening/ Disabling ☐Death	☐Unrelated ☐Unlikely ☐Probable ☐Possible ☐Definite	☐None ☐Study Intervention Interrupted ☐Study Intervention Discontinued ☐Study Intervention Modified	☐None ☐AED therapy temporarily interrupted ☐AED therapy permanently stopped ☐AED therapy modified	☐Recovered/Resolved ☐Recovered/Resolved With Sequelae ☐Recovering/Resolving ☐Not Recovered/Not Resolved ☐Fatal ☐Unknown	☐ Yes[7] ☐ No

[7] Yes should be answered when the adverse event results in death, is life-threatening, requires in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.

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Adverse Event (Please use medical terminology)	Start Date	End Date-OR-Continuing	Severity	Relatedness	Action Taken with Study Intervention	Action Taken with AED	Outcome	Serious Adverse Event
Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	☐Mild ☐Moderate ☐Severe ☐Life-threatening/ Disabling ☐Death	☐Unrelated ☐Unlikely ☐Probable ☐Possible ☐Definite	☐None ☐Study Intervention Interrupted ☐Study Intervention Discontinued ☐Study Intervention Modified	☐None ☐AED therapy temporarily interrupted ☐AED therapy permanently stopped ☐AED therapy modified	☐Recovered/Resolved ☐Recovered/Resolved With Sequelae ☐Recovering/Resolving ☐Not Recovered/Not Resolved ☐Fatal ☐Unknown	☐ Yes[7] ☐ No
Data to be filled in by site	Data to be filled in by site	Data to be filled in by site	☐Mild ☐Moderate ☐Severe ☐Life-threatening/ Disabling ☐Death	☐Unrelated ☐Unlikely ☐Probable ☐Possible ☐Definite	☐None ☐Study Intervention Interrupted ☐Study Intervention Discontinued ☐Study Intervention Modified	☐None ☐AED therapy temporarily interrupted ☐AED therapy permanently stopped ☐AED therapy modified	☐Recovered/Resolved ☐Recovered/Resolved With Sequelae ☐Recovering/Resolving ☐Not Recovered/Not Resolved ☐Fatal ☐Unknown	☐ Yes[7] ☐ No

* All CDEs on this CRF are for all Prospective Intervention studies

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16.1 General Instructions

16.1.1 ADVERSE EVENTS

Adverse events (AEs) document medical events that occur to a participant/subject once enrolled in a study. AEs are the construct through which the safety of an intervention is recorded and assessed during a study. Typical AE descriptors include event start date, severity, relatedness, outcome, and an indication of whether the event is serious.

16.1.2 RECORDING ADVERSE EVENTS

All AEs, both serious and non serious, regardless of relationship to the study intervention, should be recorded on the AE case report form (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). The form may be modified so that a separate CRF is filled out at each study visit, rather than maintaining a running log.

16.1.3 SERIOUS ADVERSE EVENTS

A serious adverse event is (SAE) defined as any untoward medical occurrence that at any dose results in one of the following outcomes:

- Death
- A life-threatening adverse drug experience
- Results in inpatient hospitalization or prolongation of existing hospitalization
- A persistent or significant disability/incapacity
- A congenital anomaly/birth defect

Important medical events that may not result in death, be life threatening, or require hospitalization may be considered a serious adverse drug event when, based upon appropriate medical judgment, they may jeopardize the patient 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 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 IRB, sponsor, FDA, and DSMB and responses 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 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 case report forms nor entered into the study data management system.

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17 Devices Log

[Study Name/ID pre-filled]

Site Name:

Subject ID:

Complete this form if the participant/subject has utilized an implantable device based therapy for their epilepsy either in the past or ONGOING.

Table for Recording Device Data Details

Line #	Device Name	Date of Initial Implant (mm/dd/yyyy)	Device Manufacturer	Device Registration # or Serial #	Stimulation Target	Type of Lead (Depth; Strip; VNS) and # of Contacts (if applicable)	Location of Neurostimulator	[8]Date of Permanent Explant (if applicable) (mm/dd/yyyy)	Is any part of the device left in the body?	If applicable, Reason for Discontinuation
#	☐ VNS ☐ DBS ☐ RNS ☐ Other, specify:	//	Data to be entered.	☐ INS ☐ Lead ☐ Extension (if applicable):	☐ Left Vagus Nerve ☐ Hippocampus ☐ Left side ☐ Right side ☐ AN ☐ Unilateral ☐ Bilateral ☐ Other, specify:	☐ VNS ☐ Depth; # Contacts ☐ Strip; # Contacts ☐ Other, specify:	☐ Right Chest ☐ Left Chest ☐ Other, specify:	//	☐ No ☐ Yes If Yes, specify:	☐ Serious Device Adverse Effect(s), specify: ☐ Intolerable Stimulation Related Adverse Event, specify: ☐ Other Adverse Event, specify: ☐ Inadequate Seizure Control ☐ Other, specify:

[8] If not explanted, complete Implanted Devices Log

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Line #	Device Name	Date of Initial Implant (mm/dd/yyyy)	Device Manufacturer	Device Registration # or Serial #	Stimulation Target	Type of Lead (Depth; Strip; VNS) and # of Contacts (if applicable)	Location of Neurostimulator	[8]Date of Permanent Explant (if applicable) (mm/dd/yyyy)	Is any part of the device left in the body?	If applicable, Reason for Discontinuation
#	☐ VNS ☐ DBS ☐ RNS ☐ Other, specify:	//	Data to be entered.	☐ INS ☐ Lead ☐ Extension (if applicable):	☐ Left Vagus Nerve ☐ Hippocampus ☐ Left side ☐ Right side ☐ AN ☐ Unilateral ☐ Bilateral ☐ Other, specify:	☐ VNS ☐ Depth; # Contacts ☐ Strip; # Contacts ☐ Other, specify:	☐ Right Chest ☐ Left Chest ☐ Other, specify:	//	☐ No ☐ Yes If Yes, specify:	☐ Serious Device Adverse Effect(s), specify: ☐ Intolerable Stimulation Related Adverse Event, specify: ☐ Other Adverse Event, specify: ☐ Inadequate Seizure Control ☐ Other, specify:

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17.1 General Instructions

This Case Report Form (CRF) Module is used to collect data from participants/subjects who have utilized an implantable device based therapy for their epilepsy in the past, or are currently using an implantable device. The CDEs on this CRF are highly recommended for all Prospective Intervention studies. Additional data about implantable devices providing ongoing therapy should also be collected on the Implanted Devices Log CRF Module.

The device name and manufacturer must be specified in the Log. If any part of the device was left inside the body after explant, it must be recorded in the log along with the location of the part. Discontinuation of a device must also be addressed along with reasoning for discontinuation and any adverse events should be reported on the Adverse Event CRF.

The form may be modified so that a separate CRF is filled out at each study visit, rather than maintaining a running log.

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18 Device Revision/Replacement Log

[Study Name/ID pre-filled] Site Name:

Subject ID:

Complete this form if the device has been modified (e.g., battery replacement; lead revision etc). If the entire device is explanted, complete the Devices Log.

3: Device Revision/Replacement Log Details Table

Line #	Device (link to line# on Devices Log)	Date of Revision (m m/d d/y y y y)	INS	Lead (LEFT)	Lead (RIGHT) if applicable	Extension (LEFT) if applicable	Extension (RIGHT) if applicable	Other	Clinical Condition If applicable, reason for the device revision/replacement
Data to be filled out by site	Data to be filled out by site	Data to be filled out by site	☐Explant and replace on same day ☐Explant only ☐Replacement only (previously explanted) ☐Repositioned Model # of new INS: **Device registration # of new INS:	☐Explant and replace on same day ☐Explant only ☐Replacement only (previously explanted) ☐Repositioned Model # of new lead: *Device registration # of new lead:	☐Explant and replace on same day ☐Explant only ☐Replacement only (previously explanted) ☐Repositioned Model # of new lead: *Device registration # of new lead:	☐Explant and replace on same day ☐Explant only ☐Replacement only (previously explanted) ☐Repositioned Model # of new extension: *Device registration # of new extension:	☐Explant and replace on same day ☐Explant only ☐Replacement only (previously explanted) ☐Repositioned Model # of new extension: *Device registration # of new extension:	☐Explant and replace on same day ☐Explant only ☐Replacement only (previously explanted) ☐Repositioned Model # of new component: **Device registration # of new component:	☐Serious Adverse Device Effect, specify: ☐Intolerable Stimulation Related Adverse Event, specify: ☐Other Adverse Event, specify: ☐Inadequate Seizure Control ☐Other, specify:

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Line #	Device (link to line# on Devices Log)	Date of Revision (m m/d d/y y y y)	INS	Lead (LEFT)	Lead (RIGHT) if applicable	Extension (LEFT) if applicable	Extension (RIGHT) if applicable	Other	Clinical Condition If applicable, reason for the device revision/replacement
Data to be filled out by site	Data to be filled out by site	Data to be filled out by site	☐Explant and replace on same day ☐Explant only ☐Replacement only (previously explanted) ☐Repositioned Model # of new INS: **Device registration # of new INS:	☐Explant and replace on same day ☐Explant only ☐Replacement only (previously explanted) ☐Repositioned Model # of new lead: *Device registration # of new lead:	☐Explant and replace on same day ☐Explant only ☐Replacement only (previously explanted) ☐Repositioned Model # of new lead: *Device registration # of new lead:	☐Explant and replace on same day ☐Explant only ☐Replacement only (previously explanted) ☐Repositioned Model # of new extension: *Device registration # of new extension:	☐Explant and replace on same day ☐Explant only ☐Replacement only (previously explanted) ☐Repositioned Model # of new extension: *Device registration # of new extension:	☐Explant and replace on same day ☐Explant only ☐Replacement only (previously explanted) ☐Repositioned Model # of new component: **Device registration # of new component:	☐Serious Adverse Device Effect, specify: ☐Intolerable Stimulation Related Adverse Event, specify: ☐Other Adverse Event, specify: ☐Inadequate Seizure Control ☐Other, specify:

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18.1 GENERAL INSTRUCTIONS

This CRF Module is intended to collect details about how a participant's/ subject's implanted device is modified (e.g., battery replacement, lead revision, etc.) while enrolled in a study. If the entire device is explanted, the Devices Log CRF Module should also be used.
The model and device number should be recorded. Reasons for replacement and/or revision must be specified for the device. Any Adverse Event (AE) that occurred prior to revision or replacement must also be recorded in the AE Tracking Log. Add additional rows and indicate page number for additional devices.

The form may be modified so that a separate CRF is filled out at each study visit, rather than maintaining a running log.

[ii] Fisher RS, Cross JH, French JA, Higurashi N, Hirsch E, Jansen FE, Lagae L, Moshé SL, Peltola J, Roulet Perez E, Scheffer IE, Zuberi SM. Operational classification of seizure types by the International League Against Epilepsy: Position Paper of the ILAE Commission for Classification and Terminology. Epilepsia 2017;58(4):522-530.
Fisher RS, Cross JH, D'Souza C, French JA, Haut SR, Higurashi N, Hirsch E, Jansen FE, Lagae L, Moshé SL, Peltola J, Roulet Perez E, Scheffer IE, Schulze-Bonhage A, Somerville E, Sperling M, Yacubian EM, Zuberi SM. Instruction manual for the ILAE 2017 operational classification of seizure types. Epilepsia 2017;58(4):531-542.

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