ESETT HUM00096708	**Study Title: Established Status Epilepticus Treatment Trial (ESETT)** A multicenter, randomized, blinded, comparative effectiveness study of fosphenytoin, valproic acid, or levetiracetam in the emergency department treatment of patients with benzodiazepine-refractory status epilepticus. PI Adult: R. Silbergleit, MD, PI PEDS: A. Rogers, MD

RESEARCH COORDINATOR ENROLLMENT GUIDE

ENROLLMENT PROCEDURE

☐ 1. Ensure ESETT box is in resus bay
- ☐ Press 'Start Protocol' on PAD **AT SAME TIME** as drug infusion! (If this window is missed, do not 'Start Protocol')
- ☐ *Verbalize* status and ask recording nurse to *note in patient's chart*: When ***"seizure stopped"*** and if ***"seizure resumes"***

☐ 2. Complete Drug Administration Card (located front, inside cover)
- ☐ Put Patient ID sticker on ESETT Drug Admin Card
- ☐ Write down vial number. Once done, dispose vial in black plastic bin for glass.

☐ 3. **Check:** Ensure ED Patient Timeline depicts accurate drug infusion start time – should be 10 minutes before medication stop time.
- ☐ If you know *for a fact* when drug infusion started, ask recording nurse to correct in timeline.

☐ 4. **Be sure recording nurse notes pt's status in chart at the 20 and 60 min assessments time points!**
- ☐ After 60 min assessment: if unblinding is needed press 'Unblind; on PAD' if not, press 'Complete Protocol.' (Unblinding will not be an option through the PAD after pressing 'Complete Protocol' must then call hotline. Unblinding before 60 min is a protocol violation)

☐ 5. When calm, approach family for consent (may consult with social work if they have already met w/family).
- ☐ Give family copy of consent and signature page
- ☐ Ask the subject or surrogate to complete the ESETT survey after consent or withdraw (Highlight Q4b only needs **one** answer response)
- ☐ Complete the Demographics CRF (Form 505)
- ☐ Complete the Prior Relevant Home Medications CRF (Form 108) and ask family if pt had taken any current medications listed in EMR in the last 24 hrs.
- ☐ If a child (7-14 yo) is enrolled, continue to monitor for assent. If they are not able (cognitive impairment, medically unstable up to discharge, etc.) write a NTF as to why assent was not obtained. If they refuse, complete withdrawal form that is attached to consent form

☐ 6. Complete the Informed Consent Log CRF (Form 211)
- ☐ Be thorough! (If LAR is not at bedside at time of infusion: document where they are, and if a significant amount of time has passed between start of infusion and approach for consent document why, document every attempts/contacts.)

☐ 7. PAD and back-up vial:
- ☐ Select 'Submit Results' option, exit out of app and charge device.
- ☐ Retrieve back-up vial from Adult ED pharmacy to reload the use-next box. Sign in when entering pharm fridges.
- ☐ **Set up device:** Open app → Scan back-up vial code. Log in to WebDCU → Drug Tracking → Drug Receiving → Click blue number next to back-up vial → Scan code on computer screen. Touch 'Continue Setup.' Contact info stays the same. Save. (This needs to be repeated once replacement vial comes in!)
- ☐ Ensure device is off and wifi is still connected. Disinfect PAD.

CONSENT INTRODUCTION

NOTE: Subjects who **are** deemed competent and have **no LAR present** can consent and complete the Survey. Subjects who are **not** deemed competent and have **no LAR present**, follow-up with social work on what attempts have been made to contact LAR and status. Document your efforts on Form 211.

Introduce yourself as a member of the research staff: I was asked to tell you about a research study we are doing of medications for seizures that don't stop with initial treatment. When the seizure did not stop, [**Prefix last name]** was entered into the ESETT Study.

Introduce Study: The purpose of the study is to find out which of three commonly used medicines is safer and more effective at stopping a prolonged seizure that does not stop after receiving a full dose of medicine (like Valium). This condition is known as Established Status Epilepticus. The study is called ESETT or Established Status Epilepticus Treatment Trial.

When patients have seizures that do not stop after treatment with benzodiazepines, doctors commonly use one of three meds:

- fosphenytoin (**Cerebyx**)
- levetiracetam (**Keppra**)
- valproic acid (**Depacon**)

Despite being **commonly used**, we do not have any **scientific evidence** on which is most effective.

Therefore, we (UMich) are involved in a study to systematically study the drugs. Because **seizures** require **immediate treatment** and any delay can be dangerous, we have **permission** to obtain **informed consent after the seizure has been treated**.

Your loved one has been treated under the study protocol. The FDA has asked us to continue collecting information from the medical record to help determine which medicine is the **safest and most effective**.

We **do require your consent as the LAR** to continue to collect this information.

If you agree to continue to participate we will:

- Collect medical information until discharge from the hospital
- No aspect of your medical care will be affected by the study enrollment
- No further medications or tests will be required.

We will collect:

- Demographics
- Info on your condition and treatment in the emergency department,
- Medical history,
- Information on recurrent seizures in the hospital,
- Some tests and laboratory results during your hospitalization,
- Adverse events,
- Dates of hospital admission and discharge.

Your **participation will end when you are discharged** from the hospital.

If you decide not to continue, no further information will be collected about you. Data collected prior to withdraw will remain in the study in order that we can monitor the safety of these medications.
Do you have any questions for me at this time?

CONSENT TALKING POINTS

Consent Checklist

- □ Study explanation and enrollment
- □ Standard care vs. study procedure
- □ EFIC explanation
- □ Participation is voluntary
- □ Risks and benefits

Talking points for each page of consent form:

P1. **Study Explanation and Enrollment:** This **study** is being done at about **40 hospitals around the country.** As noted, [**Prefix last name]** was enrolled in the study at the time of seizure treatment and the outcome of the treatment has been noted for the study.

Standard care vs. study procedure: The drugs used in this study are all commonly and routinely used for treatment of seizures that do not respond to benzodiazepines (valium)

P2. All people over the **age of 2 who come to these hospitals with an ongoing seizure that has not responded to initial treatments** are being given medication that is systematically chosen by the study.

P3. **Risks and Benefits**: The risks and benefits are comparable to that of **normal clinical treatment** for a seizure like this. The different **medications** used by doctors that we are testing have different side effects, which you can read more about here. But they are all **thought to be safe for clinical use** and have a low incidence of serious side effects.

The only **risk** to allowing us to continue collecting information from the medical record is the low risk of **breach of confidentiality**. Any time information is recorded somewhere, there's a chance it could end up somewhere it's not supposed to be; but we have many security measures in place, and only HIPAA-certified study team members will handle [**Prefix last name]** information for this study.

P4. **Participation is Voluntary:** You can ask us to stop collecting medical data at any time. Some of his/her data may still be used just to help us know if the medicine he/she was given was safe and effective. If you agree to continue in the study, we will only collect his/her information until the end of the hospital visit.

P5. The medicine we are studying was provided free of charge. There will be **no costs to you related to being in the study**.

P6. All of the information we collect in this study is **protected by HIPAA**, the Health Insurance Portability Act, which is the same set of regulations that govern your medical record. **This means that no one will see your information except for study team members who are trained in privacy laws.**

Now, if you would like to continue in the study and give us permission to collect [**Prefix last name]** medical information until he/she is out of the hospital, I will have you sign this page.

If you do not want to continue in the study and you would like to withdraw now, I will have you sign this page.

POST ENROLLMENT

NOTE: Paper DCFs are to be completed first. Hierarchy of initial source information: 1.) Discussion with treatment team (also live observation), 2.) Patient's electronic medical record, and 3.) PAD.

☐ 1. Check the survey after it is returned for 1) completion and 2) Q4b has only **one** answer selected.

☐ 2. If a child (7-14 yo) is enrolled, continue to monitor for assent until end-of-study. If they are not able (cognitive impairment, medically unstable up to discharge, etc.) be sure to write a NTF as to why assent was not obtained. If subject refuses (regardless if consent was signed from LAR previously), complete withdrawal form (attached to consent form), no further data will be collected.

☐ 3. Enter patient information in MBECT. (MBECT batch loads to MiChart every few hours, cannot associate patient with research study until this happens. You CAN, however, upload the research note.)

☐ 4. Go to WebDCU → Add New Subject, complete information, save record, click green arrow for Subject CRF Binder. Most other DCFs can wait (based on CRF Completion Timeline on back) if necessary.

☐ 5. Complete F102 Randomization. Once submitted, this will trigger a drug resupply.

☐ 6. Complete F108 Prior Home Medications in case there is anything you need to ask the patient.

☐ 7. Enter Research Note and upload Informed Consent Document (ICD) to MiChart **ASAP**.
- ☐ **Follow instructions!** Located in S:// drive → MiChart → Training.
- ☐ Save scanned ICDs to S:// drive under POST Enrollment.
- ☐ If Sherry or PI enrolls a patient: Contact RC coming into office next

☐ 8. Upload Patient/Surrogate survey to the PECARN-Michigan folder in MBox. Alternatively, you can email the completed survey to: upload.PECARN_.lpcciollku@u.box.com.
- ☐ Save uploaded survey in S://drive under POST Enrollment.

☐ 9. Enter enrollment in ESETT Internal Log excel spreadsheet and any notes located in S:// drive under POST Enrollment.

☐ 10. Recognize any outstanding RNs and pharmacists to receive "Making a Difference" award at: http://www.med.umich.edu/umhshr/recognition/

☐ 11. Add to GCal 24 hour mark:
- ☐ Check for any S/AEs and schedule 24 hour audit
- ☐ Check if replacement vial has come in. Continually check for this!! When it does, program device with new vial ***immediately*** and place back-up back in Adult pharm fridge. Ensure receipt of drug has been documented in WebDCU by IDS pharmacy. Log this information in ESETT Internal Log spreadsheet.

☐ 12. Audit patient at 24 hours and End of Study.
- ☐ All S/AEs are to be documented in paper DCFs, WebDCU, and ESETT Internal Log.
- ☐ Refer to AE Reporting Guidelines by the IRB located in S/AE tab under POST Enrollment.

☐ 13. End of Study:
- ☐ Complete Clinical Summary Packet. Folder with instructions located in S:// drive POST Enrollment. Upload to WebDCU and save to S:// drive.
- ☐ Email PI after all DCFs completed and folder audited to sign Form 126: End of Study in WebDCU. Be sure this information is documented in the paper DCF.
- ☐ Upload incomplete clinical summary packet if waiting on a physician to sign off on a note. Have PI sign form in order to submit it before the 5 day deadline. Write in notes the form is incomplete.

ESETT - CRF Completion Timeline		
Form#	**Form Name**	**Timeline of Submittal**
	Enrollment Form	Within 8 hours of enrollment
F102	Randomization	Within 8 hours of enrollment
F101	Eligibility	Within 8 hours of enrollment
F501	Treatment Effect	Within 8 hours of enrollment
F503	Secondary Outcomes	Within 24 hours of enrollment
F211	Informed Consent Log	Within 24 hours of enrollment
F104	Adverse Events*	Through End of Study*
F504	Study Drug Infusion	Within 8 hours of enrollment
F508	Affirmation of Adverse Event Assessment	Within 5 days of enrollment
F108	Prior Relevant Home Medications	Within 5 days of enrollment
F117	Baseline Vital Signs	Within 5 days of enrollment
F123	Hospital Discharge	Within 5 days of End of Study
F506	ED Arrival	Within 5 days of enrollment
F505	Demographics	Within 5 days of enrollment
F126	End of Study	Within 5 days of End of Study
*Serious Adverse events must be reported with 24 hours of discovery.		

UNBLINDING	• Unblinding is an option on the PAD after 60 minute questions have been answered. • If after 60 minutes and the device is no longer available, call PI Hotline (855-ESETT-PI) • Emergency unblinding (unblinding prior to 60 minutes): Call PI Hotline(855-ESETT-PI) o Unblinding should be performed by clinical team rather than study team if possible. Study team should remain blinded. o **Unblinding prior to the 60 minute primary outcome is a protocol violation.**
NON-ENGLISH	• If interpreter is coming, wait to approach family until arrival. Refer to S:// drive → Consent → Non-English speaking short forms. • If no interpreter is coming, approach clerk (maroon scrubs), ask to connect with language line or consent line on portable phone. Consent is recorded. Make NTF. o Save NTF in folder under POST Enrollment. • **<u>WORKFLOW:</u>** o Use short forms saved in the S:// drive (location above). If specific language is not offered in the S:// drive, search online resources for the specific short form needed. o Conduct the subject's informed consent process with the researcher and a translator fluent in English and the foreign-language present (a family member or others may also attend as long as no concerns regarding undue coercion from them on the subject is known). o The subject signs a 'short form' informed consent document written in the appropriate language if agreeing to participate o The researcher signs the currently approved informed consent document [ICD] in English o The witness (fluent in both languages) signs BOTH the short form and the English ICD. (Note, the translator may also serve as the witness **or** the investigator, but not as the investigator **and** the witness **and** the translator). o The subject is given a copy of BOTH the signed short form and signed English ICD o Provide the English ICD even though the subject may not understand English. o Copies of BOTH signed documents are maintained in the study records. • Copies of both signed documents are uploaded in the subject's medical record.

Definitions and Locations

- A subject is considered ***"enrolled" and "randomized"*** at the same time point, defined as the time that study drug infusion is initiated.

- **LAR:** Legally Authorized Representative. An LAR is typically defined as: a.) Health-care agent; b.) Adult child (18 yrs or older); c.) Parent; d.) Adult sibling; e.) Grandparent; f.) Adult grandchild (18 yrs or older). When more than one LAR is present, the closest relative, as defined above, should give consent.

- **MoP:** Manual of Procedures found here: https://docs.google.com/document/d/1XjsnRHpq8AZS_XJeyLJ0bRCRWADCt3Gd6FPIT5g8HoA/edit?pli=1

- **WebDCU:** Enter new subject here: https://webdcu.musc.edu/login.asp

- **MBECT**: Enter new subject here: https://crao-mbect.umms.med.umich.edu/flash/eThorityHome.aspx

- **Non-English-speaking consent forms and SOP:** S:// drive →ESETT →Consent → Non-English-speaking short forms

- **S/AE reporting:** See CTCAE and Safety Monitoring Plan under S:// drive ESETT →MoP →Supporting documents.

- **Research Notes** and upload **Informed Consent Documents** to MiChart instructions**:** S:// drive → MiChart → Training

- **PAD Instructions:** S:// drive ESETT → MoP → Supporting documents → PAD → User Manual

- **Change vial codes in PAD:** S:// drive ESETT → Training Materials → PAD Training

CONTACTS

Google Voice:

- 781-763-7388

Charge Nurse Desks:

- CES (phone: 734-615-9742) (page: 0974)
- AES (phone: 734-615-8836) (page: 9458)

Paging Number: 734-936-6266

PIs:

- Alex Rogers (cell: 734-255-7685) (page: 15364) alexroge@med.umich.edu
- Allison Cator (cell: 847-308-1976) (page: 11914) acator@med.umich.edu
- Robert Silbergleit (cell: 22-5446) (page: 10703) robie@med.umich.edu

RCs:

- Office Pager 33394
- Sherry Goldfarb (cell: 734-730-6071) (office: 734-763-7488) Goldfarb@med.umich.edu
- Noelle Herzog (cell: 989-889-5812) noellel@med.umich.edu
- Stephanie Johnson (cell: 734-377-8081) nuseigus@med.umich.edu
- Cate Flechsig (cell: 810-623-1615) cflechsi@med.umich.edu

PI Hotline:

- 855-ESETT-PI (855-373-8874)

Pharmacy:

- CES (mobile phone: 734-232-5198) (page: 35942)
- AES (mobile phone: 734-647-5431) (page: 32818)

SUSPEND STUDY

If an emergency comes up and there is NO coverage:

1.) First try contacting other RCs and/or PIs to cover

2.) If no coverage:

a. Call CES and AES mobile phones (CES: 734-232-5198; AES: 734-647-5431)

i. Give instruction to place the "ESETT Study Suspended" sign on the box.

1. Sign is located in the research binder.

ii. Let them know time/day of study stop and time/day of suspected study start – this information will need to be written on the sign.

1. Be sure to follow-up when study starts that the sign is taken off.

iii. Email Pam Walker plada@med.umich.edu this information.

1. She will then send a notification to all of pharmacy staff.

iv. Text ESETT Group and email to let the team know the study has been suspended and for how long.

1. Email any PI not on ESETT Group text this information.