**UCB, Inc Medical Educational Grants**

**Medical Affairs**

**Request for Proposal (RFP)**

**Advancing the Treatment of Focal Seizures in the Intensive Care Setting**

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| **Background:** | UCB, Inc is a global biopharmaceutical company focused on the discovery and development of innovative medicines and solutions to transform the lives of people living with severe diseases of the central nervous system and immune system. Seizure treatment and management of antiepileptic drug (AED) therapy in the hospital setting is a major channel in which epilepsy patients are managed. Neurointensivists and neurologists within the hospital system frequently diagnosis, treat, and manage focal (partial-onset) convulsive and nonconvulsive seizures1,2. The appropriate and safe administration of AEDs in the hospital for each individual patient is needed to lead to the best clinical outcome. Also AED selection for continued long-term treatment of focal seizures is important if the risk of reoccurrence warrants continued therapy1,3. In the intensive care unit (ICU), the reported risk of seizures as a complication or as the principal reason for ICU admission is estimated to be 3.3%; although, the actual incidence is likely to be significantly higher with one study reporting of an incidence of 34%4,5. Nonconvulsive seizures have been more recently recognized as common occurrences in the ICU, with 8%-48% of comatose patients experiencing nonconvulsive seizures, depending on the patient population studied6,7. Most patients with nonconvulsive seizures have purely electrographic seizures, but other subtle signs like face and limb myoclonus, nystagmus, eye deviation, pupillary abnormalities, and autonomic instability can accompany a nonconvulsive seizure8. These symptoms are not specific for nonconvulsive seizures in critically ill patients; therefore, routine or continuous EEG monitoring is necessary for the diagnosis and treatment of nonconvulsive seizures8,1. Primary causes of seizures in the ICU are AED noncompliance, alcohol or drug withdrawal, stroke, anoxic brain injury, head trauma or traumatic brain injury, central nervous system infection, sepsis, metabolic disorders, and other acute drug toxicity states or withdrawal1,9. To provide additional information on the occurrence of seizures in these populations, estimates for the rate of acute convulsive seizures after stroke are 2%-9%10,11. Additionally, the incidence of convulsive seizures within the first week (early seizures) after traumatic brain injury is estimated between 4%-15%12,13. In current treatment algorithms, with the widespread use of seizure prophylaxis after traumatic brain injury the rate of clinical seizures has decreased in these patients. Acute convulsive seizures in the ICU should be actively and timely treated with AED therapy for several reasons. Timely administration of effective AEDs within 5 to 10 minutes has been shown to be essential in the prevention of the emergence of status epilepticus, which can lead to neuronal damage and permanent cerebral injury. Additionally, early treatment of seizures is associated with better patient outcomes and survival14,15. In several studies, increased mortality has been shown to be associated with the occurrence of convulsive seizures in patients following an ischemic stroke16.  |
| **Key Identified Gaps:** | Seizures occurring in the ICU are caused from diverse structural lesions and metabolic disturbances, each with a distinct risk of seizures that the health care provider must understand1,9. Outside of the ongoing acute brain insult, treatment of seizures in the critically ill patients can be further complicated by numerous elements. Some of these elements include multisystem organ dysfunction, metabolic abnormalities, hypermetabolism, the induction of therapeutic paralysis, and other patient co-morbidities and concomitant medications1,17. These challenges lead to difficulty in choosing the best AED(s) for treatment, as well as, challenges in providing the appropriate dose and distribution of therapy that will lead to effective seizure treatment within the ICU population18.When selecting an AED(s) for the treatment of focal seizures based on the individual acute seizure etiology, seizure type, co-morbidities, and co-medications in the ICU patient population, class one evidence with randomized, placebo controlled trials are lacking3,14. There are over 25 AEDs currently available for the treatment of seizures. Some AEDs are available in a variety of dosing formulations, which could be an important consideration when choosing an AED(s)19,20. Additional AED treatment considerations for the ICU patient population include the safety profile, the pharmacokinetic and metabolic properties, and the potential for drug interactions of the AED therapy3, 25. Outside of basic AED characteristics that help drive AED selection, comparative effectiveness data is missing within epilepsy to drive treatment selection among the AED class21. Additionally, there is an absence of dosing or pharmacokinetic studies that have been conducted in the critically ill population. To help address these data gaps pharmacokinetic modeling has been applied to clinical trial outpatient data of AEDs to examine the effect of some individual characteristics on the individual AED’s pharmacokinetic profile22,23. As a result, current dosing and administration of AEDs in ICU patients relies upon dosing and pharmacokinetic data from outpatient epilepsy populations and from real world reports of clinical experience20,23,24. With these considerations, the choice of AED for the treatment of seizures in the ICU patient population should be individualized based upon seizures etiology, patient characteristics, and acute symptoms in order to provide the best outcomes and quality of life for patients; however, specialized skills and knowledge is needed to select and administer the correct treatment for each patient5,9,21.The treatment of ICU patients requires the coordination, communication, and expertise of a multidisciplinary team consisting of neurointensivists, nurses, neurologists, pharmacists, rehabilitation professionals, and social workers3,21. This multidisciplinary team is not only tasked with managing acute seizures for each patient, but also for continued long-term treatment of seizures if the risk of reoccurrence warrants continued therapy1,26. Selecting the correct therapy for the long-term treatment of seizures will have different patient considerations than the selection of an acute therapy to help assure the best long-term quality of life for patients5. Based upon current treatment practices, knowledge and skills of the long-term epilepsy treatment considerations needed to improve patient quality of life seem to be lacking5,21.  |
| **Specific Interest of this RFP:**  | It is our intent to financially support an independently developed comprehensive proposal that will improve health care provider knowledge and skills in treating focal (partial-onset) seizures in the intensive care hospital environment. Proposals should consider learning materials that incorporate the dosing and administration of AEDs, individual patient characteristics informing AED selection, and considerations for selecting an AED at time of patient discharge. The learning objectives for this proposal are intended for the treatment of partial-onset and secondarily generalized seizures and not for the treatment of status epilepticus. Proposals should include identification and mapping of educational gaps towards knowledge, skills, attitude, and performance including inter-professional team gaps in order to strive towards improving health care providers’ skills in treating partial-onset seizures in the intensive care setting. Proposals with broad reach and impact to US healthcare providers will be given priority. Another key consideration is the need for more than one touch point with the audience members to assure acquisition of knowledge and skills (level 3 & 4 according to the Moore Scale) or improving performance (level 5), dependent on identified and validated clinical gaps. Innovative medical educational platforms with demonstrated effectiveness in learner engagement and long term knowledge retention are encouraged.  |
| **Eligibility Criteria:**  | The program should target the US geographic region. The education must offer credit and meet the accreditation or certification requirements and standards of the ACCME, AOA, AMA, AAFP, or ADA CERP or other recognized accrediting body. If accepted, the provider must attest to the terms, conditions and purposes of an educational grant as described in the electronic UCB letter of agreement.  |
| **RFP Release Date:**   | August 17, 2016 |
| **Clinical Area:** | Epilepsy  |
| **Target Audience:** | US neurointensivists, hospitalists, intensive care nurses and discharge nurses, and neurologists |
| **Outcomes:** | Minimum outcome measurement level will demonstrate learner competence (practical application and conceptual understanding).  |
| **Expected Monetary Range of Applications:**  | The anticipated program cost is expected to be achievable with a budget of no more than $250,000. The final awarded amount will depend upon the review panel’s evaluation of the proposal and costs involved. |
| **Key Dates:** | RFP release date: August 17, 2016Full Proposal Deadline: October 7, 2016 Please note the deadline is midnight Eastern Time Review of Full Proposals by External Review Panel: October 7-31, 2016 Anticipated Full Proposal Notification Date: November 1, 2016 Period of Performance: November 2016 - December 2017 Please note an interim progress report will be requested depending upon timelines of the program. |
| **Submission Instructions:**  | Submit applications online through the UCB eRequest system which can be accessed via <http://erequest.ucb.com>. Applicants must register for the UCB eRequest system if you are not a current registrant.Select **UCB.EP-RFP2016** in the RFP Number field in the application, and include **UCB.EP-RFP2016** within the Request Title as well. Select **Epilepsy** as the Area of Interest. Complete all required sections of the online application and upload the proposal. Approvals and denials will be communicated to the applicant via the eRequest system by email by the dates provided above.  |
| **Application Section Requirements:** | Learning objectivesNeeds assessment with classification of identified gaps into knowledge, skills, attitudes optionally performance according to the Moore levels of outcomes based planningIntended outcome level to be achieved according to the Moore ScaleActivity type and delivery format following instructional design principlesProgram faculty including respective qualification criteriaAudience Line item budget (template provided on application)Document uploads for inclusion:1. A formal dated Letter of Request for the funding
2. A comprehensive learning needs assessment plan
3. Detailed program plan
4. Accreditation certificate(s)
5. W-9 for payee organization
6. Outcomes measures plan

Be sure to review the USA FAQ document on the website for other application information. |
| **Questions:** | Please direct any questions that you may have to the UCB Grants Office at grants@ucb.com  |

References:

1. Ziai WC and Kaplan PW. [Seizures and status epilepticus in the intensive care unit.](http://www.ncbi.nlm.nih.gov/pubmed/19115173) Semin Neurol. 2008 Nov;28(5):668-81.
2. Friedman D et al. [Continuous electroencephalogram monitoring in the intensive care unit.](http://www.ncbi.nlm.nih.gov/pubmed/19608827)

Anesth Analg. 2009 Aug;109(2):506-23.

1. Varelas PN et al. [Seizures and the neurosurgical intensive care unit.](http://www.ncbi.nlm.nih.gov/pubmed/23809033) Neurosurg Clin N Am. 2013 Jul;24(3):393-406.
2. Bleck TP et al. [Neurologic complications of critical medical illnesses.](http://www.ncbi.nlm.nih.gov/pubmed/8420739) Crit Care Med. 1993 Jan;21(1):98-103.
3. Jordan KG. [Continuous EEG monitoring in the neuroscience intensive care unit and emergency department.](http://www.ncbi.nlm.nih.gov/pubmed/10082089) J Clin Neurophysiol. 1999 Jan;16(1):14-39.
4. [Persistent nonconvulsive status epilepticus after the control of convulsive status epilepticus.](http://www.ncbi.nlm.nih.gov/pubmed/9701373) DeLorenzo RJ, Waterhouse EJ, Towne AR, Boggs JG, Ko D, DeLorenzo GA, Brown A, Garnett L. Epilepsia. 1998 Aug;39(8):833-40.
5. Towne AR. [Prevalence of nonconvulsive status epilepticus in comatose patients.](http://www.ncbi.nlm.nih.gov/pubmed/10668693) Neurology. 2000 Jan 25;54(2):340-5.
6. Jirsch J and Hirsch LJ. C[onvulsive seizures: developing a rational approach to the diagnosis and management in the critically ill population.](http://www.ncbi.nlm.nih.gov/pubmed/17588812) Clin Neurophysiol. 2007 Aug;118(8):1660-70.
7. Mirski MA et al. [Seizures and status epilepticus in the critically ill.](http://www.ncbi.nlm.nih.gov/pubmed/18241782) Crit Care Clin. 2008 Jan;24(1):115-47.
8. Bladin CF et al. [Seizures after stroke: a prospective multicenter study.](http://www.ncbi.nlm.nih.gov/pubmed/11074794) Arch Neurol. 2000 Nov;57(11):1617-22.
9. Szaflarski JP et al. [Incidence of seizures in the acute phase of stroke: a population-based study.](http://www.ncbi.nlm.nih.gov/pubmed/18248443) Epilepsia. 2008 Jun;49(6):974-81.
10. Annegers JF et al. [Seizures after head trauma: a population study.](http://www.ncbi.nlm.nih.gov/pubmed/7190235) Neurology. 1980 Jul;30(7 Pt 1):683-9.
11. Temkin NR et al. [A randomized, double-blind study of phenytoin for the prevention of post-traumatic seizures.](http://www.ncbi.nlm.nih.gov/pubmed/2115976) N Engl J Med. 1990 Aug 23;323(8):497-502.
12. [No authors listed]. [Treatment of convulsive status epilepticus. Recommendations of the Epilepsy Foundation of America's Working Group on Status Epilepticus.](http://www.ncbi.nlm.nih.gov/pubmed/8340986) JAMA. 1993 Aug 18;270(7):854-9.
13. Pellock JM et al. [Time to treatment in prolonged seizure episodes.](http://www.ncbi.nlm.nih.gov/pubmed/15123020) Epilepsy Behav. 2004 Apr;5(2):192-6.
14. Vernino S et al. [Cause-specific mortality after first cerebral infarction: a population-based study.](http://www.ncbi.nlm.nih.gov/pubmed/12855836) Stroke. 2003 Aug;34(8):1828-32.
15. Wu C et al. [Hypermetabolism in the Initial Phase of Intensive Care Is Related to a Poor Outcome in Severe Sepsis Patients.](http://www.ncbi.nlm.nih.gov/pubmed/26044971) Ann Nutr Metab. 2015;66(4):188-95.
16. UCB Consulting. Intravenous Antiepileptic Drug Loading Dose Steering Committee. 2015 Sept.
17. Glauser T et al. Updated ILAE evidence review of antiepileptic drug efficacy and effectiveness as initial monotherapy for epileptic seizures and syndromes. ILAE Subcommission on AED Guidelines. Epilepsia. 2013 Mar;54(3):551-63
18. Wasim M et al. [Nonconvulsive seizure control in the intensive care unit.](http://www.ncbi.nlm.nih.gov/pubmed/25677444) Curr Treat Options Neurol. 2015 Mar;17(3):340.
19. England M et al. Epilepsy across the spectrum: promoting health and understanding. The National Academies Press: Institute of Medicine Report. 2012.
20. Gidal B et al. Concentration effect relationships with perampanel in patients with pharmacoresistant partial-onset seizures. Epilepsia. 2013;54(8):1490-7.
21. Schoemaker R et al. [Brivaracetam Population Pharmacokinetics and Exposure-Response Modeling in Adult Subjects with Partial-Onset Seizures.](http://www.ncbi.nlm.nih.gov/pubmed/27146213) J Clin Pharmacol. 2016 May 5.
22. Caballero GC et al. [Retrospective analysis of levetiracetam compared to phenytoin for seizure prophylaxis in adults with traumatic brain injury.](http://www.ncbi.nlm.nih.gov/pubmed/24421550) Hosp Pharm. 2013 Oct;48(9):757-61.
23. Gidal B et al. [Drug interactions in epilepsy care: perspective on the newer generation antiepileptic drugs.](http://www.ncbi.nlm.nih.gov/pubmed/19810913) Expert Rev Neurother. 2002 Nov;2(6):801-8.
24. Goldstein LB. [Potential effects of common drugs on stroke recovery.](http://www.ncbi.nlm.nih.gov/pubmed/9561971) Arch Neurol. 1998 Apr;55(4):454-6.