Pfizer Independent Grants for Learning & Change
Request for Proposals (RFP)
Pediatric and Adolescent Migraine

I. Background

The mission of Pfizer Independent Grants for Learning & Change (IGL&C) is to partner with the global healthcare community to improve patient outcomes in areas of mutual interest through support of measurable learning and change strategies. "Independent" means that the projects funded by Pfizer are the full responsibility of the recipient organization. Pfizer has no influence over any aspect of the projects and only asks for reports about the results and the impact of the projects in order to share them publicly.

The intent of this document is to encourage organizations with a focus in healthcare professional education and/or quality improvement to submit a letters of intent (LOI) in response to a Request for Proposal (RFP) that is related to education in a specific disease state, therapeutic area, or broader area of educational need. The RFP model is a two-stage process. Stage 1 is the submission of the LOI. After review of the LOI, you may be invited to submit your Full Grant Proposal. Stage 2 is the submission of the Full Grant Proposal.

When a RFP is issued, it is posted on the Pfizer IGL&C website (www.pfizer.com/independentgrants) and is sent via e-mail to all registered users in our grants system. Some RFPs may also be posted on the websites of other relevant organizations, as deemed appropriate.

II. Eligibility

Geographic Scope:	☐ United States Only ☑ International (specify country/countries) **U.S., Canada, and** European Union
Applicant Eligibility Criteria:	The following may apply: medical, dental, nursing, allied health and/or pharmacy professional schools; healthcare institutions (both large and small); professional associations; and other not-for-profit entities with a mission related to healthcare improvement. Collaborations within institutions (e.g., between departments and/or inter-professional), as well as between different institutions/organizations/associations, are encouraged. Please note all partners must have a relevant role and the requesting organization must have a key role in the project.

III. Requirements

Date RFP Issued:	April 29, 2014
Clinical Area:	Pediatric and Adolescent Migraine
Specific Area of Interest for this RFP:	It is our intent to support projects that focus on the design and implementation of a comprehensive learning and change strategy that facilitates improving a clinician's understanding of the appropriate diagnosis and management of migraines in the pediatric and adolescent patient. Multi-disciplinary collaborations are encouraged when appropriate, but all partners must have a relevant role. It is expected that projects will be evidence-based (education and/or quality improvement) and the proposed research/evaluation will follow generally accepted scientific principles. During review, the intended outcome of the project is given careful consideration and, if appropriate based on the project goal, projects with the maximum likelihood to directly impact patient care will be given high priority. There is a considerable amount of interest in receiving responses from projects that utilize system-based changes. Although educational efforts for providers and patients may be entirely appropriate components in responses to this RFP, projects that include an overt description of system changes will be given high priority.
Target Audience:	Pediatricians Primary Care/General Practitioners Emergency Department Medical Personnel Neurologists Pain Specialists Child Psychologists Multi-disciplinary team approaches adopting a holistic or multidimensional means of therapeutic disease-state management that addresses the co-morbidities and unique sequelae of pediatric and adolescent migraine are highly encouraged.

Disease Burden Overview:	The overall prevalence of migraine headaches in children up to 20 years of age is approximately 7.7% • Prevalence of migraines in female children and adolescents is 9.7% and is 6.0% in male children and adolescents. • Migraines are more common in adolescents over the age of 14 years. • Migraines affect males and females equally at a young age (<14y) and more females than males in adolescence and young adulthood. • There is higher prevalence of child and adolescent migraines in Europe and the Middle East as compared to USA and the Far East [1] Migraines are the most common recurring pain syndrome in childhood and adolescence [2] A recent study showed that 40% of children who present to the emergency department (ED) with a headache have a primary headache disorder, with migraine being the most common (74%) [3] Migraines significantly impair quality of life (QOL) for a broad age-range of children and adolescents, thus raising the importance of early and appropriate recognition and treatment. [4] • The impact of headaches on QOL is similar to that found for other chronic illness conditions, with impairments in school and emotional functioning being the most prominent. [5] • Adolescents with migraines reported the greatest impairment on their curricular and extracurricular lives (e.g., school, play, social, or leisure activities). [6] • Headaches have the ability to affect all aspects of a child's functioning which may lead to negative affective states (e.g., anxiety, depression, and anger) and increased psychosocial problems (e.g., school absences and problematic social interactions). [7] • Given that headaches are a major factor contributing to school absenteeism and poorer quality of life in childhood and in adolescence, understanding the natural history and the management of different headache forms is vital for our future. • Children with headaches beginning before the age of 6 were found to have a 4.2 times greater risk of an unfavorable evolution than those whose symptoms appeared between 6 and 10 years of age. [8]

Recommendations and Target Metrics:	**Related Guidelines and Recommendations** **Diagnosis:** International Classification of Headache Disorders, 2nd Revision (ICHD-II) (http://ihs-classification.org/en/) In children: • In children and adolescents (aged under 18 years), attacks may last 2-72 hours (the evidence for untreated durations of less than 2 hours in children has not been substantiated). • Migraine headache in children and adolescents (aged less than 18 years) is more often bilateral than is the case in adults; unilateral pain usually emerges in late adolescence or early adult life. • In young children, photophobia and phonophobia may be inferred from their behavior. • Episodic Syndromes: Recurrent gastrointestinal disturbance, Cyclic vomiting syndrome, Abdominal migraine, Benign paroxysmal vertigo, Benign paroxysmal torticollis [9] **Management:** Appropriate management of headache disorders may include, for example, professional training of healthcare professionals, accurate diagnosis and recognition of the condition, appropriate treatment, lifestyle and dietary modifications, and patient education.[10] The goals of long-term migraine management, both pharmacologic and non-pharmacologic are: • reduce attack frequency, severity, and disability; • reduce reliance on poorly tolerated, ineffective, or unwanted acute pharmacotherapies; • improve quality of life; • avoid acute headache medication escalation; • educate and enable patients to manage their disease and to enhance personal control of their migraine; and • reduction of headache-related distress and psychological symptoms.[11] To achieve this, a balanced, flexible and individually tailored treatment regimen may include bio-behavioral strategies and non-pharmacological methods as well as pharmacological measure. [2]

Gaps Between Actual and Target, Possible Reasons for Gaps:	The program should aim to address the following gaps:
	
	Diagnosis of Pediatric and Adolescent Migraine:
	
	• Headaches in children and adolescents are under-diagnosed. [7]
	• Child and adolescent migraines often go unrecognized or are misattributed to causes such as sinus disease or emotional disorders.[2, 12]
	• Early recognition and intervention is essential for minimizing the impact on a child's quality of life and may be important in preventing long term disability.[7]
	
	• There is significant variability in the evaluation and treatment of pediatric headaches in the emergency department (ED). Despite official recommendations and guidelines available to ED providers, the ED management of pediatric headaches is highly variable.[13]
	  ○ A large number of children continue to receive unnecessary testing and unproved treatments in the ED. [14]
	
	Management of Pediatric and Adolescent Migraine:
	
	• Headache disability as determined by the impact of recurrent headaches on a patient's quality of life has been demonstrated in adults with migraines but is only beginning to be assessed in children and adolescents.[15]
	• The management of pediatric headache should be addressed at each visit. A recent study shows that this is not occurring.
	  ○ Need to increase the role and the involvement of family doctors in the management of primary headache in children in general, and of pediatric migraine in particular. [16]

Barriers:	• In young children the presence of headaches is often overlooked.[9] • Children often have difficulty expressing the associated symptoms therefore they have to be inferred from the child's behavior ○ Children have difficulty describing light and sound sensitivity [17]
Current National Efforts to Reduce Gaps:	• PedMIDAS was developed to assess migraine disability in pediatric and adolescent patients. It has been tested and validated for ages 4 to 18. http://www.cincinnatichildrens.org/service/h/headache-center/pedmidas/
Expected Approximate Monetary Range of Grant Applications:	Individual grants requesting up to $500,000 will be considered. The total available budget related to this RFP is $1,000,000. The amount of the grant Pfizer will be prepared to fund for any full proposal will depend upon the external review panel's evaluation of the proposal and costs involved, and will be stated clearly in the grant approval notification.
Key Dates:	RFP release date: April 29, 2014 Letter of Intent due date: June 10, 2014 Review of LOIs by External Review Panel: week of June 30th Anticipated LOI Notification Date: week of July 7th Full Proposal Deadline: *week of August 21st *Only accepted LOIs will be invited to submit full proposals Review of Full Proposals by External Review Panel: week of September 15th Anticipated Full Proposal Notification Date: week of September 22nd Grants distributed following execution of fully signed Letter of Agreement Period of Performance: 10/1/2014 to 9/30/2016

How to Submit:	Please go to the website at www.pfizer.com/independentgrants and click on the button "Go to the Grant System." If this is your first time visiting this site you will be prompted to take the Eligibility Quiz to determine the type of support you are seeking. Please ensure you identify yourself as a first-time user. Select the following Area of Interest: Pediatric and Adolescent Migraine Requirements for submission: Complete all required sections of the online application and upload the completed LOI template (see Appendix). If you encounter any technical difficulties with the website, please click the "Need Support?" link at the bottom of the page.
Questions:	If you have questions regarding this RFP, please direct them in writing to the Grant Officer, Amanda Stein, at amanda.j.stein@pfizer.com, with the subject line "Pediatric and Adolescent Migraine 4/29/14."
Mechanism by which Applicants will be Notified:	All applicants will be notified via email by the dates noted above. Applicants may be asked for additional clarification or to make a summary presentation during the review period.

References:

1. Abu-Arafeh, I., et al. (2010). "Prevalence of headache and migraine in children and adolescents: a systematic review of population-based studies." Developmental Medicine & Child Neurology **52**(12): 1088-1097.
2. Brenner, M. and D. Lewis (2008). "The Treatment of Migraine Headaches in Children and Adolescents." J Pediatr Pharmacol Ther **13**(1): 17-24.
3. Conicella, E., et al. (2008). "The Child With Headache in a Pediatric Emergency Department." Headache: The Journal of Head and Face Pain **48**(7): 1005-1011.
4. Powers, S., et al. (2004). "Quality of life in paediatric migraine: characterization of age-related effects using PedsQL 4.0." Cephalalgia **24**(2): 120-127.
5. Powers, S. W., et al. (2003). "Quality of life in childhood migraines: clinical impact and comparison to other chronic illnesses." Pediatrics **112**(1 Pt 1): e1-5.
6. Fuh, J.-L., et al. (2010). "Headache Disability Among Adolescents: A Student Population-Based Study." Headache: The Journal of Head and Face Pain **50**(2): 210-218.
7. Kabbouche, M., et al. (2008). "Management of Migraine in Adolescents." Neuropsychiatr Dis Treat. 4(3): 535–548.
8. Antonaci, F., et al. (2014). "The evolution of headache from childhood to adulthood: a review of the literature." The Journal of Headache and Pain **15**(1): 15.

9. Society, H. C. C. o. t. I. H. (2013). "The International Classification of Headache Disorders, 3rd edition (beta version)."Cephalalgia **33**(9): 629-808.
10. World Health Organization: Headache Disorders Fact Sheet. http://www.who.int/mediacentre/factsheets/fs277/en/index.html. Accessed March 20, 2014.
11. Silberstein (2000). "Practice parameter: Evidence-based guidelines for migraine headache (an evidence based review)." Pediatrics **55**(6): 754-762.
12. Hershey, A.D. (2010). "Recent developments in pediatric headache." Current Opinion in Neurology. 23:249–253
13. Richer, L. P., et al. (2010). "Treatment of children with migraine in emergency departments: national practice variation study." Pediatrics **126**(1): e150-155.
14. Sheridan, D. C., et al. (2013). "Diagnostic testing and treatment of pediatric headache in the emergency department." J Pediatr **163**(6): 1634-1637.
15. Hershey, A. D., Powers, S.W., Vockell, A.-L. B., et al. (2001). " PedMIDAS: Development of a questionnaire to assess disability of migraines in children." Neurology **57**(11): 2034-2039.
16. Cuvellier JC, Fily A, Joriot S, et al. French general practitioners' management of children's migraine headaches. Headache 2007; 47:1282–1292.
17. Hershey, A. D., et al. (2005). "Use of the ICHD-II Criteria in the Diagnosis of Pediatric Migraine." Headache: The Journal of Head and Face Pain **45**(10): 1288-1297.

IV. Ethical Framework for Projects Involving Children

Evidence-based quality-improvement innovations should be designed with an underlying ethical framework that promotes the alliance among health care providers, patients, parents, and caregivers in the management of children with pediatric and adolescent migraine. Inter-professional collaborations that foster a comprehensive systems-based approach and accommodate the unique ethical obligations and protections of children are highly encouraged. Ultimately, the expectation is that such ethical considerations for children will be incorporated in the intervention design, with the overall intent of proposed projects resulting in robust and sustainable direct patient outcomes improvement. As such, proposals should include measures to protect the interests of pediatric and adolescent participants. These types of measures can be found in the following:

- American Academy of Pediatrics Clinical Report: Guidelines for the Ethical Conduct of Studies to Evaluate Drugs in Pediatric Populations; *Pediatrics Vol. 125 No. 4 April 1, 2010 pp. 850-860.*
- Code of Federal Regulations, 21 CFR 50 Subpart D: Additional Protections for Children Involved as Subjects in Research.
- Council for International Organizations of Medical Sciences (CIOMS), in collaboration with the World Health Organization (WHO): International Ethical Guidelines for Biomedical Research Involving Human Subjects.
- European Union: Ethical Considerations for Clinical Trials on Medicinal Products Conducted with the Paediatric Population; *Eur JHealth Law 15 (2):223-250.*
- Institute of Medicine Committee on Clinical Research Involving Children: Ethical Conduct of Clinical Research Involving Children.

- International Conference on Harmonization: Guidance for Good Clinical Practice and Clinical Investigation of Medicinal Products in the Pediatric Population.
- World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects.

Any internal or external review bodies with project oversight should include members with pediatric and adolescent expertise, and are knowledgeable about the special medical, psychological, ethical, and social needs of this vulnerable population. Additionally, projects must incorporate a robust and independent data- and safety-monitoring plan to safeguard the welfare of pediatric and adolescent project participants and ensure the integrity of the outcomes evaluation.

ADDITIONAL REFERENCES

- Ethical Considerations in Conducting Pediatric Research; *Pediatric Clinical Pharmacology, 1st Edition.*
- Everyday Ethics Issues in the Outpatient Clinical Practice of Pediatric Residents; *Arch Pediatr Adolesc Med 2009 Sep, 163(9):838-843.*
- Food and Drug Administration: Additional Safeguards for Children in Clinical Research. *Federal Register 66 (79):20589-20600*

V. Terms and Conditions

1. This RFP does not commit Pfizer or its partners to award a grant or a grant of any particular size if one is awarded, nor to pay any costs incurred in the preparation of a response to this request.

2. Pfizer reserves the right to accept or reject any or all applications received as a result of this request, or to cancel this RFP in part or in its entirety, if it determines it is in the best interest of Pfizer to do so.

3. For compliance reasons and in fairness to all applicants, all communications about the RFP must come exclusively to Pfizer IGL&C. Failure to comply will disqualify applicants.

4. Consistent with its commitment to openness and transparency, Pfizer reports education grants provided to medical, scientific and patient organizations in the United States. Pfizer reserves the right to announce the details of successful grant application(s) by whatever means insures transparency, such as on the Pfizer website, in presentations, and/or in other public media. In the case of this RFP, a list of all LOIs selected to move forward may be publicly disclosed. In addition, all approved full proposals, as well as all resulting materials (e.g., status updates, outcomes reports, etc.) may be posted on the IGL&C website and/or any other Pfizer document or site.

5. Pfizer reserves the right to share with organizations that may be interested in contacting you for further information (e.g., possible collaborations) the title of your proposed project, and the name, address, telephone number, and e-mail address of the applicant for the requesting organization.

6. To comply with the Patient Protection and Affordable Care Act ("Sunshine Act") under non-exempt conditions, Provider (sponsor) must provide names and other required information for the US-licensed physicians and US teaching hospitals ("Covered Recipients," as defined by Centers for Medicare and Medicaid Services) to whom the Provider (sponsor) furnished payments or other transfers of value stemming from the original independent grant awarded by Pfizer, if applicable. This includes compensation, reimbursement for expenses, and meals provided to faculty (planners, speakers, investigators, project leads, etc.) and "items of value" (items that possess a value on the open market, such as textbooks) provided to faculty and participants, if such faculty and/or participants meet the definition of Covered Recipient. Such required information is to be submitted during the reconciliation process or earlier upon Pfizer's request in order to meet certain Sunshine Act reporting commitments. Be advised Pfizer will not make any payments to any individuals; grant funding shall be paid directly to Provider (sponsor).

7. No portion of a Pfizer independent grant may be used for food and/or beverages for learners and/or participants in any capacity. Provider (sponsor) will be required to certify during the reconciliation process and/or the periodic collection of Sunshine reporting that funds were not used for food and/or beverages for learners and/or participants.

8. In the performance of all activities related to an independent grant, the Provider (sponsor) and all participants must comply with all applicable Global Trade Control Laws. "Global Trade Control Laws" include, but are not limited to, U.S. Export Administration Regulations; the International Traffic in Arms Regulations; EU export controls on dual-use goods and technology; Financial Sanctions Laws and Restrictive Measures imposed within the framework of the CFSP - Treaty on European Union; and the economic sanctions rules and regulations administered by the U.S. Treasury Department's Office of Foreign Assets Control.

Appendix: Letter of Intent Submission Guidance

LOIs should be single-spaced using Calibri 12-point font and 1-inch margins. Note there is a 3-page limit in the main section of the LOI. ***LOIs not meeting these standards will not be reviewed.***

LOIs should include the following sections

Main Section (not to exceed 3 pages):

A. Title

B. Goal
    1. Briefly state the overall goal of the project. Also describe how this goal aligns with the focus of the RFP and the goals of the applicant organization(s).

C. Objectives
    1. List the *overall* objectives you plan to meet with your project both in terms of learning and expected outcomes. Do not include individual activity objectives.
        - Objectives should describe the population as well as the outcomes you expect to achieve as a result of conducting the project.

D. Assessment of Need for the Project
    1. Please include quantitative baseline data summary, initial metrics (e.g., quality measures), or project starting point (please cite data on gap analyses or relevant patient-level data that informs the stated objectives) in *your* target area. Describe the source and method used to collect the data. Describe how the data was analyzed to determine that a gap existed. The RFP includes a international assessment of the need for the project. Please do not repeat this information within the LOI (you may reference the RFP, if necessary). Only include information that impacts your specific project, linking regional or local needs to those identified on the international basis, if appropriate

    2. Describe the primary audience(s) targeted for this project. Also indicate whom you believe will directly benefit from the project outcomes. Describe the overall population size as well as the size of your sample population

E. Project Design and Methods
    1. Describe the planned project and the way it addresses the established need.
        - If your methods include educational activities, please describe succinctly the topic(s) and format of those activities.

F. Innovation
    1. Explain what measures you have taken to assure that this project idea is original and does not duplicate other projects or materials already developed.
    2. Describe how this project builds upon existing work, pilot projects, or ongoing projects, etc., developed either by your institution or other institutions related to this project.

G. Design of Outcomes Evaluation
    1. In terms of the metrics used for the needs assessment, describe how you will determine if the practice gap was addressed for the target group.
        - Identify the sources of data you anticipate using to make the determination.
        - Describe how you expect to collect and analyze the data.
        - Explain the method used to control for other factors outside this project (e.g., use of a control group, comparison with baseline data).
    2. Quantify the amount of change expected from this project in terms of your target audience.
    3. Describe how you will determine if the target audience was fully engaged in the project.
    4. Describe how the project outcomes might be broadly disseminated.

H. Project Timeline

I. Requested Budget
    1. A total amount requested is the only information needed at this time.
    2. The budget amount requested must be in U.S. dollars (USD).
    3. While estimating your budget please keep the following items in mind:
        - Institutional overhead and indirect costs may be included within the grant request. Examples include human resources department costs, payroll processing and accounting costs, janitorial services, utilities, property taxes, property and liability insurance, and building maintenance as well as additional project expenses such as costs for publication, IRB/IEC review fees, software license fees, and travel. Please note: Pfizer does not provide funding for capital equipment.
        - It should be noted that grants awarded through IGLC cannot be used to purchase therapeutic agents (prescription or non-prescription).
        - Pfizer maintains a company-wide, maximum allowed overhead rate of 28% for independent studies and projects.

J. Additional Information
    1. If there is any additional information you feel Pfizer should be aware of concerning the importance of this project, please summarize it in within the page limitations.

Organizational Detail (not to exceed 1 page)

Describe the attributes of the institutions/organizations/associations that will support and facilitate the execution of the project and the leadership of the proposed project. Articulate the specific role of each partner in the proposed project.

LOIs should be single-spaced using Calibri 12-point font and 1-inch margins. There is a 3-page limit for the main section and a 1-page limit for organizational detail. If extensive, references may be included on 1 additional page. **Final submissions should not exceed 5 pages in total** (3 pages for the main section, 1 page for organizational detail, and 1 page for references).

Make every effort to submit as **few** documents as possible—you are encouraged to include all required sections in one document. There is no need to submit the organization detail or references in a separate document from the main section of the LOI.

Please note the formatting and page limit for the LOI. The LOI is inclusive of additional information of any kind. A submission exceeding the page limit ***WILL BE REJECTED*** *and* ***RETURNED UNREVIEWED****.*