



# OPIOID STEWARDSHIP REQUEST FOR PROPOSAL

Publish Date: [Date]

## PURPOSE AND INTENT:

This Request for Proposals (RFP) is issued by Pacira Pharmaceuticals, Inc. for educational programs regarding Opioid Stewardship Centers of Excellence. This RFP is funded through the educational grant program at Pacira Pharmaceuticals. Funding is available for the fiscal year 2018.

Pacira Pharmaceuticals, Inc. (NASDAQ:PCRX) is a specialty pharmaceutical company focused on the clinical and commercial development of new products that meet the needs of acute care practitioners and their patients. The company's flagship product, EXPAREL<sup>®</sup> (bupivacaine liposome injectable suspension) was commercially launched in the United States in April 2012. EXPAREL and two other products have successfully utilized DepoFoam<sup>®</sup>, a unique and proprietary product delivery technology that encapsulates drugs without altering their molecular structure, and releases them over a desired period of time. Additional information about Pacira is available at [www.pacira.com](http://www.pacira.com).

Pacira is focused on the clinical and commercial development of new products for use primarily in hospitals and ambulatory surgery centers (ASCs). The corporate mission of Pacira is to drive innovation in postsurgical pain management to provide an opioid alternative to as many patients as possible and strive to improve patient care through low or no opioid use strategies. Pacira embraces educational programs and activities that serve the needs of our patients, as well as the needs of the medical, scientific and advocacy organizations supporting them.

The focus of this RFP is intended to support regional and/or national organizations that support health care institutions and/or practices in creating opioid stewardship centers of excellence across the United States and seeks to find organizations that champion opioid minimization and opioid alternative treatment options in postsurgical pain management.

## BACKGROUND: POSTSURGICAL OPIOID USE AND THE OPIOID EPIDEMIC

### **The Opioid Crisis**

*91 Americans die of an opioid overdose each day.*

In 2015, there were 33,091 opioid overdose-related deaths in the United States<sup>1</sup>, an epidemic level leading to heightened national attention and the recent establishment of a government commission to combat this growing health problem.<sup>2</sup> Opioid overdose-related deaths increased exponentially between 1999 and 2014<sup>2</sup>, a 15-year trend that was driven primarily by prescription opioids.<sup>3</sup> High opioid prescribing and overprescribing for postsurgical pain<sup>4</sup> carries

not only acute risks related to opioid-related adverse effects (ORAEs) but also a long-term risk of chronic opioid use, both of which are associated with substantial costs.<sup>5-8</sup>

### **Acute Impact of Opioid Use for Postsurgical Pain Management**

*99% of surgical patients receive opioids while in the hospital; therefore opioid related adverse events are common and costly.*

A mainstay of postsurgical pain management, 99% of surgical patients receive opioids while in the hospital.<sup>8,10</sup> As a result, a variety of ORAEs are common particularly in the short-term after surgery when the highest dose of opioids are administered, and can linger well into the post-operative period. Common ORAEs impact the respiratory, gastrointestinal, and genitourinary systems and disproportionately affect patients who are elderly, obese, or have comorbid illness.<sup>8-12</sup> In addition, patient deaths have been attributed to programming errors of IV PCA devices commonly used to deliver opioids in a hospital setting.<sup>53</sup>

ORAEs are associated with longer hospital stays, higher readmission rates, and increased mortality risk<sup>8</sup> and can necessitate costly interventions, such as increased monitoring, additional medication, and urinary catheterization.<sup>8,12,13</sup> A study of administrative records of patients who underwent common orthopaedic and soft-tissue in-patient procedures at twenty-six (26) hospitals in the US, showed that patients who experienced ORAEs had 55% (3-day) longer hospital stays, 47% higher hospital cost (\$21,012 vs. \$14,291), a 36% higher 30-day readmission rate (7.5% vs. 5.6%) and a 3.4 times greater risk of mortality.<sup>8</sup> Similarly, a study which examined administrative claims for 17,876 patients who underwent inpatient colectomy at over 500 hospitals in the US found the incidence of post-operative ileus to be 17%, and its occurrence increased LOS by 55% (13.8 vs. 8.9 days) and costs by 48% (\$25,089 vs. \$16,907).<sup>54</sup> Studies have shown that common gastrointestinal ORAEs impose substantial costs, with estimated excesses of \$126 to \$4000 per month to manage chronic constipation, \$9000 to \$10,000 for postoperative ileus, and \$33,000 for opioid-related bowel obstruction.<sup>14-16</sup>

### **Long-Term Chronic Opioid Abuse After Surgery**

*1 in 15 patients prescribed an opioid may develop long-term use, due in part to the widespread use of opioids for pain management, the prevalence of risk factors for persistent use, and the increased risk of long-term use as soon as 3 days after the initial dose is given. Left over medication after surgery is also common and often leads to first exposure in adolescents and young adults.*

Postsurgical pain management with opioids can lead to chronic use,<sup>6,19,20</sup> with the risk of chronic opioid use increasing as soon as 3 days after initial exposure.<sup>21</sup> Trends suggest that 1 in 15 patients prescribed an opioid may go on to long-term use.<sup>6,19,55</sup>

Risk factors for chronic opioid use include characteristics inherent to the procedure, as well as common patient characteristics and behaviors.<sup>22,23</sup> Groups with increased risk for chronic opioid use after surgery include women; middle-age or older patients; obese patients; and

patients with a history of opioid use, substance abuse, smoking, mental health conditions such as anxiety and depression, or pain disorders.<sup>6,20,22-25</sup>

Although a reported 20 million Americans have a substance use disorder as of 2015 and at least 9% of all surgery patients have a history of chronic opioid use or abuse,<sup>23,26,27,56</sup> the actual rate is likely higher due to underreporting of substance abuse. Large database studies have shown increased risk of persistent opioid use across both major and minor procedures including bariatric surgery (8%), colectomy (10%) and, total joint arthroplasty (9%) among many others.<sup>6,24,30</sup>

In addition to the risk of chronic opioid use in surgical patients themselves, leftover medication is a major source of diversion.<sup>32,33</sup> Up to 92% of patients report unused opioids after surgery,<sup>31</sup> and for adolescents, in whom misuse and abuse of prescription opioids is prevalent, first exposure commonly occurs at home.<sup>5,34</sup>

### **Economic Impact of Chronic Opioid Abuse**

*In 2013, the estimated economic burden related to prescription opioid abuse exceeded \$78.5 billion, with costs related to health-care, criminal justice and lost workplace productivity.*

Along with adverse health consequences, the opioid crisis imposes a profound economic burden. From 2002 to 2012, the number of outpatients who purchased prescription opioids increased by nearly 10 million, and total expenses for these medications increased by \$5.1 billion.<sup>35</sup> Between 1997 and 2005, there was nearly a 6-fold increase in the number of oxycodone prescriptions alone.<sup>36</sup> In commercially insured patients, a  $\geq 2$ -fold increase in all-cause pharmacy and medical costs has been demonstrated after the onset of chronic opioid therapy.<sup>37</sup>

There are multiple costs related to opioid misuse and abuse, including costs related to healthcare utilization (eg, emergency department, hospital stays, outpatient visits, and medications) as well as substance abuse treatment, lost workplace productivity, and criminal justice.<sup>7,36,38-41,45</sup> An administrative claims database study encompassing sixteen self-insured employer health plans reported an 8-fold increase in healthcare costs for opioid abusers (\$15,884) compared with non-abusers (\$1,830).<sup>42</sup> In 2001, the estimated cost of treating prescription opioid abuse in the United States was \$8.6 billion<sup>43</sup> and by 2013, estimated costs related to prescription opioid abuse exceeded \$78.5 billion.<sup>44</sup>

### **Addressing the Opioid Crisis**

*Stringent prescribing practices and greater use of multimodal opioid- minimizing/eliminating pain management strategies provides the opportunity to dramatically reduce or eliminate the use and availability of opioids and make a substantial impact on the opioid crisis.*

Despite efforts to decrease opioid abuse and associated risks and healthcare costs via the development of abuse-deterrent opioid formulations,<sup>46-48</sup> the opioid epidemic has not abated.

Prescription opioids have become cheap and easy to acquire, and the costs associated with ORAEs and chronic opioid use are climbing.<sup>10</sup> In tandem with federal efforts to combat the opioid epidemic,<sup>52</sup> there is a need for increased commitment from payers, surgeons, and family physicians to increase awareness and education about the long-term consequences of prescription opioid use. Thoughtful consideration must be given to patient characteristics that indicate a higher risk for chronic opioid use. Through stringent prescribing practices and greater use of multimodal, opioid-minimizing pain management strategies<sup>49,50</sup> with effective non-opioid analgesics, there is the opportunity to reduce or eliminate the use and availability of opioids, and make a substantial impact on the opioid crisis.

#### WHO CAN APPLY?:

To be eligible for consideration for this RFP, the requestor must be an independent third party. Examples of appropriate Requesters include, but are not limited to:

- Healthcare Professional organizations;
- Hospitals, health systems or academic medical centers;
- Accredited educational providers;
- Patient advocacy groups;
- Disease-related organizations;
- Medical education companies; or
- Charitable Organizations.

#### SCOPE OF WORK:

Successful applicants will have protocols and procedures regarding opioid minimization and how they will collaborate with the hospital staff to ensure coordination and adherence.

The Grantee will work with the opioid stewardship evaluation team, and other collaborative partners to identify specific program outcomes demonstrating the effectiveness of this opioid stewardship model. The Grantee will then be expected to report on these outcomes every three months, as applicable.

#### PROPOSAL SUBMISSION REQUIREMENTS:

All requestors must submit a written proposal that addresses the following topics, and adheres to all instructions and includes required supporting documentation noted at <https://www.pacira.com/depoforam-platform/grants.php>:

- Organization's contact information
- Primary contact name, title, address, phone, and email
- Describe organization's primary mission and/or current activities relevant to proposal
- Project description and specific proposal objectives



- Available data/information relevant to proposal submission (e.g. guidelines, educational brochures, etc.)
- Examples of proposed framework to enact grant to have broad national impact (e.g. guidelines, conferences, targeted institutions or practices, etc.)
- Describe how proposal will improve patient care in alignment with grant objectives
- Provide financial support justifications, such as:
  - Supportive activities or materials (e.g. development of educational materials/banners, forums, etc.);
  - Enhanced recovery after surgery (ERAS), multimodal pain management, infiltration administration technique(s); and
  - Postsurgical pain quality improvement outcomes and assessments.
- Proposed timeline for completion with associated deliverables. If possible, attach a flow chart outlining the operational steps of the proposed program.
- Proposed budget. Budgets should be reasonable and reflect the scope of responsibilities in order to accomplish the goals of this project. No funding match is required; however, bidders will need to identify any other sources of funding, both in-kind and monetary, that will be used.

All grant requests can be submitted at <https://www.pacira.com/depof foam-platform/grants.php>

#### PACIRA PHARMACEUTICALS, INC. CONTACT INFORMATION:

Maureen Chlopik  
Manager, Medical Health Science  
Pacira Pharmaceuticals, Inc.  
5 Sylvan Way  
Parsippany NJ 07054  
[MaureenChlopik@pacira.com](mailto:MaureenChlopik@pacira.com)  
973-254-4321 (direct)

#### CONFIDENTIALITY:

This Request for Proposal constitutes the confidential and proprietary information of Pacira Pharmaceuticals, Inc. and may not, in whole or in part, be copied, reproduced, or otherwise used in any manner whatsoever without the prior express written permission of Pacira Pharmaceuticals, Inc. All information provided herein is proprietary to Pacira Pharmaceuticals, Inc. and is to be used only by your company in its response hereto. Any other use or communication of this information is prohibited.

#### REFERENCES

1. Rudd RA, Seth P, David F, Scholl L. Increases in drug and opioid-involved overdose deaths-United States, 2010-2015. *MMWR Morb Mortal Wkly Rep.* 2016;65(5051):1445-1452.

2. President Donald J. Trump Signs an Executive Order Establishing the President's Commission on Combating Drug Addiction and the Opioid Crisis. Available at: <https://www.whitehouse.gov/the-press-office/2017/03/30/president-donald-j-trump-signs-executive-order-establishing-presidents>. Accessed August 18, 2017.
3. Centers for Disease Control and Prevention. Understanding the epidemic. Drug overdose deaths in the United States continue to increase in 2015. Available at: <https://www.cdc.gov/drugoverdose/epidemic/>. Accessed April 7, 2017.
4. Hernandez NM, Parry JA, Taunton MJ. Patients at Risk: Large Opioid Prescriptions After Total Knee Arthroplasty. *J Arthroplasty*. 2017;32(8):2395-2398.
5. Volkow ND, McLellan TA. Curtailing diversion and abuse of opioid analgesics without jeopardizing pain treatment. *JAMA*. 2011;305(13):1346-1347.
6. Brummett CM, Waljee JF, Goesling J, et al. New persistent opioid use after minor and major surgical procedures in US adults. *JAMA Surg*. 2017:e170504.
7. Oderda GM, Lake J, Rudell K, Roland CL, Masters ET. Economic Burden of Prescription Opioid Misuse and Abuse: A Systematic Review. *J Pain Palliat Care Pharmacother*. 2015;29(4):388-400.
8. Kessler ER, Shah M, Gruschkus SK, Raju A. Cost and quality implications of opioid-based postsurgical pain control using administrative claims data from a large health system: opioid-related adverse events and their impact on clinical and economic outcomes. *Pharmacotherapy*. 2013;33(4):383-391.
9. Baratta JL, Gandhi K, Viscusi ER. Perioperative pain management for total knee arthroplasty. *J Surg Orthop Adv*. 2014;23(1):22-36.
10. Minkowitz HS, Gruschkus SK, Shah M, Raju A. Adverse drug events among patients receiving postsurgical opioids in a large health system: risk factors and outcomes. *Am J Health Syst Pharm*. 2014;71(18):1556-1565.
11. Pizzi LT, Toner R, Foley K, et al. Relationship between potential opioid-related adverse effects and hospital length of stay in patients receiving opioids after orthopedic surgery. *Pharmacotherapy*. 2012;32(6):502-514.
12. Oderda G. Challenges in the management of acute postsurgical pain. *Pharmacotherapy*. 2012;32(9 suppl):6S-11S.
13. Suh DC, Kim MS, Chow W, Jang EJ. Use of medications and resources for treatment of nausea, vomiting, or constipation in hospitalized patients treated with analgesics. *Clin J Pain*. 2011;27(6):508-517.
14. Kane-Gill SL, Rubin EC, Smithburger PL, Buckley MS, Dasta JF. The cost of opioid-related adverse drug events. *J Pain Palliat Care Pharmacother*. 2014;28(3):282-293.
15. Gan TJ, Robinson SB, Oderda GM, et al. Impact of postsurgical opioid use and ileus on economic outcomes in gastrointestinal surgeries. *Curr Med Res Opin*. 2015;31(4):677-686.

16. Wan Y, Corman S, Gao X, et al. Economic burden of opioid-induced constipation among long-term opioid users with noncancer pain. *Am Health Drug Benefits*. 2015;8(2):93-102.
17. Oderda GM, Evans RS, Lloyd J, et al. Cost of opioid-related adverse drug events in surgical patients. *J Pain Symptom Manage*. 2003;25(3):276-283.
18. Oderda GM, Said Q, Evans RS, et al. Opioid-related adverse drug events in surgical hospitalizations: impact on costs and length of stay. *Ann Pharmacother*. 2007;41(3):400-406.
19. Alam A, Gomes T, Zheng H, et al. Long-term analgesic use after low-risk surgery: a retrospective cohort study. *Arch Intern Med*. 2012;172(5):425-430.
20. Clarke H, Soneji N, Ko DT, Yun L, Wijesundera DN. Rates and risk factors for prolonged opioid use after major surgery: population based cohort study. *BMJ*. 2014;348:g1251.
21. Shah A, Hayes C, Martin B. Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use — United States. *MMWR CDC Surveill Summ*. 2017;66(10):265- 269.
22. Inacio MC, Hansen C, Pratt NL, Graves SE, Roughead EE. Risk factors for persistent and new chronic opioid use in patients undergoing total hip arthroplasty: a retrospective cohort study. *BMJ Open*. 2016;6(4):e010664.
23. Jiang X, Orton M, Feng R, et al. Chronic Opioid Usage in Surgical Patients in a Large Academic Center. *Ann Surg*. 2017;265(4):722-727.
24. Kim SC, Choudhry N, Franklin JM, et al. Patterns and predictors of persistent opioid use following hip or knee arthroplasty. *Osteoarthritis Cartilage*. 2017;25(9):1399-1406.
25. Bedard NA, Pugely AJ, Westermann RW, et al. Opioid Use After Total Knee Arthroplasty: Trends and Risk Factors for Prolonged Use. *J Arthroplasty*. 2017;32(8):2390-2394.
26. Cauley CE, Anderson G, Haynes AB, et al. Predictors of In-hospital Postoperative Opioid Overdose After Major Elective Operations: A Nationally Representative Cohort Study. *Ann Surg*. 2017;265(4):702-708.
27. Inacio MC, Hansen C, Pratt N, Graves S, Roughead E. Risk factors for persistent and new chronic opioid use in patients undergoing total hip arthroplasty: a retrospective cohort study. *BMJ Open*. 2016;6.
28. Sun EC, Darnall BD, Baker LC, Mackey S. Incidence of and risk factors for chronic opioid use among opioid-naive patients in the postoperative period. *JAMA Intern Med*. 2016;176(9):1286-1293.
29. Raebel MA, Newcomer SR, Reifler LM, et al. Chronic use of opioid medications before and after bariatric surgery. *JAMA*. 2013;310(13):1369-1376.
30. Raebel MA, Newcomer SR, Bayliss EA, et al. Chronic opioid use emerging after bariatric surgery. *Pharmacoepidemiol Drug Saf*. 2014;23(12):1247-1257.

31. Bicket MC, Long JJ, Pronovost PJ, Alexander GC, Wu CL. Prescription Opioid Analgesics Commonly Unused After Surgery: A Systematic Review. *JAMA Surg.*
32. Maughan BC, Hersh EV, Shofer FS, et al. Unused opioid analgesics and drug disposal following outpatient dental surgery: A randomized controlled trial. *Drug Alcohol Depend.* 2016;168:328-334.
33. Volkow ND, McLellan AT. Opioid Abuse in Chronic Pain--Misconceptions and Mitigation Strategies. *N Engl J Med.* 2016;374(13):1253-1263.
34. Zosel A, Bartelson BB, Bailey E, Lowenstein S, Dart R. Characterization of adolescent prescription drug abuse and misuse using the Researched Abuse Diversion and Addiction-related Surveillance (RADARS((R))) System. *J Am Acad Child Adolesc Psychiatry.* 2013;52(2):196-204.e192.
35. Stagnitti MN. Trends in Prescribed Outpatient Opioid Use and Expenses in the U.S. Civilian Noninstitutionalized Population, 2002-2012. *Statistical Brief (Medical Expenditure Panel Survey (US)).* Rockville (MD); 2015.
36. Meyer R, Patel AM, Rattana SK, Quock TP, Mody SH. Prescription opioid abuse: a literature review of the clinical and economic burden in the United States. *Popul Health Manag.* 2014;17(6):372-387.
37. Kern DM, Zhou S, Chavoshi S, et al. Treatment patterns, healthcare utilization, and costs of chronic opioid treatment for non-cancer pain in the United States. *Am J Manag Care.* 2015;21(3):e222-234.
38. Strassels SA. Economic burden of prescription opioid misuse and abuse. *J Manag Care Pharm.* 2009;15(7):556-562.
39. Baser O, Xie L, Mardekian J, et al. Prevalence of diagnosed opioid abuse and its economic burden in the veterans health administration. *Pain Pract.* 2014;14(5):437-445.
40. Ronan MV, Herzig SJ. Hospitalizations Related To Opioid Abuse/Dependence And Associated Serious Infections Increased Sharply, 2002-12. *Health Aff (Millwood).* 2016;35(5):832-837.
41. White AG, Birnbaum HG, Mareva MN, et al. Direct costs of opioid abuse in an insured population in the United States. *J Manag Care Pharm.* 2005;11(6):469-479.
42. White PF. The changing role of non-opioid analgesic techniques in the management of postoperative pain. *Anesth Analg.* 2005;101(5 Suppl):S5-22.
43. Birnbaum HG, White AG, Reynolds JL, et al. Estimated costs of prescription opioid analgesic abuse in the United States in 2001: a societal perspective. *Clin J Pain.* 2006;22(8):667-676.
44. Florence CS, Zhou C, Luo F, Xu L. The Economic Burden of Prescription Opioid Overdose, Abuse, and Dependence in the United States, 2013. *Med Care.* 2016;54(10):901-906.
45. Birnbaum HG, White AG, Schiller M, Waldman T, Cleveland JM, Roland CL. Societal



- costs of prescription opioid abuse, dependence, and misuse in the United States. *Pain medicine*. 2011;12(4):657-67.
46. Descoteaux A, Borrelli E, Kogut S. A budget impact analysis of abuse deterrent opioid formulation. *Value Health*. 2017;20:A295.
47. Schatman ME, Webster LR. The health insurance industry: perpetuating the opioid crisis through policies of cost-containment and profitability. *J Pain Res*. 2015;8:153-158.
48. White AG, Birnbaum HG, Rothman DB, Katz N. Development of a budget-impact model to quantify potential cost savings from prescription opioids designed to deter abuse or ease of extraction. *Appl Health Econ Health Policy*. 2009;7(1):61-70.
49. American Society of Anesthesiologists Task Force on Acute Pain Management. Practice guidelines for acute pain management in the perioperative setting: an updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. *Anesthesiology*. 2012;116(2):248-273.
50. Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of postoperative pain: a clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. *J Pain*. 2016;17(2):131-157.
51. Philip BK, Reese PR, Burch SP. The economic impact of opioids on postoperative pain management. *J Clin Anesth*. 2002;14(5):354-364.
52. US Department of Health and Human Services. Secretary price announces HHS strategy for fighting opioid crisis. Available at: <https://www.hhs.gov/about/leadership/secretary/speeches/2017-speeches/secretary-price-announces-hhs-strategy-for-fighting-opioid-crisis/index.html>. Accessed August 24, 2017.
53. Wong M, Mabuyi A, Gonzalez B. First National Survey of Patient-Controlled Analgesia Practices. *Physician-Patient Alliance for Health & Safety*; 2013.
54. Iyer S, Saunders WB, Stemkowski S. Economic burden of postoperative ileus associated with colectomy in the United States. *J Managed Care Pharmacy: JMCP*. 2009;15(6):485-94.
55. Carroll I, Barelka P, Wang CK, Wang BM, Gillespie MJ, McCue R, et al. A pilot cohort study of the determinants of longitudinal opioid use after surgery. *Anesth Analg*. 2012;115(3):694-702.
56. Center for Behavioral Health Statistics and Quality. (2016). Key substance use and mental health indicators in the United States: Results from the 2015 National Survey on Drug Use and Health (HHS Publication No. SMA 16-4984, NSDUH Series H-51). Retrieved from <http://www.samhsa.gov/data/>. Accessed September 12, 2017.