REQUEST FOR (GRANT) APPLICATIONS (RFA)

Overview Information

Sponsoring Organization	Risk Evaluation and Mitigation Strategy Program Companies (RPC)
RFA Title	Extended-Release and Long-Acting Opioid Analgesics: Risk Evaluation and Mitigation Strategy (REMS)
RFA Code	ER/LA 040314
RFA Goal	The goal of this RFA is to support high-quality REMS-compliant Continuing Education (CE) designed to assist in ensuring that the benefits of Extended Release/Long-Acting (ER/LA) opioid analgesics outweigh the risks (in patients whose clinicians have determined ER/LA opioid analgesics to be an appropriate treatment option). The mechanism by which this is intended to occur is by educating healthcare providers (HCPs), **particularly, as specified by the FDA REMS goals, those HCPs who prescribe ER/LA opioid analgesics**. The education will be based on the *Food & Drug Administration (FDA) Blueprint for Prescriber Education for ER/LA Opioid Analgesics* (FDA Blueprint or Blueprint), with the aim to optimize both knowledge acquisition and the translation of that knowledge into practice. Successful proposals will detail educational initiatives that ultimately assist in positively impacting safe and appropriate patient care while meeting all REMS requirements detailed in the next section.
RFA Elements Essential to Meet REMS-Compliant CE Requirements	**Educational design of proposed CE activities must incorporate all of the requirements for REMS-compliant CE training:** • All activities within each educational program must cover all FDA Blueprint elements contained within the six sections of the document. • All activities must include an assessment that covers all six sections of the FDA Blueprint. Preferred consideration will be given to grant applications that integrate the assessment throughout the activity in order to increase the likelihood of learners completing the assessment, an FDA requirement for the learner to be counted toward the REMS goals. (Please note: The related MedBiquitous specification states that "successfully completing" the REMS education means "Completing all components of an education activity and meeting education provider's

	criteria for passing. Components of an educational activity include instruction, assessment of learning, and potentially evaluation." For a full list of REMS-related definitions developed by the MedBiquitous Working Group, please see Appendix A. • The educational activities are subject to independent audit by the CE Accrediting Bodies. ➢ This audit is intended to occur prior to learners encountering the activity, and as such, Providers conducting CE under RPC-supported grants agree to submit all materials to their Accrediting Body at least 45 days before the activity start date. ➢ RPC-supported Providers whose activities are not selected for audit by the Accrediting Bodies agree to provide documentation to RPC in which a medical expert, independent of, but chosen by the Provider, attests that the activity meets the REMS-compliant CE requirements. • The activities must be conducted in accordance with the standards for accredited CE set by the appropriate Accrediting Body or Bodies (ACCME, AOA, AANP, AMA, AAFP, or ADA CERP). **FDA has set explicit definitions and goals regarding the primary target audience for REMS education and how many learners from this target audience will complete REMS-compliant CE by certain time frames (see Section 1). Since RPC is held responsible by FDA for meeting these goals, the Provider's proposed approach to engaging the primary target audience to "complete" REMS-compliant CE is a key criterion on which all proposals will be evaluated.**
Key Dates	RFA Posted: March 19th, 2014 Application Due Date: April 30th, 2014 Award Notification Date: Q3 2014
RFA Document Parameters	Grant applicants should submit applications in MS Word.
Submission Link	Grant applications must be submitted via the Grant Management System (GMS), which will be accepting new grant applications in response to this RFA beginning on **March 21st, 2014**. The GMS may be accessed by way of

	the RPC website at www.ER-LA-OpioidREMS.com via the right-hand-side link, “Continuing Education Provider Information.” For this specific RFA, the appropriate RFA code is **RFA 040314**.
Questions on RFA?	Please contact Polaris Grant Coordinator Brad Hill. Phone: 1-800-376-9756; Email: grants@er-la-opioidrems.com

Table of Contents

Section 1: Scope of Problem and Background on ER/LA Opioid REMS

Scope of the Problem

According to the 2011 Institute of Medicine (IOM) Report "*Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research,"* as many as 100 million adults in the US report having a common chronic pain condition, exceeding the number affected by heart disease, cancer, and diabetes.

The economic burden of pain to society is staggering. The IOM Report suggests that the annual health economic impact of pain represents a $560 billion to $635 billion burden to the US (in 2010 dollars) and the morbidity and disability associated with chronic pain represents a significant public health issue. At the same time, however, the misuse and abuse of opioid analgesics, one class of medications used for managing moderate-to-severe chronic pain, has emerged as a major public health/patient safety problem.

The most recent national data available indicate that:

- At the patient-health level, numerous clinical reports suggest that chronic pain remains undertreated; the percentage of patients receiving appropriate and adequate treatment has been reported to be as low as 10% to 25%.[1]

- Patients with chronic pain have difficulty finding physicians who can effectively treat their pain, with nearly 50% of patients changing physicians at least once and nearly 25% making at least three physician changes.1

- Based on the 2012 National Survey on Drug Use and Health, public health experts estimate more than 37 million Americans age 12 and older used an immediate release (IR) or ER/LA opioid analgesic for non-medical use some time in their life—an increase from about 30 million in 2002.[2]

- In 2012, there were more than 366,000 emergency department visits involving nonmedical use of opioid analgesics.[1]

- 257 million prescriptions for opioids were dispensed in 2009—a 48% increase compared with figures for 2000.[3]

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[1] Drug Abuse Warning Network 2011 http://www.samhsa.gov/data/2k13/DAWN2k11ED/DAWN2k11ED.htm#5 Accessed January 2014

[2] Substance Abuse and Mental Health Services Administration. 2012. *Results from the 2012 National Survey on Drug Use and Health: Detailed Table*, Table 1.54A.a. Rockville, MD.
http://www.samhsa.gov/data/NSDUH/2012SummNatFindDetTables/NationalFindings/NSDUHresults2012.htm

[3] Warner M, Chen LH, Makuc DM, Anderson RN, and Miniño AM. 2011. Drug Poisoning Deaths in the United States, 1980–2008, in U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics, *NCHS Data*

- Total societal costs of prescription opioid abuse, including costs related to workplace, healthcare, and criminal justice, were estimated at $55.7 billion in 2009.[4]

ER/LA Opioid REMS and the REMS Program Companies

The ER/LA Opioid Analgesics REMS is designed to ensure that the benefits of ER/LA opioid analgesics outweigh the risks (in patients whose clinicians have determined ER/LA opioid analgesics to be an appropriate treatment option). The goal of this REMS is to reduce serious adverse outcomes resulting from inappropriate prescribing, misuse, and abuse of ER/LA opioid analgesics while maintaining patient access to pain medications. Adverse outcomes of concern include addiction, unintentional overdose, and death.[5]

The FDA has developed a Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics, which is posted on the FDA website for use by accredited CE Providers to develop the actual CE activities. (http://www.fda.gov/downloads/drugs/drugsafety/informationbydrugclass/ucm277916.pdf)

The FDA determined that a single shared system was to be implemented for all products within this drug class. As a result, the RPC was created, comprising the 19 companies[6] that have ER/LA opioid products. RPC-supported REMS education will be provided through accredited continuing education (CE) activities supported by independent educational grants from the RPC. For a complete listing of the RPC member companies, see www.ER-LA-OpioidREMS.com.

Desired Outcomes and FDA Expectations of RPC-Supported REMS Education

The desired outcome of ER/LA opioid analgesic REMS-compliant CE is to increase understanding of appropriate patient assessment and prescribing practices, as well as other information that can help reduce misuse, abuse, and overdose deaths associated with ER/LA opioids analgesics. Education that is focused on the expected results outlined below should result in healthcare professionals incorporating practices that can assist in maintaining that the benefits of opioid analgesic medications outweigh the risks.

The expected results of the REMS education as described by the FDA in the FDA Blueprint introductory section are that prescribers of ER/LA opioid analgesics will:

- Understand how to assess patients for treatment with ER/LA opioid analgesics

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Brief, *No 81*. December 2011. Hyattsville, MD. http://www.cdc.gov/nchs/data/databriefs/db81.pdf. Accessed on March30, 2012.

[4] Birnbaum, Howard G., Alan G. White, Matt Schiller, Tracy Waldman, Jody M. Cleveland, and Carl L. Roland. "Societal Costs of Prescription Opioid Abuse, Dependence, and Misuse in the United States." *Pain Medicine* 12, no. 4 (2011): 657–667.

[5] Adapted from the FDA Approved ER/LA Opioid Analgesics REMS document (October 2012 version). ER/LA Opioid Analgesics REMS (http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf)

[6] As of March 2013

- Be familiar with how to initiate therapy, modify dose, and discontinue use of ER/LA opioid analgesics

- Be knowledgeable about how to manage ongoing therapy with ER/LA opioid analgesics

- Know how to counsel patients and caregivers about the safe use of ER/LA opioid analgesics, including proper storage and disposal

- Be familiar with general and product-specific drug information concerning ER/LA opioid analgesics

In order to be REMS-compliant, and therefore eligible for educational grant support from the RPC, the education must address all elements of the FDA Blueprint. (http://www.fda.gov/downloads/drugs/drugsafety/informationbydrugclass/ucm277916.pdf) While these are the overall FDA REMS expectations, successful proposals should translate these into CE-compliant objectives and outcomes.

The FDA has set goals/time frames for the number of ER/LA opioid prescribers completing REMS-compliant CE.

The first FDA-mandated CE goal[7] stipulates that 80,000 ER/LA opioid analgesic prescribers will have successfully completed REMS-compliant CE, as defined at the bottom of page 1, by February 28, 2015.

Subsequent goals established by the FDA in the REMS are:

- ***160,000 ER/LA opioid analgesic prescribers will have successfully completed REMS-compliant CE by February 28, 2016.***

- ***192,000 ER/LA opioid analgesic prescribers will have successfully completed REMS-compliant CE by February 28, 2017.***

Definitions and Clarifications:

As part of the REMS, the FDA characterized prescribers that were the intended audience for the REMS CE. CE-compliant definitions were then developed and finalized by the MedBiquitous Working Group, which included representation from Accreditors, national CE Provider organizations, Providers, FDA, RPC, and other REMS CE-related stakeholders. For a full list of definitions developed by the MedBiquitous Working Group, please see Appendix A.

Key definitions relevant to this RFA include:

[7] FDA. "Blueprint for Prescriber Education for Extended-release and Long-acting Opioid Analgesics," 2013.

- ER/LA_opioid_prescriber: "An individual clinician who is registered with the DEA (Drug Enforcement Agency) to prescribe schedule 2 and/or 3 controlled substances and has written at least one ER/LA opioid script in the past year." (Please see MedBiquitous website for reference: http://www.medbiq.org/mems/definitions)
  Note: To be counted toward these FDA mandated CE-goals, a learner must meet the MedBiquitous definition of "prescribers successfully completing"[8] all components of an educational activity.
- "Prescribers successfully completing" a REMS educational activity: "FDA REMS defined ER/LA opioid prescribers that have completed all components of an educational activity and met the education provider's criteria for passing. Components of an educational activity include instruction, assessment of learning, and potentially evaluation." (Please see definition of "prescribers_successfully _completing" at the MedBiquitous website: http://medbiq.org/mems/definitions)

The FDA Blueprint and additional information on REMS-compliant CE can be found on the RPC website at www.ER-LA-OpioidREMS.com.

[8]MedBiquitous Medical Education Metrics Definitions http://medbiq.org/mems/definitions. Accessed January 2014.

Section 2: Funding Opportunity and Award Information

Anticipated Number of Awards	The number of submissions and their ability to address the full FDA Blueprint and assessment requirements will determine the number of grants awarded in 2014. Because of the need to engage large numbers of learners in "successfully completing" all components of the educational activities described in the MedBiquitous definition,[8] grant applicants are encouraged to incorporate effective co-sponsorships, partnerships, and/or collaborations among organizations that have already established ongoing relationships/regular communication with the primary audience for REMS CE. (See Section 4, #5).
Award Budget	***Budgets should be consistent with the realistic total number of ER/LA opioid prescribers that the Provider estimates will complete both education on the full FDA Blueprint and an assessment covering all six sections of the Blueprint.*** Preference will be given to cost-effective, collaborative, and innovative educational activities that minimize redundancies in development costs and leverage potential synergies. Providers may propose budget models with multiple levels of support, which would enable RPC to award funds for a subset of activities. **Note:** The RPC will ONLY support budget proposals in full compliance with Transparency Reports and Reporting of Physician Ownership Interests provisions of the Social Security Act (42 U.S.C. 1320a-7h) (Physician Payment "Sunshine Act" or "Open Payments"). • Providers will ensure that no grant funds from the RPC will be used for payments associated with the provision of food, beverages, travel, or lodging for meeting attendees.
Award Project Period	Because of the need to report ongoing progress to the FDA, the expectations are that: • The initial activity within the proposed program must begin within four months of signing the Letter of Agreement (LOA). • If an educational program contains multiple activities, all activities

	must start within twelve months of signing the LOA. • Any portion of a proposal with a start date more than twelve months beyond the execution of the initial LOA will require a separate grant application (although an activity that begins within twelve months of LOA execution may overlap two calendar years). **Note:** The RPC is open to receiving proposals to extend grant support for CE Providers who have already been awarded funding from the RPC. • Based on the number of applications received, it is the intent of the RPC to complete the review process and notify selected grantees approximately in the middle of the third quarter, 2014.
Other Award Information	To optimize the learning opportunities, the RPC intends to fund multiple grant applications from different Accredited Providers and educational partners with different, yet complementary, initiatives. Preference will be given to those grant requests that permit the RPC to support multiple high-quality, diverse programs that will enable achievement of the education participation goals and outcomes as described in the FDA-approved ER/LA Opioid REMS. Grant applications will be considered that demonstrate how the proposed education will fully meet or exceed the criteria for being REMS-compliant, are cost-effective for the scope of the proposal, and satisfy the RFA Criteria outlined in Section 4 (e.g., innovation, number of ER/LA opioid prescribers expected to complete all components of the REMS-compliant CE, etc.).

Section 3: Applicant Eligibility Criteria

- ❒ The Requestor must be an Accredited Provider who will serve as the Provider of Record for the proposed activities.

- ❒ The Requestor must be accredited to provide CE by a national accrediting body (e.g., ACCME, AAFP, AANP, AAPA, ACPE, ADA, ANCC, AOA, or equivalent accrediting body) or by an official state accrediting agency, and must demonstrate that their organization is in good standing at the time of submission.

- ❒ The Requestor must have demonstrated capabilities in the design and successful implementation of innovative, interactive, engaging, multimodal educational activities, and effective communication skills, as evidenced by solid partnerships and collaborations.

Section 4: RFA Submission Information

Grant proposals must include *all of the following components;* Providers should use the below numbered sections in their response submission, following the outline below.

	Application Component	Description
1	**Provider of Record**	Name of Accredited Provider and person(s) responsible for this project including contact information
2	**Partner Organizations**	Name of any partner organizations involved with the proposed education, along with roles/responsibilities, and contact information
3	**Overview of Proposed Educational Program**	A one (1) to two (2) page summary description of overall project goals, target audience, findings from needs assessment, proposed educational activities to fill gaps identified in the needs assessment, method for measuring outcomes, and amount of grant funds being sought
4	**Faculty Selection Criteria/Team Member Qualifications**	• Description of methods and criteria used to select faculty, and/or individuals involved in the development and implementation of proposed educational initiatives • Description and qualifications of the members of the team responsible for implementing the project
5	**Audience(s)**	The primary audience for REMS CE, as outlined by the FDA, are clinicians who are registered with the DEA, eligible to prescribe schedule 2 or 3 drugs, and have written at least one ER/LA opioid prescription in the past year. Other audiences, who care for patients who require these medications in order to manage their pain, may be encouraged to participate in the educational activities. Within this broadly defined target audience, specify clearly your *target audience(s)*. Why this particular audience? What expertise do you have both reaching this audience and motivating them to "successfully complete" all components of your educational program (including assessment of learning)?

	Application Component	Description
6	**Scope/Populations**	Specify the scope of your educational program: • National • Regional (Multi-City, Multi-State) • State • Health System or Integrated Health System • Hospital or Medical Center • Other Community Practice Collaboratives
7	**Needs Assessment**	Needs assessment should be concise, properly referenced and include one or more of the following: (a) Evidence of knowledge and/or practice gaps of your target audience in the geographic area where the proposed program will occur, and/or in general audience where proposed program will be implemented (i.e., primary care vs. specialist). (b) Results from any surveys or assessments you have executed that provide greater detail of the knowledge and/or practice gaps of your specific target audience beyond what you provided for (a). (c) Results from any surveys or assessments you have executed with your specific target audience, where the survey tool was *specifically based on the FDA Blueprint.*

	Application Component	Description
8	**Description of Educational Program & Design** **Note: See Section 5 for details on how proposals will be reviewed and evaluated**	Detailed description of proposed educational program and its activities, and how it will: • Align with all elements of the FDA Blueprint. • Meet all REMS-compliant CE requirements (See Overview Information). • Meet the goals and close the gaps in knowledge, competence, and/or performance for your target audience based on your needs assessment. • Be based on adult learning principles, utilize instructional design principles, and employ best educational and practices/methods, so as to optimize both knowledge acquisition and the transfer of that knowledge into clinical practice for the intended audience. • Reinforce the value of including a multidisciplinary team in patient care. • Include an attestation regarding full compliance with all applicable standards of your accrediting body, as well as other relevant standards, guidelines, and requirements as they apply to the conduct of independent medical education. (Include documentation that the Provider of Record is in good standing at the time of application.) • Include a statement that your organization will cooperate with the independent third parties (independent of RPC) conducting the FDA-required Long-Term REMS Evaluations of REMS-supported CE activities six to twelve months following activity completion.

	Application Component	Description
9	**Validation of Clinical Content**	Detailed description of process by which the following will be validated: • All elements of the FDA Blueprint are covered in the educational activity/materials to ensure completeness of content. • Content of the activity reflects the most current evidence-based information and that the content of the FDA Blueprint is represented accurately. Note: Due to internal FDA review timelines, it is possible that new ER/LA opioid information may be posted to the FDA website before being integrated into the Blueprint. Prior to finalizing activity content, it is the Provider's responsibility to check the FDA REMS website for any new information that may affect the content of the REMS CE. • Provider has ensured fair balance and controlled for bias. Note, all REMS-compliant activities are subject to independent audit by the Accrediting Bodies, and all audit-required materials must be submitted to the Accrediting Bodies in advance of the activity start date, as per the timelines/processes defined by the Accreditor. The proposed process should take these requirements into account.

	Application Component	Description
10	**Outcome Evaluation/Knowledge Assessment**	Provide detailed description of how you intend to measure successful educational outcomes associated with your educational program, including the *valid and reliable measures* you intend to employ in your evaluation activities/assessment of learning. Educational impact on healthcare professional's knowledge, competence, and performance may include attitudes, perceptions, and skills. In addition to educational programs covering all elements of the FDA Blueprint, as per the FDA REMS requirements, the program must: • Include an assessment that covers all *six sections of the FDA Blueprint.* Preferred consideration will be given to grant applications which integrate the assessment throughout the activity in order to increase the likelihood of learners completing the assessment, an FDA requirement for the learner to be counted toward the REMS goals. (*To be counted toward the FDA goals, ER/LA opioid prescriber-completers must have "successfully completed" all components of an education activity* and met the education provider's criteria for passing. See MedBiquitous "FDA ER/LA Opioid REMS defined: successfully_completing"). • Be subject to independent audit by the Accreditors to confirm that conditions of the REMS education have been met.
11	**Marketing Plan for the Proposed CE Program**	Detail your *marketing strategy* for how the target audience will be reached, motivated to participate in your program, and be engaged to complete all components of the education activity, including assessment of learning. Include steps you will take if it appears you may fall short of meeting the commitments to educate the estimated number of ER/LA opioid prescribers that you proposed in your grant application.
12	**Budget**	Detail budget using the template residing in the REMS Grant Management System portal.

	Application Component	Description
		FDA has required RPC-supported CE to be provided at no cost, or at a nominal cost to the participant (e.g., a small amount to cover costs such as parking). In keeping with the FDA's requirements, the RPC thus discourages charging a fee for RPC-supported CE. In the event the provider chooses to include a nominal registration fee, this fee should not exceed $25 per participant completing CE covering the full FDA Blueprint. RPC will cover the cost of REMS service fees the Accreditors may require for reimbursement of costs the Accreditor incurs in conjunction with FDA-mandated independent audits and data aggregation/reporting. There is a specific line on the budget template which indicates how to estimate REMS Service Fees for the activities you propose. Explanation of rationale, efficiencies, and cost-effective approaches to both the live and enduring components, including an estimated cost per ER/LA opioid prescriber "completer" for both components. *Note: Rationale should include an explanation of how the proposal's estimated number of ER/LA opioid prescriber/completers was calculated.* Statement that: 1. The program activities meet the accreditation/ certification requirements and standards of the ACCME, AOA, AMA, AAFP or ADA CERP; 2. No RPC member has selected or provided suggestions for any speaker involved in the program activities; and **3.** The grant monies provided are for the program activity as a whole and are not meant to be a direct payment to any speaker since ultimate disbursement of the grant monies is within the sole control of the Provider. **Proposed cost per ER/LA opioid prescriber completer as defined in Section 1 for entire project should be calculated and provided as part of the budget.**

	Application Component	Description
13	**Timeline of Project**	Detailed project timeline for each phase and milestone. This will serve as the basis for the milestone payments in the grant as described below: • Thirty (30) days after execution of LOA and submission of initial activity listing to RPC for FDA-required CE search page: 35% • Start of first activity and upon acceptance of update report: 25% • Mid-term of grant timeline and upon acceptance of update report (including progress against the grant metrics that the Provider submitted in the approved proposal): 30% • Completion of last activity and receipt/acceptance of required grant-related documentation (including final metrics for the education activity and budget reconciliation): 10%
14	**Optional Organizational Change Elements**	See below for details

Section 5: Grant Application Review Criteria

Grant applications will be thoroughly and critically reviewed by members of the RPC Grant Review Committee and the RPC Oversight Committee. Grants will be awarded based on Providers' ability to include elements in their proposals that clearly and sufficiently address the following criteria:

Criteria	Description
Compliance	Requestor (Provider of Record) meets eligibility criteria outlined in Section 3.
Alignment[7]	Includes all elements of the FDA Blueprint and presents a detailed mapping of how all elements will be covered in educational programs/materials. Also explicitly states that all six sections of the FDA Blueprint will be covered in the assessment.
Number of ER/LA opioid prescribers fully completing the REMS-compliant CE	Relative to the FDA goals and MedBiquitous definitions described in Section 1 of this document, realistic estimate of the number of ER/LA opioid prescribers expected to fully complete CE covering all elements of the FDA Blueprint and all components of educational activity and to have met the education provider's criteria for passing. Components of an educational activity include instruction, assessment of learning that covers all six sections of the FDA Blueprint, and potentially evaluation. As described in the Budget section of the RFA on page 16, your grant application should include an explanation of how the proposal's estimated number of ER/LA opioid prescriber/completers was calculated.
Qualifications of Provider and partners	Employs effective partnerships/coalitions across professional, governmental, and/or community organizations that can achieve broad reach, engagement, and impact. Consider the inclusion of community health programs and/or patient-focused organizations.
Needs assessment [9,10,11]	Specific to the audience, ensuring the content of the educational material is relevant and adapted to the needs and clinical practice

[9] Bordage, G., B. Carlin, and P. E. Mazmanian. "Continuing Medical Education Effect on Physician Knowledge Effectiveness of Continuing Medical Education: American College of Chest Physicians Evidence-Based Educational Guidelines." CHEST Journal 135, no. 3_suppl (2009): 29S–36S.
[10] Greiner, A., and Elisa Knebel. Health Professions Education: a Bridge to Quality. National Academy Press, 2003.
[11] Moore, D. E., J. S. Green, and H. A. Gallis. "Achieving Desired Results and Improved Outcomes: Integrating Planning and Assessment Throughout Learning Activities." Journal of Continuing Education in the Health Professions 29, no. 1 (2009): 1–15.

	circumstances of the learners.
Educational design/methods[8,10,12,13,14,15,16]	• *Multi-method, multi-media:* Content is delivered using evidence-based methods and multiple *formats*—including, but not limited to, audio, visual, case discussions, role plays and other features of active learning and problem-based learning approaches—to guide learners in reflection and application of new knowledge to their practice settings. • Activities are innovative/creative in nature, motivating learners to participate and complete all activities. *Multi-exposure (education sessions):* For multi-exposure formats, content is delivered in digestible chunks or modules, over time, in ways that optimize learning.
Knowledge transfer[17]	• Principles from the field of implementation science are incorporated into overall learning program to address barriers to the application of the knowledge conveyed in the program. • *Application of CE-compliant outcomes measures of knowledge, competence, performance, etc.*
Interprofessional education[14,18]	• Facilitates interprofessional education and educational activities, particularly for healthcare providers practicing in settings in which care is delivered by multidisciplinary teams.
Valid and reliable outcome measures[14,19,20,21]	Educators should provide evidence for the validity and reliability of CE evaluation and outcome assessment methods. Preference will be given to proposals that integrate assessments throughout the

[12] Bloom, B. S. "Effects of Continuing Medical Education on Improving Physician Clinical Care and Patient Health: a Review of Systematic Reviews." International Journal of Technology Assessment in Health Care 21, no. 3 (2005): 380–385.
[13] Chiauzzi, E., K. J. Trudeau, K. Zacharoff, and K. Bond. "Identifying Primary Care Skills and Competencies in Opioid Risk Management." Journal of Continuing Education in the Health Professions 31, no. 4 (2011): 231–240.
[14] Van Hoof, T. J., and T. P. Meehan. "Integrating Essential Components of Quality Improvement into a New Paradigm for Continuing Education." Journal of Continuing Education in the Health Professions 31, no. 3 (2011): 207–214.
[15] Institute of Medicine. Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. National Academy Press, 2011.
[16] Mansouri, M., and J. Lockyer. "A Meta-analysis of Continuing Medical Education Effectiveness." Journal of Continuing Education in the Health Professions 27, no. 1 (2007): 6–15.
[17] Ratanawongsa, N., P. A. Thomas, S. S. Marinopoulos, T. Dorman, L. M. Wilson, B. H. Ashar, J. L. Magaziner, R. G. Miller, G. P. Prokopowicz, and R. Qayyum. "The Reported Validity and Reliability of Methods for Evaluating Continuing Medical Education: a Systematic Review." Academic Medicine 83, no. 3 (2008): 274–283.
[18] Sargeant, J., F. Borduas, A. Sales, D. Klein, B. Lynn, and H. Stenerson. "CPD and KT: Models Used and Opportunities for Synergy." Journal of Continuing Education in the Health Professions 31, no. 3 (2011): 167–173.
[19] Marinopoulos SS, Dorman T, Ratanawongsa N, Wilson LM, Ashar BH, Magaziner JL, MillerRG, Thomas PA, Prokopowicz GP, Qayyum R, Bass EB**.** Effectiveness of Continuing MedicalEducation. Evidence Report/Technology Assessment No. 149 (Prepared by the Johns

	educational activity (versus waiting until the end of the entire activity), to optimize ER/LA opioid prescriber-completion, since completing the assessment is part of "prescribers successfully completing" the activity, as per the MedBiquitous definitions (see Appendix A).
Budget	Reasonable cost per learner given the proposed educational program (see Section 2)
Marketing plan for CE program	Detailed marketing strategy outlined for how target audience will be reached, motivated to participate in the educational activity, engaged to complete all components of the educational activity, and to meet the education provider's criteria for passing. Components of an educational activity include instruction, assessment of learning that covers all six sections of the FDA Blueprint, and potentially evaluation.

HopkinsEvidence-based Practice Center, under Contract No. 290-02-0018.) AHRQ Publication No.07-E006. Rockville, MD: Agency for Healthcare Research and Quality. January 2007.

[20] Price, D. W., E. K. Miller, A. K. Rahm, N. E. Brace, and R. S. Larson. "Assessment of Barriers to Changing Practice as CME Outcomes." Journal of Continuing Education in the Health Professions 30, no. 4 (2010): 237–245.

[21] Brownson, R. C., G. A. Colditz, and E. K. Proctore (eds). Dissemination and Implementation Research in Health: Translating Science to Practice. New York: Oxford University Press, 2012.

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1. Drug Abuse Warning Network 2011 http://www.samhsa.gov/data/2k13/DAWN2k11ED/DAWN2k11ED.htm#5. Accessed January 2014
2. Substance Abuse and Mental Health Services Administration. 2012. *Results from the 2012 National Survey on Drug Use and Health: Detailed Table*, Table 1.54A.a. Rockville, MD. http://www.samhsa.gov/data/NSDUH/2012SummNatFindDetTables/NationalFindings/NSDUHresults2012.htm. Accessed January 2014
3. Warner M, Chen LH, Makuc DM, Anderson RN, and Miniño AM. 2011. Drug Poisoning Deaths in the United States, 1980–2008, in U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics, *NCHS Data Brief*, *No 81*. December 2011. Hyattsville, MD. http://www.cdc.gov/nchs/data/databriefs/db81.pdf. Accessed on March 30, 2012.
4. Birnbaum, Howard G., Alan G. White, Matt Schiller, Tracy Waldman, Jody M. Cleveland, and Carl L. Roland. "Societal Costs of Prescription Opioid Abuse, Dependence, and Misuse in the United States." *Pain Medicine* 12, no. 4 (2011): 657–667.
5. Adapted from the FDA-Approved ER/LA Opioid Analgesics REMS document (October 2012 version).
6. There are 19 RPC member companies as of December 2013.
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Appendix A: Medical Education Metrics Definitions

Medical Education Metrics (MEMS 2.0) provides a standard XML format for CE outcomes data, including data related to FDA ER/LA Opioid Risk Evaluation and Mitigation Strategy (ER/LA Opioid REMS) education. One key component of evaluating the reach of ER/LA opioid REMS is evaluating the number of learners by category. One particular important category is the number of prescribers successfully completing REMS-compliant education.

MEMS 2.0 uses the following definitions:

FDA ER/LA Opioid REMS defined: ER/LA_opioid_prescriber: An individual clinician who is registered with the DEA to prescribe schedule 2 and/or 3 controlled substances and has written at least one ER/LA opioid script in the past year.

FDA ER/LA Opioid REMS defined: successfully_completing: Completing all components of an educational activity and meeting the education provider's criteria for passing. Components of an educational activity include instruction, assessment of learning, and potentially evaluation.

FDA ER/LA Opioid REMS defined: prescribers_successfully_completing: FDA REMS defined ER/LA opioid prescribers that have completed all components of an educational activity and met the education provider's criteria for passing. Components of an educational activity include instruction, assessment of learning, and potentially evaluation.

practice_type: A description of the clinician's practice by broad category (e.g. primary care). For a vocabulary of practice types related to the evaluation of pain management, see the Medical Education Metrics Vocabularies (http://medbiq.org/mems/vocabularies#practice_type).

schedule_2_or_3_registered_clinician: An individual clinician who is registered with the DEA to prescribe schedule 2 and/or 3 controlled substances.

schedule_2_or_3_registered_clinicians_successfully_completing: Schedule 2 or 3 registered clinicians that have completed all components of an educational activity and met the education provider's criteria for passing. Components of an educational activity include instruction, assessment of learning, and potentially evaluation.

Appendix B: Overdose Deaths Related to ER/LA Opioid Analgesics and Understanding the Audience of ER/LA Opioid Prescribers

The contents of this Appendix is intended to provide background information on two topics of particular relevance to the REMS:

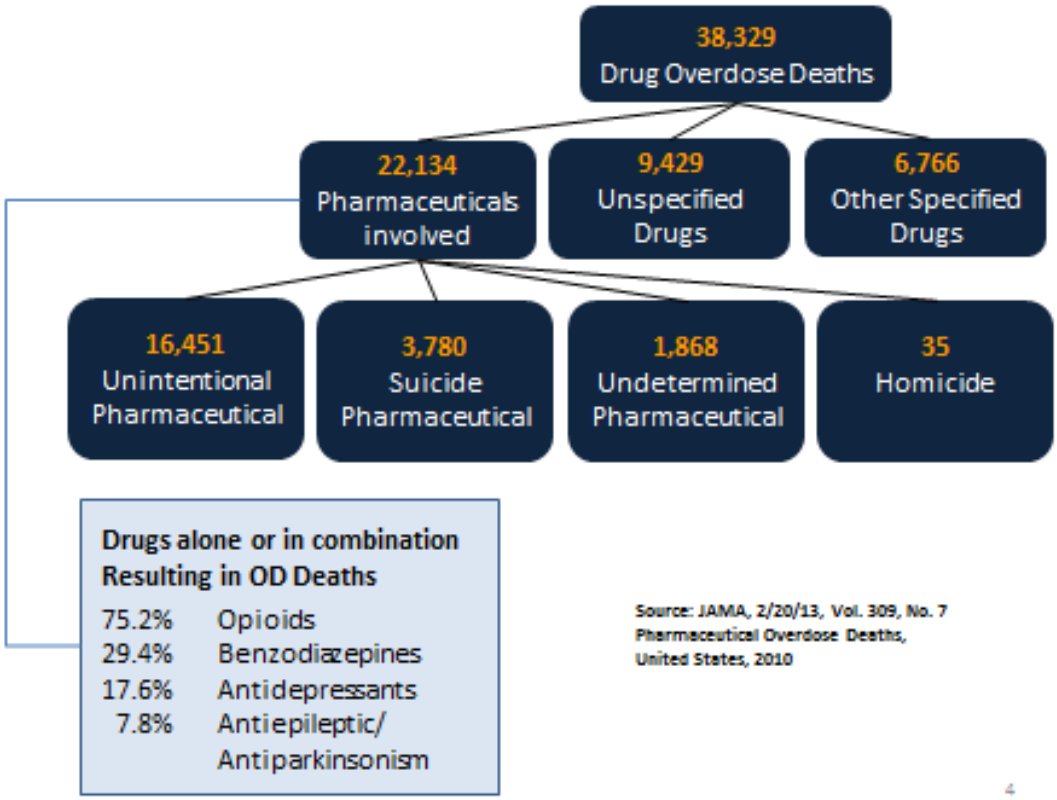
- Overdose deaths related to ER/LA opioid analgesics
- Demographic information on ER/LA opioid prescribers

What do we know about ER/LA opioid analgesics (opioid pain relievers (OPRs)) overdose deaths?

FDA REMS-compliant prescriber CE training, based on the FDA Blueprint, is largely motivated by the precipitous rise in prescription opioid medication abuse and overdose death during the past decade.

Figure 1 illustrates the total number of OPR deaths as a percentage of all drug overdose deaths in which pharmaceuticals were involved.

Figure 1. Breakdown of overdose deaths by type of drug, 2010 data from the National Vital Statistics System



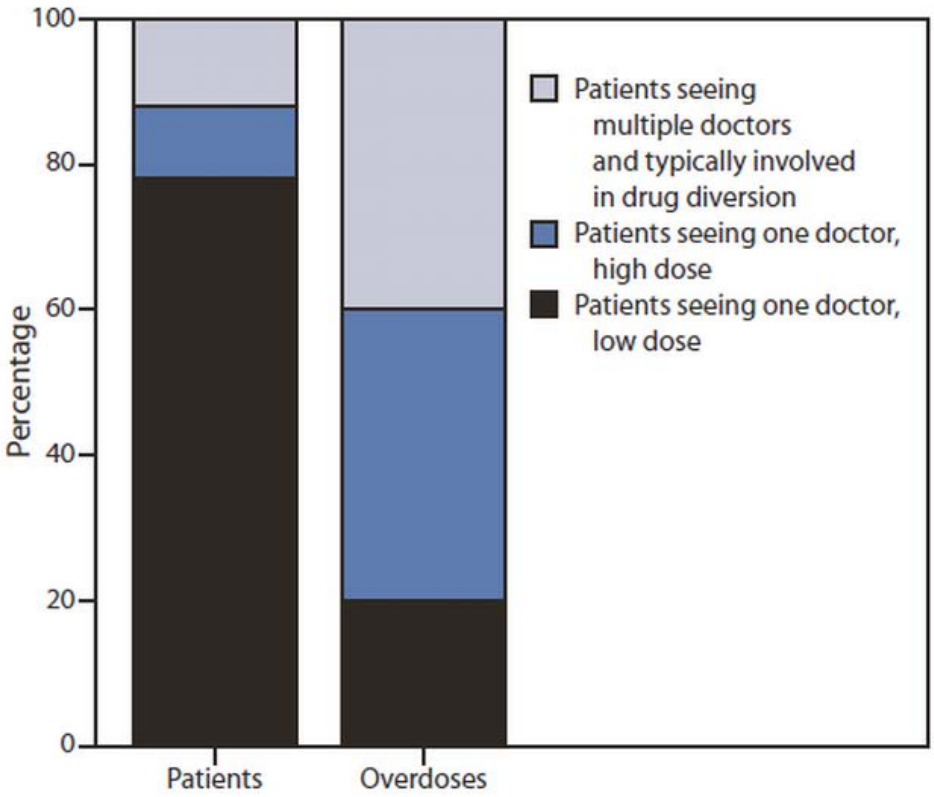
Key Findings on OPR overdose death:

- *Multiple prescription drugs* often play a role in OPR overdose death, the most common being benzodiazepines, antidepressants, antiepileptic and antiparkinsonism drugs, and antipsychotics and neuroleptics.
- Methadone accounts for only 2% of OPR prescriptions in the US but is involved in *more than 30% of overdose deaths* (*July 2012: Prescription Painkiller Overdoses: Use and Abuse of Methadone as a Painkiller).*
- Both immediate and extended-release formulations contribute to overdose death.

Populations most at risk for OPR overdose death:

- People who obtain multiple OPR prescriptions from multiple providers (e.g., doctor shoppers)
- People who take high daily dosages of OPR and those who misuse multiple abuse-prone prescription drugs
- About 60% of OPR overdose deaths are male, while 40% are female. But, OPR deaths increased fivefold between 1999 and 2010 for women, while the increase among men was 3.6 times.
- Low-income people and those living in rural areas: People on Medicaid are prescribed OPR at twice the rate of non-Medicaid patients and are at six times the risk of OPR overdose.
- People with mental illness and those with a history of substance abuse

Figure 2. Percentage of patients and prescription drug overdoses, by risk group—US



Hall et al. paper, JAMA 2008

This study by Hall et al. (JAMA 2008) was among the most rigorous attempts to understand OPR overdose death. The study investigated 295 decedents in West Virginia in 2006 since this state experienced the nation's largest increase in drug overdose death rates during 1999-2004. The drug overdose death rate in 2006 was 16.2.

Results:

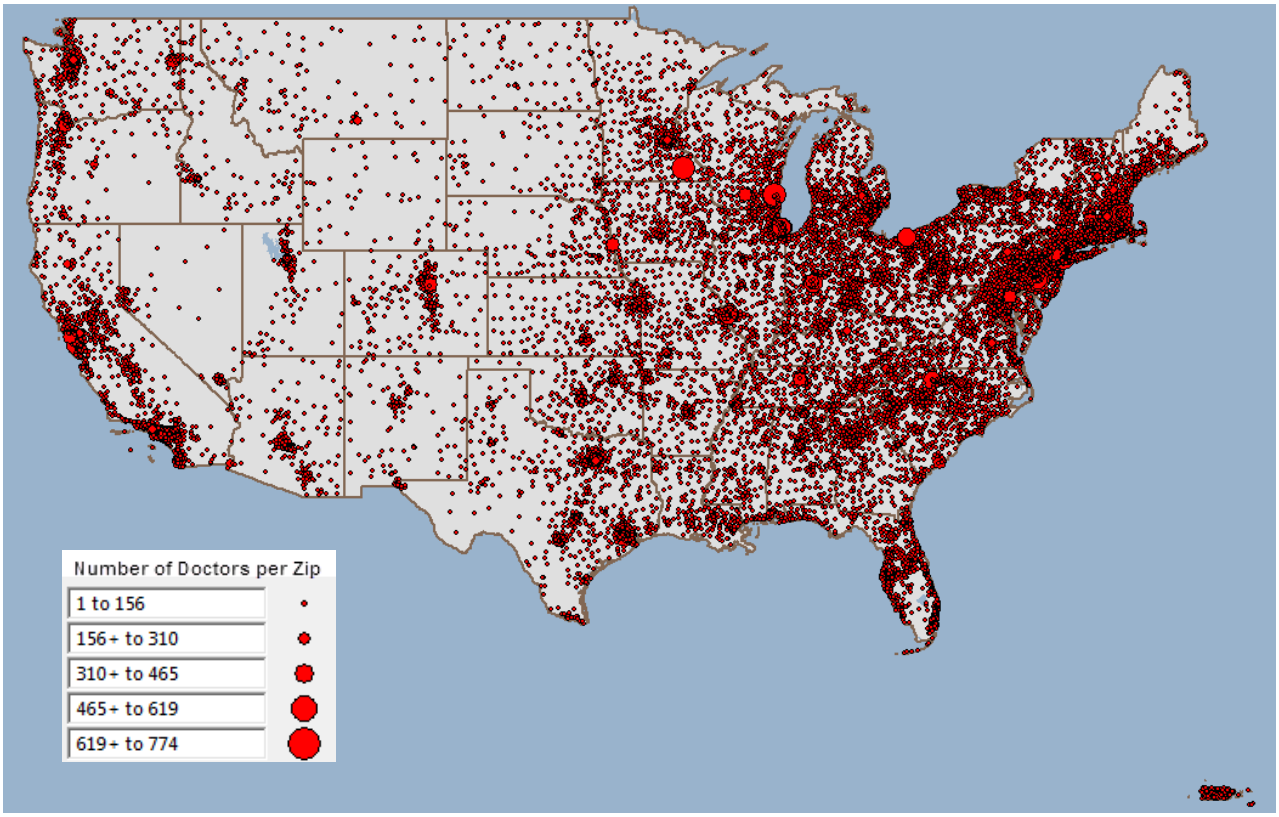
- Opioid analgesics were taken by 93.2% of the decedents, of whom only 44% had ever been prescribed these drugs.
- 67.1% were male.
- 91.9% were aged 18-54.
- Pharmaceutical diversion occurred in 63.1% of deaths, and 21.4% were accompanied by doctor shopping.
- Diversion was highest among 18- to 24-year-olds and decreased across successive age groups.
- Having a controlled prescription from five or more doctors in the year prior to death was more common among women (30.9%) and decedents aged 35-44 (30.7%) compared with men (16.7%) and other age groups (18.2%).

- Methadone was responsible for more single-drug deaths and was involved in far more deaths than any other drug (40% vs. #2 hydrocodone 22.7%).
- 94.6% of decedents had indicators of substance abuse, including nonmedical routes of exposure and illicit contributory drugs particularly prevalent among drug diverters.
- Multiple contributory substances were involved in 79.3% of deaths.

What do we know about the target audience of ER/LA opioid prescribers?

Based on an analysis of prescribers who wrote *at least one* ER/LA opioid prescription in the 12 months ending March 2013, the total target audience is about 334,000.

Figure 3. Prescribers who wrote at least one ER/LA opioid prescription in the 12 months ending March 2013 by ZIP code

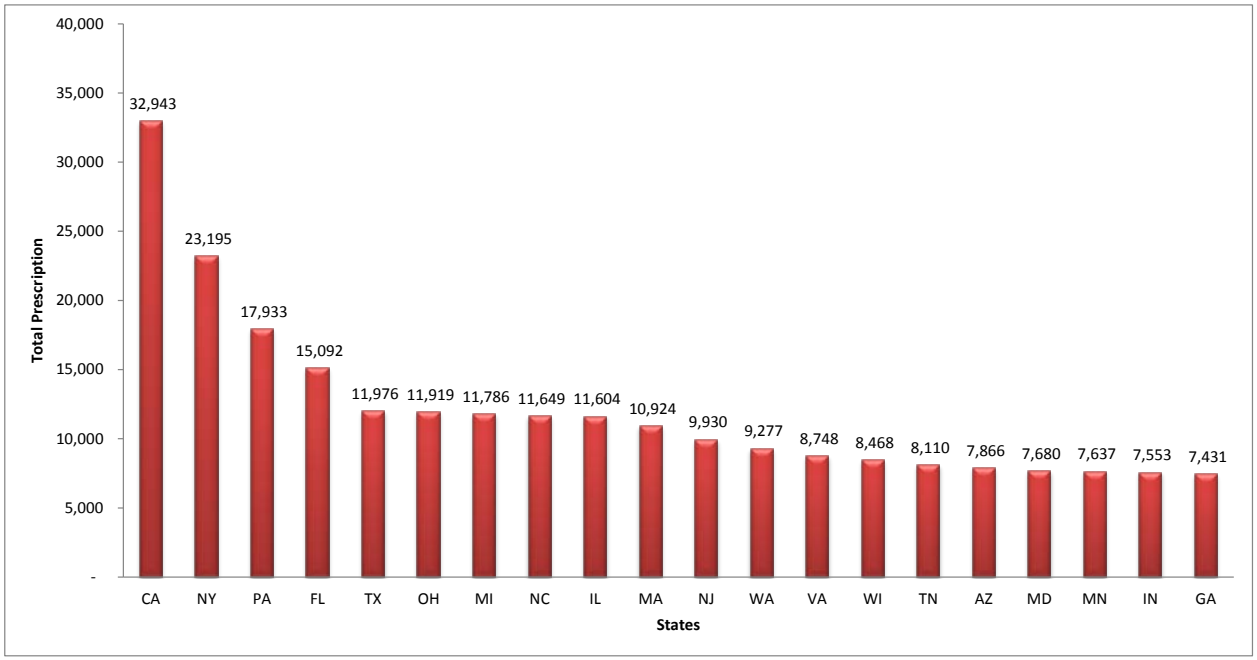


The map in Figure 3 indicates that prescribers of ER/LA opioid products are distributed throughout the US, with great concentrations occurring in large urban city areas as expected.

Source: IMS HEALTH Confidential and Proprietary; IMS Health Incorporated, IMS Xponent Plantrak

As shown in Figure 4, a follow-up analysis of the top twenty states based on highest number of ER/LA opioid prescribers was done.

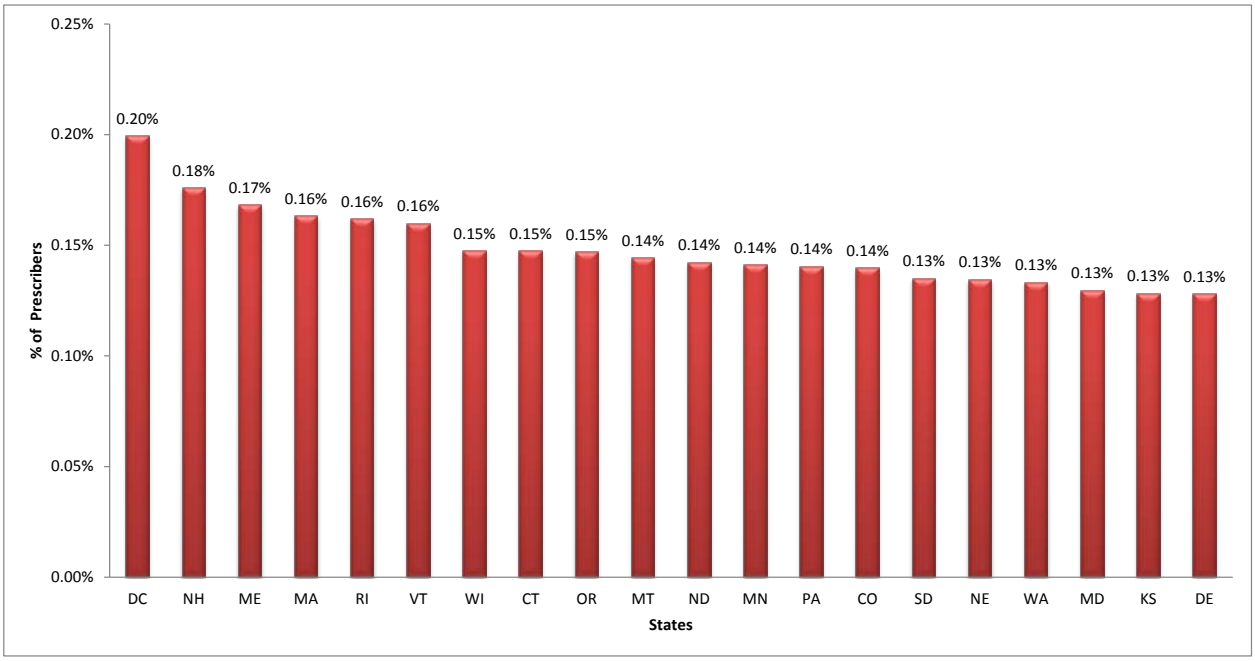
Figure 4. ER/LA Opioid Prescribers by State—Top Twenty States



Source: IMS HEALTH Confidential and Proprietary; IMS Health Incorporated, IMS Xponent Plantrak

As an alternative analysis, the following graph in Figure 5 divides total prescribers in a given state by the 2013 population census for that state.

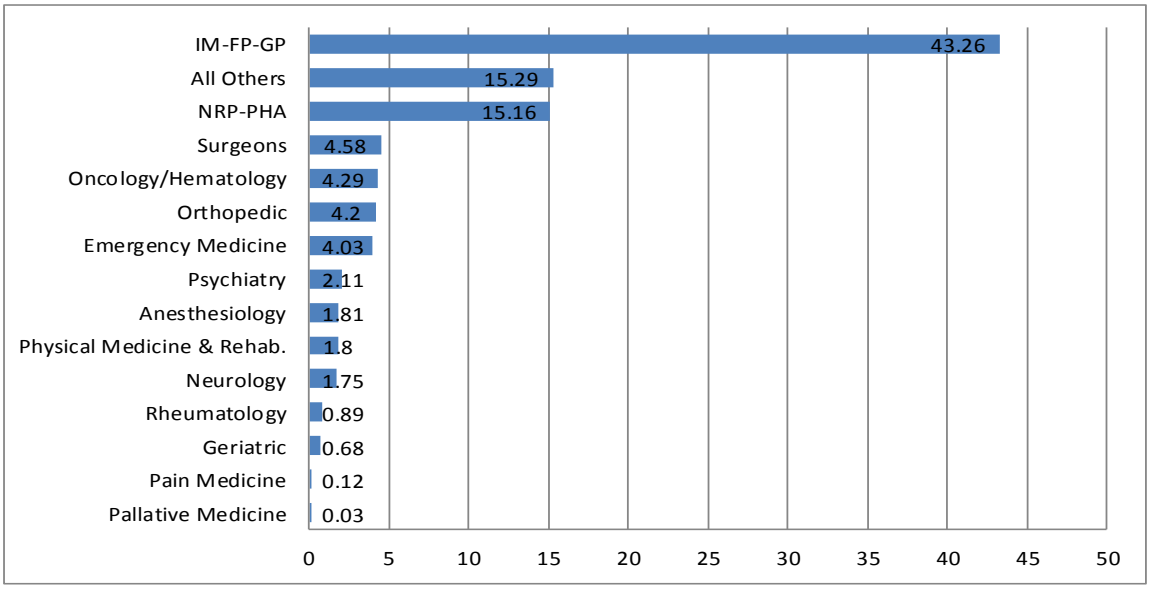
Figure 5. ER/LA Opioid Prescribers by State divided by 2013 population census



Further analysis of ER/LA opioid prescribers by *specialty group*, revealed:

- *43%* of the total ER/LA opioid prescriber target audience are internal medicine, family practice, and general practitioners, and that this group significantly dwarfs all other specialty groups.
- The second largest group, *all others*, represents approximately 130 specialties that represent very small specialty prescriber groups not shown in the graph (e.g., sleep medicine, pediatric, urology, dermatology).
- The third-largest specialty group, *nurse practitioners and physician assistants*, represents 15% of the total audience of prescribers.

Figure 6. Percentage of total ER/LA opioid prescribers by specialty group



Source: IMS HEALTH Confidential and Proprietary; IMS Health Incorporated, IMS Xponent Plantrak

Note: IM=Internal Medicine, FP=Family Practice, GP=General Practitioner, NRP=Nurse Practitioners, and PHA=Physician Assistants