Title:	Extended-Release (ER) and Long-Acting (LA) Opioid Analgesics Risk Evaluation and Mitigation Strategy (REMS) Program Six-Month Assessment Report
Document Number:	Version 1.0
Product Name:	All Extended-release (ER) and Long-acting (LA) Opioid Analgesic Products
Sponsors:	REMS Programs Companies (RPC)
Date:	21DEC2012

Mark A. Collins, PhD
Director, Pharmacovigilance and Risk Management
ENDO

02 Jan 2013

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ACCME	Accreditation Council for Continuing Medical Education
AE	Adverse Event
AMA	American Medical Association
BAC	Business Activity Codes
BPS	Baseline Prescriber Survey
CME/CE	Continuing Medical Education/Continuing Education
CMSS	Council of Medical Specialty Societies
DDRP	Dear DEA-Registered Prescriber
DEA	Drug Enforcement Administration
ER	Extended-Release
ET	Eastern Time
ETASU	Elements to Assure Safe Use
FAQs	Frequently-Asked Questions
FDA	Food and Drug Administration
FSMB	Federation of State Medical Boards
GMS	Grant Management System
GRC	Grant Review Committee
HCP	Healthcare Professional
LA	Long-Acting
PARS	Program and Activity Reporting System (ACCME's)
PCD	Patient Counseling Document
POLB	Professional Organization/Licensing Board
REMS	Risk Evaluation and Mitigation Strategy
RFA	Request for Application
RPC	REMS Program Companies
US	United States
USPS	United States Postal Service

1. BACKGROUND

In April 2011, in accordance with section 505-1 of the Federal Food Drug and Cosmetic Act, the Food and Drug Administration (FDA) determined that a Risk Evaluation and Mitigation Strategy (REMS) was necessary for all extended-release and long-acting (ER/LA) opioid analgesic drug products to ensure that their benefits outweighed their risks, especially with regard to specific adverse outcomes. The goal of the ER/LA Opioid Analgesics 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 particular interest include addiction, unintentional overdose, and death. In the interest of public health and to minimize the burden on the healthcare delivery system of having multiple unique REMS programs, the FDA determined that a single shared system should be used to implement this REMS.

The sponsors of branded and generic drug products meeting the following requirements are obligated to participate in the ER/LA Opioid Analgesics REMS: extended-release, oral-dosage formulations containing hydromorphone, morphine, oxycodone, oxymorphone, and tapentadol; transdermal delivery systems containing fentanyl or buprenorphine; and methadone formulations that are indicated for use as analgesics.

Pharmaceutical companies subject to this REMS (the REMS Program Companies, or RPC) joined together to implement a REMS for all ER/LA opioid analgesic drug products. The RPC was actively involved in providing input to FDA as it developed the shared ER/LA Opioid Analgesics REMS. The ER/LA Opioid Analgesics REMS provides a structure for all of the companies of the RPC to efficiently implement risk evaluation and mitigation activities across all ER/LA opioid analgesics in a uniform manner. The REMS was approved by FDA on July 9, 2012 (http://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm163647.htm).

The elements of the REMS include Medication Guides, Elements to Assure Safe Use (ETASU) and a Timetable for Submission of Assessments. Under the REMS, the NDA/ANDA holders must do the following:

- Ensure that training is available to prescribers who prescribe the ER/LA opioid analgesics
- Provide to prescribers information that the prescriber can use to educate patients about the risks of ER/LA opioid analgesics, and their safe use, storage and disposal
- Inform prescribers of the existence of the ER/LA Opioid Analgesics REMS and the need to successfully complete the necessary training.

Training will be considered “REMS-compliant training” under this REMS if: 1) it, for training provided by Continuing Education (CE) providers, is offered by an accredited provider to licensed prescribers, 2) it includes all elements of the FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics (“FDA Blueprint”), 3) it includes a post-course knowledge assessment of all of the sections of the FDA Blueprint, and 4) it is subject to independent audit to confirm that conditions of the REMS training have been met.

As part of the REMS, performance goals were established for availability of the REMS-compliant training. These goals are:

- Not later than March 1, 2013, the first REMS-compliant training will be made available
- Within two years from the time the first REMS-compliant training becomes available, 80,000 prescribers (based on 25% of the 320,000 active prescribers in 2011) will have been trained
- Within three years from the time the first REMS-compliant training becomes available, 160,000 prescribers (based on 50% of the 320,000 active prescribers in 2011) will have been trained
- Within four years from the time the first REMS-compliant training becomes available, 192,000 prescribers (based on 60% of the 320,000 active prescribers in 2011) will have been trained.

The REMS includes a plan to inform prescribers and potential prescribers identified via the Drug Enforcement Administration (DEA) registration database about the REMS and the need to complete the necessary training. The primary communication methods to disseminate this information include Dear DEA Registered Prescriber (DDRP) Letters and Letters to Professional Organizations and Licensing Boards (POLB). Performance goals established for these communications are:

- DDRP Letter 1 will be sent not later than 60 days after the initial approval of this REMS
- DDRP Letter 2 will be sent not later than 30 days before the first prescriber REMS-compliant training required by the REMS is offered by providers
- At least annually from the date of initial approval of the REMS, the DEA Registration Database will be reviewed and Prescriber Letter 3 will be sent to all newly DEA-registered prescribers who are registered to prescribe Schedule II and III drugs
- POLB Letter 1 will be sent not later than 60 days after REMS approval
- POLB Letter 2 will be sent not later than 30 days before the first prescriber REMS-compliant training is available

Educational materials must be developed for prescribers to use in educating their patients. The REMS includes a Patient Counseling Document on Extended-Release and Long-Acting Opioid Analgesics (PCD), and Medication Guides. These materials must be accessible to prescribers; the RPC has developed an ER/LA Opioid Analgesics REMS website and has established a Call Center to provide easy access. Performance goals regarding information availability include:

- An interim single toll-free number Call Center must be implemented no later than July 23, 2012, and a fully operational centralized Call Center must be implemented no later than 90 calendar days after the approval of the REMS (October 21, 2012).

A critical aspect of the REMS is assessment of the effectiveness of the program in meeting its goals. The FDA has indicated eight key areas for assessment as well as evaluation of the functional components of the REMS implementation. These elements are shown in Table 1 below.

Table 1: FDA-Required REMS Assessments

FDA Requirements
Evaluation of Functional Components **Dates when the following were initiated:** REMS Website Prescriber Letter 1 Professional Organizations and Licensing Boards Letter 1 Call Center
Assessment 1: Assessment of how many prescribers of ER/LA opioids have successfully completed the training. Specify performance goals for number of prescribers trained by time.
Assessment 2: Independent audit of the quality of the content of the educational materials used by the CE providers to provide the education. The audit should evaluate the quality of the content against the content approved by the FDA as part of the REMS, as well as against the ACCME's and other accrediting bodies' standards for Commercial Support.
Assessment 3a: Prescriber survey. Evaluation of healthcare providers' (HCPs) awareness and understanding of the serious risks associated with these products (eg, through surveys of HCPs) and specification of measures that would be taken to increase awareness if surveys of HCPs indicate that HCP awareness is not adequate
Assessment 3b: Long-term Evaluation grants
Assessment 4: Patient survey
Assessment 5: Surveillance for misuse, abuse, overdose, addiction, death and any intervention to be taken resulting from signals of these metrics, including information for different risk groups (eg, teens, chronic abusers) and different settings (eg, emergency rooms, addiction treatment centers, poison control Call Centers). As much as possible, the information should be drug-specific.
Assessment 6: Evaluation of drug utilization patterns (IMS data)
Assessment 7: Evaluation of changes in prescribing behavior
Assessment 8: Evaluation of changes in access to ER/LA opioid analgesics

REMS assessments will be submitted to the FDA at six months and twelve months after REMS approval and annually thereafter. To facilitate inclusion of as much information as possible, while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment will conclude no earlier than 60 days before the submission date for that assessment.

This report is the first assessment of the ER/LA Opioid Analgesics REMS, covering the time period from REMS approval to 60 days prior to submission of the report to the FDA, from July 9, 2012 through November 9, 2012. The report will be submitted in order to be received by the FDA on or before the due date six months after REMS approval, January 9, 2013. This report includes an evaluation of the REMS Functional Components cited in Table 1 above and describes the progress that has been made toward addressing the eight key assessments. These eight assessments will be included in subsequent reports as the REMS Program is fully developed and implemented. The time frame for addressing the eight key assessments and the types of evaluation metrics to be used are shown in Table 2 below.

Table 2: Individual Assessments Required for Assessment Reports and 'Umbrella Metrics' Vendor Activities[1]

Individual Assessments	Key Activities[2]				
	Assessment Report #1 (6 months)	**Assessment Report #2 (12 Months)**	**Assessment Report #3 (Year 2)**	**Assessment Report #4 (Year 3)**	**FDA Subsequent Reports**
Functional Components Assessment	Dates, call centers FAQs	Dates, call centers FAQs	-	-	-
Assessment 1 Prescribers successfully completing training	Grant reports	# of Prescribers trained; estimate of future trained	Target 80,000 Prescribers	Target 160,000 Prescribers	Target 192,000 Prescribers – YR 4
Assessment 2 Independent audit of CE activities	-	-	√	√	√
Assessment 3a[1] Evaluation of prescriber understanding (ie, Prescriber Survey)	Qualitative Research and Baseline Survey	-	-	√	Per FDA Request
Assessment 3b: Long-term Evaluation grants Grants to CE orgs. to assess prescribers' knowledge/practice changes 6-12 mo after REMS-compliant training	# of proposals and grants, list of grantees, date of training and evaluation	# of proposals and grants, list of grantees, date of training and evaluation	# of proposals and grants, list of grantees, date of training and evaluation	# of proposals and grants, list of grantees, date of training and evaluation	Per FDA Request
Assessment 4 Evaluation of patient understanding (ie, Patient Survey)	-	-	√	√	Per FDA Request
Assessment 5 Surveillance monitoring for misuse, abuse, overdose, addiction, death and intervention taken	-	-	√	√	√
Assessment 6 Evaluation of drug utilization patterns (IMS data, claims data)	-	-	√	√	√
Assessment 7 Evaluation of changes in prescribing behavior	-	-	√	√	√
Assessment 8 Changes in Access to ER/LA opioid analgesics	-	-	√	√	√

[1]Assessment 3a was not a requirement for inclusion in the Six-Month FDA Assessment Report

[1] Checkmark indicates that reporting on this Individual Assessment is required for this Assessment Report.

[2] To facilitate inclusion of as much information as possible, while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment will conclude no earlier than 60 days before the submission date for that assessment.

2. REMS ASSESSMENT RESULTS

2.1 Assessment 1 – Prescribers Successfully Completing Training

2.1.1 Requirements

Healthcare professionals who prescribe ER/LA opioid analgesics are in a key position to balance the benefits of prescribing ER/LA opioid analgesics to treat pain against the risks of serious adverse outcomes including addiction, unintentional overdose, and death. As such, a main feature of the REMS is to educate HCPs on the risks of ER/LA opioid analgesics. One method of delivering these educational messages to prescribers is through one or more REMS-compliant Continuing Education (CE) programs. In accordance with the REMS, the RPC must ensure that REMS-compliant training is made available to prescribers of ER/LA opioid products.

As described in section VII.D.1 of the REMS Supporting Document, the Six-Month FDA Assessment Report will contain information related to the accredited continuing education that constitutes RPC-supported REMS-compliant training. The following section summarizes the outcome of the RPC's efforts during this initial reporting period to support accredited continuing education and thus make REMS-compliant training available to prescribers.

2.1.2 Support of Continuing Education Activities through Grants

In order to include CE activities as part of the REMS, the RPC prepared and disseminated two Requests for Grant Applications (RFA), informing organizations of the availability of grant funds to support accredited independent continuing education. The goal of each RFA was to support high quality education using evidence-based methods intended to assist in ensuring 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).

This report includes an update on the status of the grant submissions in response to the RFAs for REMS-compliant training, including: 1) the two posted RFAs (Appendix E); 2) the number of proposals submitted in response to each RFA; 3) the number of grants awarded; 4) a list of the grantees; 5) the date when each grantee will make their REMS-compliant training available; 6) a high-level description of each awarded program (eg, web-based, live), and 7) an estimate of how many prescribers will be trained under each program.

The first RFA (RFA010812) for educational grant support of the REMS-compliant training activities had an accelerated timeframe and was posted to the ER/LA Opioid Analgesic REMS website (www.ER-LA-opioidREMS.com) on August 22, 2012, six weeks after REMS approval. The accelerated timeframe was implemented to meet the requirement of REMS-compliant CE training being available by March 1, 2013. Grant applications in response to this RFA were due on September 24, 2012.

A second RFA (RFA020912) was issued on September 10, 2012, with applications due on November 5, 2012. The purpose of this RFA was to encourage submission of additional grant applications, according to a more standard timeline, thereby allowing sufficient time for those providers who may have required additional planning time. As a result of Hurricane Sandy's effects on East Coast-based providers, the RPC decided to extend the deadline for the second

RFA from November 5, 2012 to November 12, 2012. Results of the second RFA process will be included in the One-Year FDA Assessment Report, since the deadline occurred after Report #1 data lock.

The RFAs were disseminated via posting on the RPC website and Grant Management System (GMS). RPC raised awareness about the RFAs through mass e-mail dissemination to accreditors, organizations representing accredited providers, CE providers, and other outcomes-focused CE stakeholders.

The RFAs indicated that the proposals must:

- Address all elements of the approved FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics;
- Include a post-course knowledge assessment of all sections of the FDA Blueprint;
- Be subject to independent audit to confirm that the conditions of the REMS training have been met;
- Employ MedBiquitous ER/LA REMS standards to provide a uniform data set to FDA (ER/LA REMS standards are currently in development with MedBiquitous);
- Include additional details on evidence-based adult learning principles/preferences; and,
- Adhere to standards for program planning and commercial support promulgated by the Accreditation Council for Continuing Medical Education (ACCME), or of another CE accrediting body appropriate to the prescribers' medical specialty or healthcare profession.

The full text of RFA010812 and RFA020912 can be found in Appendix E.

All grant applications submitted in response to the two RFAs were reviewed by the RPC Grant Review Committee (GRC) against established objective criteria. There are twelve standard categories of criteria employed to review grant requests, described in Appendix F.

Those grant applications recommended by the GRC to the RPC Oversight Committee:

- Met the twelve established objective criteria;
- Presented an anticipated likelihood of reaching and engaging the greatest number of HCPs to participate in/complete the REMS compliant training; and,
- Presented the greatest potential for achieving the REMS goals, and improving the knowledge, competence and performance of prescribers who completed the activities.

Table 3 provides the information for RFAs issued by the RPC:

- new grant requests for applications issued
- the number of proposals submitted in response to each request, and the subsequent disposition of these requests
- the number of grants awarded at the time of Report #1 data lock

Thirty-six (36) submissions were received in response to the first RFA for CE grants (RFA010812). The applications were reviewed utilizing the Grant Request Review Criteria (Appendix F). One grant has been awarded to date (Table 4 below).

The second RFA (RFA020912) was issued approximately two weeks later, and 45 applications were received. These applications are currently undergoing evaluation using the same objective criteria mentioned above. Since the submission deadline for this second RFA occurred shortly before the data lock for Report #1, grants awarded under the second RFA will be described in the One-Year FDA Assessment Report.

Table 3: Requests for Grant Applications (RFAs)

RFA Data Detail	RFA010812	RFA020912
RFA Publication Date	August 22, 2012	September 10, 2012
Grant Requests Due Date	September 24, 2012	November 12, 2012
Total Number of Grant Requests Submitted	36	45
Number of Grants Declined for Non-Compliance[1]	8	Final evaluation ongoing at time of Report #1 data lock
Number of Grants Declined for Other Reasons[2]	23	Final evaluation ongoing at time of Report #1 data lock
Number of Grants Moved to Standard RFA020912	4	N/A[3]
Number of Grants Awarded at the time of Report #1 Data Lock	1[4]	TBD[5,6]

[1]Non-compliant grants were those that did not cover the entire FDA Blueprint, did not demonstrate that the activity would include assessment of all sections of the FDA Blueprint, or were not an eligible provider (see Criteria 1-3 in Appendix F).

[2]Other reasons include: low-likelihood of achieving REMS performance goals; low likelihood of achieving the expected results detailed in the FDA Blueprint; insufficient demonstration of understanding prescriber needs and knowledge gaps; poorly supported program/educational design

[3] N/A = Not Applicable

[4]One grant from RFA010812 had been awarded at the time of Report #1 data lock. Others are undergoing final evaluation, after being transferred to RFA020912 to permit comparison of those grants with the greatest likelihood of achieving REMS goals.

[5] TBD = To Be Determined

[6]Grants under RFA020912 are currently under final evaluation; award decisions will be made after Report #1 data lock and detailed in One Year Assessment Report.

Thirty-six submissions were received in response to the first RFA to be issued for CE grants (RFA010812). The applications are under review, following the review process shown in Table 4 below. One grant has been awarded to date. The second RFA (RFA020912) was issued

approximately two weeks later, and 45 applications have been received. These applications are following the same review process, and no awards have been made to date.

Table 4 provides the information for the accelerated grant that was approved for RFA010812, including:

- grantee name;
- the date when the grantee will make its REMS-compliant training available;
- a high-level description of the program (eg, web-based, live); and,
- an estimate of how many prescribers will be trained under the program.

Table 4: Grants Awarded in this Reporting Period

Grant Number	Grantee	Partner Organizations	Projected Date of CE Availability	High Level Program Description	Estimated Prescribers To Be Trained (Estimated Completers of CE on Full Blueprint)
EG-000101	Trustees of Boston University	Federation of State Medical Boards (FSMB), Council of Medical Specialty Societies (CMSS), and ExtendMed, Inc.	March 1, 2013	National program intended to improve the knowledge, competence, and performance of a multidisciplinary, inter-professional audience of HCPs (physicians, nurse practitioners, and physician assistants). Executed in conjunction with the FSMB (comprising 70 state medical boards), CMSS (comprising 39 professional societies), and ExtendMed, a web-based CME partner.	(b) (4)

Summary Description of Grant Request EG-000101's Program:

Trustees of Boston University (Boston University), in partnership with the Federation of State Medical Boards (FSMB) and joint sponsors Council of Medical Specialty Societies (CMSS) and ExtendMed, Inc., were awarded a grant in support of their national initiative entitled "Ensuring

Safe and Effective Opioid Prescribing for Chronic Pain: Incorporating ER/LA Opioids REMS in Practice." The overall goal of the initiative is to improve the knowledge, competence, and performance of a multidisciplinary, inter-professional audience of healthcare practitioners (physicians, nurse practitioners, and physician assistants) throughout the United States (US) who provide chronic opioid therapy using ER/LA analgesics to treat patients suffering from chronic pain.

Boston University will be partnering with the FSMB and CMSS, as well as ExtendMed, Inc., with the goal of reaching and engaging a broad number of HCPs to participate in/complete the continuing education. FSMB represents 70 medical and osteopathic boards of the US and its territories; CMSS is an independent forum focused on influencing policy and medical education and accreditation, and currently represents 39 US professional societies. An additional partner will be ExtendMed, Inc., the initiative's web-based partner in offering a suite of online services.

In addition to the partnerships stated above, Boston University has relationships with insurers, payers, managed care organizations, and specialty organizations, etc., to assist with this initiative, if needed.

Boston University is well qualified to execute this initiative as it has already established a pilot program educating on safe and effective opioid prescribing for chronic pain, where over (b) (4) HCPs have participated in their activities thus far.

The comprehensive REMS-compliant CE training is expected to launch by March 1, 2013, and will consist of the following:

- One national three-hour online program, covering the essential REMS content, including three modules, which address all REMS-approved content
- Online state-specific (10 states) Policy and Resource Panels: on-demand, web-based modules providing information on state-specific ER/LA opioid prescribing regulations and resources such as state Drug Prescription Monitoring Program information and specialty pain and addiction treatment programs (novel activity)
- Ten live regional meetings which address all FDA REMS requirements [locations/recruitment assisted by FSMB and CMSS]
- Ten, three-hour Train-the-Trainer live sessions offered as adjunct sessions to the live regional meetings to train physician-educators to teach the essential FDA Blueprint content to cohorts of colleagues at their home organizations (novel activity)
- Fifteen, three-hour cohort live sessions
- Dedicated website with tools/resources, Ask-the-Faculty forum, and FAQ page

Boston University and cosponsors will be partnering with AXDEV, a well-respected outcomes company, to build, track, and measure program outcomes (eg, changes in performance) including data based on MedBiquitous metrics that are reportable via the ACCME Program and Activity System (PARS).

2.1.3 Conclusion

The RPC initiated the process for making available the required accredited CE by issuing two RFAs within six weeks after REMS approval. To date, the top-rated CE grant from the first round of RFA submissions has been awarded, and with CE expected to be available by March 1, 2013, which will meet the established performance goal of the first REMS-compliant training becoming available by this date. Final evaluation of additional grants from the first round of submissions, as well as the 45 grants submitted in response to the second RFA are ongoing in order to assure the most robust offering of REMS compliant CE activities. Details on these subsequent grant awards will be included in the One-Year FDA Assessment Report.

2.2 Assessment 2- Independent Audit of CE Activities

The independent audit will be done by the CE Accreditors. This process will be described in the One-Year FDA Assessment Report.

2.3 Assessment 3a – Evaluation of Prescriber Understanding

2.3.1 Prescriber Knowledge Survey

2.3.1.1 Prescriber Baseline Survey

The REMS Assessment Plan specifies that an evaluation of HCPs' awareness and understanding of the serious risks of long-acting opioid analgesics will be included in the Third-Year FDA Assessment Report. The evaluation will be conducted via a survey of active prescribers of ER/LA REMS products and will also assess changes in prescriber behavior and practice as a result of the REMS, including comprehension of proper patient selection, general ER/LA opioid analgesic use, dosing and administration requirements for ER/LA products, and prescribers' self-reported practices for patient counseling. The surveys will also assess prescriber-reported ease of patient access to ER/LA opioids for general medical reasons. The RPC has elected to conduct a baseline prescriber survey (BPS) to measure prescriber awareness and understanding, as well as self-reported behaviors and practices, prior to the availability of REMS-compliant training.

The BPS will be conducted prior to the availability of the first REMS-compliant CE activity on March 1, 2013, and therefore will include only prescribers who have not completed REMS-compliant training. The baseline survey and the third-year survey will be two separate cross-sectional surveys of randomly selected active prescribers of ER/LA opioids (active prescribers are considered to be those prescribers who have prescribed at least one ER/LA opioid in the last year, as identified by the IMS XPonent database).

The survey protocol containing the detailed methods and survey instruments for the BPS and Third-Year Prescriber surveys was submitted for FDA review on October 31, 2012. These survey materials were developed by the RPC in consultation with and with assistance from an outside vendor with extensive experience in REMS and REMS Assessments. Start-up activities for the BPS have commenced and qualitative pre-testing was conducted in December 2012. Twenty-four (24) active prescribers of ER/LA opioid analgesics products (with equal numbers of prescribers of oral, transdermal, and methadone opioid analgesic products) participated in the pre-testing phase and the results are currently being reviewed for revision of survey materials

prior to launching the BPS in January, 2013. The BPS will be conducted prior to the availability of the first REMS-compliant CE activity on March 1, 2013, and therefore will include only prescribers who have not completed REMS-compliant training.

In parallel with FDA review and qualitative pre-testing of the BPS, the RPC solicited comments on the protocol and questionnaire from a number of therapeutic area and survey research experts with diverse experiences in pain management research, use of opioid analgesics, and opioid-related survey research. Responses from these non-industry affiliated experts will be reviewed by the RPC and may result in additional modifications to the final questionnaire for the BPS and/or Third-Year Prescriber survey. Any revision to survey materials based on pre-testing, FDA review, and independent therapeutic area expert review will be summarized in the final BPS report to FDA containing the survey results.

2.3.1.2 Prescriber Knowledge Survey for Third-Year FDA Assessment Report

The Third-Year FDA Assessment Report will include an evaluation of HCPs' awareness and understanding of the serious risks of ER/LA opioids. The evaluation will be conducted via a survey of active prescribers of ER/LA REMS products and will also assess changes in prescriber behavior and practice as a result of the REMS, including comprehension of proper patient selection, general ER/LA opioid analgesic use, dosing and administration requirements for ER/LA products, and prescribers' self-reported practices for patient counseling.

The survey will be implemented following the same processes used for the BPS described above. The survey will be conducted via an Internet survey of approximately 600 active prescribers three years post REMS-approval, at which time approximately 50% of active prescribers are expected to have completed REMS-compliant training.

The survey, required as part of the Third-Year FDA Assessment Report, will be referred to hereafter as the Third-Year Prescriber survey. The Third-Year Prescriber survey will be conducted in the first half of 2015 and will include prescribers that have completed a REMS-compliant CE course and prescribers that have not. The results of the Third-Year Prescriber survey will be submitted to FDA no later than July 9, 2015, and will contain an evaluation of prescriber awareness and understanding, self-reported prescribing behaviors and practices, and prescriber-reported measures of ease of patient access to ER/LA opioid for medical use. The Third-Year Prescriber survey will compare prescribers that have completed a REMS-compliant CE course with prescribers that have not. In addition, responses to the Third-Year Prescriber survey will be compared to a baseline prescriber survey that RPC has elected to conduct to measure prescriber awareness and understanding, as well as self-reported behaviors and practices, prior to the availability of REMS-compliant training.

2.3.1.3 Conclusion

The RPC is proactively instituting a prescriber baseline survey prior to the launch of the CE programs in order to establish a baseline of prescriber awareness and understanding about the serious risks and appropriate prescribing of the ER/LA opioid products included in the REMS. The survey and protocol have been developed and submitted to FDA for review. Qualitative pre-testing is ongoing with a sample of 24 prescribers to refine the survey in terms of clarity of questions, content and understanding.

2.4 Assessment 3b - Long-term Evaluation Grants

An RFA will be issued to solicit applications for special grants to CE providers who also agree to conduct long-term evaluations. The grants will be for activities to evaluate prescribers of ER/LA opioid analgesics who have completed REMS-compliant training to determine their knowledge retention and practice changes six months to one year after completing the training.

Since the long-term evaluation grants will not begin until six to twelve months after learners complete REMS-compliant CE training, the details of the Evaluation Grants process are in development. Additional information will be provided in the One-Year FDA Assessment Report.

2.5 Functional Components

2.5.1 Dear DEA-Registered Prescriber Letter 1 (DDRP Letter 1)

A series of DDRP Letters was planned as part of the prescriber outreach for the REMS. DDRP Letter 1 was intended to announce the approval of the ER/LA Opioid Analgesics REMS. The target audience for the letter was all DEA-registered prescribers. To enhance initial communication efforts, pharmacies and hospitals were also sent DDRP Letter 1.

DEA classifies registrants by Business Activity Codes (BAC). Most doctoral-level HCPs are in BAC C (Practitioners). This code includes allopathic and osteopathic physicians, dentists, etc. Most HCPs with limited scope of practice, such as nurse practitioners and physician assistants, are in BAC M (Mid-level Practitioners). Hospitals and clinics are registered as BAC B, while pharmacies are in BAC A.

A well-recognized vendor with expertise in delivering drug safety alerts electronically, by facsimile, and by mail was contracted by RPC to develop a distribution plan and to deliver DDRP Letter 1. A process of identifying unique prescribers within the DEA Master Registrant File was conducted. After removal of duplicate registrations, registrations with address errors, records from deceased registrants, and one registration involving an AMA record issue, 1,321,019 unique DEA-registered prescribers (BAC C + M) and 82,651 hospitals and pharmacies (BAC B +A) were identified as of July 18, 2012.

The vendor employed several methods of communication to maximize the probability of successful delivery. Electronic distribution of the letter by e-mail or facsimile was used first. The vendor used its proprietary database of healthcare professionals who have “opted in” to receive electronic communications on drug safety alerts and “Dear HCP” letters. The database of opt-in HCPs was matched to the list of DEA-registered prescribers to identify those prescribers who had chosen to receive electronic communications. Electronic distribution commenced on July 24, 2012, well within the required 60-days following REMS approval.

The next wave of communication, via United States Postal Service (USPS) mail, was to prescribers listed in the DEA Master Registration File but not on the vendor’s opt-in list and to the 79,525 intended recipients not reached by electronic means. Mailing addresses were obtained from the either the DEA File or, if need be, from the American Medical Association Physician Masterfile. Mailing was completed by July 31, 2012.

The tables below summarize the strategy, attempted methods of communication, and results of DDRP Letter 1.

Table 5: DDRP Letter 1 Communication Strategy

Row	Description	DEA Registrants
1	DEA Master Registration File [as of 07/18/12]	1,431,153
2	(Less) Deceased + Duplicates + Address Errors	(27,483)
3	Unique Registered Prescribers [C + M]	1,321,019
4	Hospitals/Clinics + Pharmacies [B + A]	82,651
5	**Targeted Audience for DDRP Letter 1**	**1,403,670**

Row 1 = Total registrations of *all* Business Activity Codes (including manufacturers, researchers, etc.)
Row 2 = Registrations for: deceased registrants, duplicate registrations, registrations with address errors
Row 3 = Unique individual registrants with prescribing authority ("Practitioners" + "Mid-level Practitioners")
Row 4 = Hospitals/clinics plus pharmacies
Row 5 = Total number of registrants RPC attempted to reach (Row 3 + Row 4)

Table 6: DDRP Letter 1 by Initial Communication Method DEA Registrant BAC C +M (Practitioners + Mid-level Practitioners)

Row	Description	Target	%
6	'C' by E-mail	274,132	19.6
7	'C' by Facsimile	290,188	20.7
8	'C' by USPS Mail	549, 132	44.9
9	'M' by USPS Mail	207,567	14.8
10	**Total** Individual Registered Prescribers	**1,321,019**	100

Row 6 = Practitioners initially sent DDRP Letter 1 by e-mail ("opted in" with vendor)
Row 7 = Practitioners initially sent DDRP Letter 1 by facsimile ("opted in" with vendor)
Row 8 = Practitioners initially sent DDRP Letter 1 by USPS mail (had not "opted in" with vendor)
Row 9 = Mid-level Practitioners sent DDRP Letter 1 by USPS mail (not able to "opt in" with vendor)
Row 10 = Sum of Rows 6 - 9

Table 7: DDRT Letter 1 Communication Apparent Results[1] DEA Registrant BAC C +M (Practitioners + Mid-level Practitioners)

Row	Description	Apparently Delivered	
		n	%
11	'C' by E-mail	254,966	93.0
12	'C' by Facsimile	229,829	79.2
13	'C' by USPS Mail	532,089	97.2
14	'M' by USPS Mail	201,700	97.2
15	Apparently Delivered to Prescribers	**1,299,888**	**98.4**
16			
17	Apparently Delivered to Hospitals/Pharmacies	**80,768**	**97.7**

Row 11 = Practitioners initially sent DDRP Letter 1 by e-mail with no bounce-back
Row 12 = Practitioners initially sent DDRP Letter 1 by facsimile with "OK" transmission notice
Row 13 = Practitioners initially sent DDRP Letter 1 by USPS mail, not returned as undeliverable
Row 14 = Mid-level Practitioners sent DDRP Letter 1 by USPS mail, not returned as undeliverable
Row 15 = Total number (%) of Prescribers apparently receiving DDRP Letter 1
Row 16 = Left blank intentionally, as Row 17 was not a REMS requirement
Row 17 = Total number (%) of Hospitals, Clinics, and Pharmacies apparently receiving DDRP Letter 1

[1] The term "Apparently Delivered" is used in recognition that no reliable method for accurately tracking unopened/unread e-mails exists. Industry-standard e-mail exchange services or programs (eg, Microsoft Exchange, Unix Sendmail) have limited ability to accurately track and report when an e-mail is opened or is read. An affirmative action on the part of the recipient (ie, downloading images or clicking on a hyperlink) is required to enable tracking of opening. It is not possible to know when an e-mail is read in the absence of these actions. In addition, many e-mail programs/services block images and hyperlinks by default to protect against spam, viruses, worms, etc. Also, many recipients do not download images as a matter of common practice for the same reasons. Finally, when the critical safety information for DDRP Letters and other REMS communications is embedded within the body of an e-mail, the recipient may choose to read some or all of it in a preview pane without ever downloading images or clicking on any hyperlinks. As a result, it is not possible to accurately know when or if the content of an e-mail is read. Likewise, no reliable method exists to determine if a letter delivered by facsimile or mail was, in fact, read by the intended recipient.

2.5.1.1 Conclusion

The process for distribution of the DDRP Letter began within 15 days after REMS approval, meeting the performance goal that Prescriber Letter 1 will be sent not later than 60 days after the initial approval of this REMS. Communications were directed to all DEA-registered prescribers, as well as DEA-registered hospitals, clinics, and pharmacies. Over 1.3 million prescribers and over 82,000 hospitals, clinics, and pharmacies were targeted for this initial REMS-related communication effort. Greater than 98% of the prescribers were apparently successfully contacted. Efforts are underway to identify methods of outreach to those prescribers for whom communications were returned as undeliverable.

2.5.2 Professional Organization/Licensing Board Letter

To further ensure that prescribers are aware of the existence of the ER/LA Opioid Analgesic REMS, the RPC distributed a letter to relevant Learned Societies and Professional Associations on August 24, 2012, 46 days after REMS approval. The recipients of this letter included the leadership of organizations shown in Table 8.

Table 8: Learned Societies and Professional Associations Receiving REMS Letter

Learned Societies and Professional Associations Receiving REMS Letter		
American Academy of Addiction Psychiatry	American Association of Poison Control Centers	American Osteopathic Association
American Academy of Family Physicians	American Board of Medical Specialties	American Osteopathic Association of Addiction Medicine
American Academy of Hospice and Palliative Medicine	American Board of Orofacial Pain	American Pain Society
American Academy of Neurology	American College of Nurse Practitioners	American Society of Addiction Medicine
American Academy of Nurse Practitioners	American College of Osteopathic Family Physicians	American Society for Pain Management Nursing
American Academy of Nursing	American College of Physicians	American Society of Anesthesiologists
American Academy of Orofacial Pain	American College of Rheumatology	American Society of Pain Educators
American Academy of Pain Management	American Dental Association	Association of American Medical Colleges
American Academy of Pain Medicine	American Dental Education Association	Council of Medical Specialty Societies
American Academy of Physical Medicine and Rehabilitation	American Medical Association	Hospice and Palliative Nurses Association
American Academy of Physician Assistants	American Medical Directors Association	Society of Emergency Medicine Physician Assistants
American Association of Colleges of Osteopathic Medicine	American Nurses Association	
American Association of Colleges of Nursing	American Nurses Credentialing Center	

A similar letter was sent to the following Licensing Boards on August 24, 2012, 46 days after REMS approval:

- State Licensing Boards of
    a. Medicine (allopathic and osteopathic)
    b. Nursing
    c. Dentistry
- Associations of State Licensing Boards
    a. Federation of State Medical Boards
    b. National Council of State Boards of Nursing
    c. American Association of Dental Boards

Two hundred sixty-five (265) professional organizations and healthcare professional licensing boards were targeted to receive a version of DDRP Letter 1, notifying these organizations of the REMS approval and its requirements (Table 9). Thirty-two (32) letters were sent by e-mail and 233 by USPS. There was no indication of failed delivery.

Table 9: POLB Letter 1 Communication Summary

POLB Letter 1 Communication Summary	
Targeted Professional Organizations and State Licensing Boards	265
Electronic Notifications Delivered	32
Hardcopy Notifications Sent	233
Total Notifications Sent	**265**
Returned Mail	- 0-
Total Successful Notifications Delivered	**265**

2.5.3 Conclusion

The process for distribution of the POLB Letter began within 46 days after REMS approval, ahead of the performance goal of distribution no later than 60 days after REMS approval. Letters were successfully delivered to all 265 targeted professional organizations and licensing boards.

2.5.4 RPC Call Center

The ER/LA Opioid Analgesics REMS Program established a centralized Call Center, which became operational on July 23, 2012. The primary purpose of the Call Center is to provide REMS Program support to consumers and HCPs. The Call Center is staffed by qualified and trained Call Center agents.

The Call Center agent responsibilities include, but are not limited to, the following:

- Provide responses to ER/LA Opioid Analgesics REMS-related questions
- Provide a single copy of the PCD and DDRP Letter 1 upon request

- Provide directions for obtaining ER/LA Opioid Analgesics REMS materials (such as Medication Guides, US Prescribing Information, and PCD Pads (see Section 2.5.6)
- Warm transfer calls when possible, or forward documented reports to the appropriate company, if a potential adverse event (AE) or potential product quality concern is identified or there is a medical information question
- Assist in navigating the ER/LA Opioid Analgesics REMS website
- Facilitate issue resolution of any reported problems and inquiries not covered by an existing frequently asked question (FAQ)

The Call Center has access to all REMS materials and the ER/LA Opioid Analgesics REMS website. In addition, the Call Center staff has access to a controlled list of FAQs and RPC approved responses.

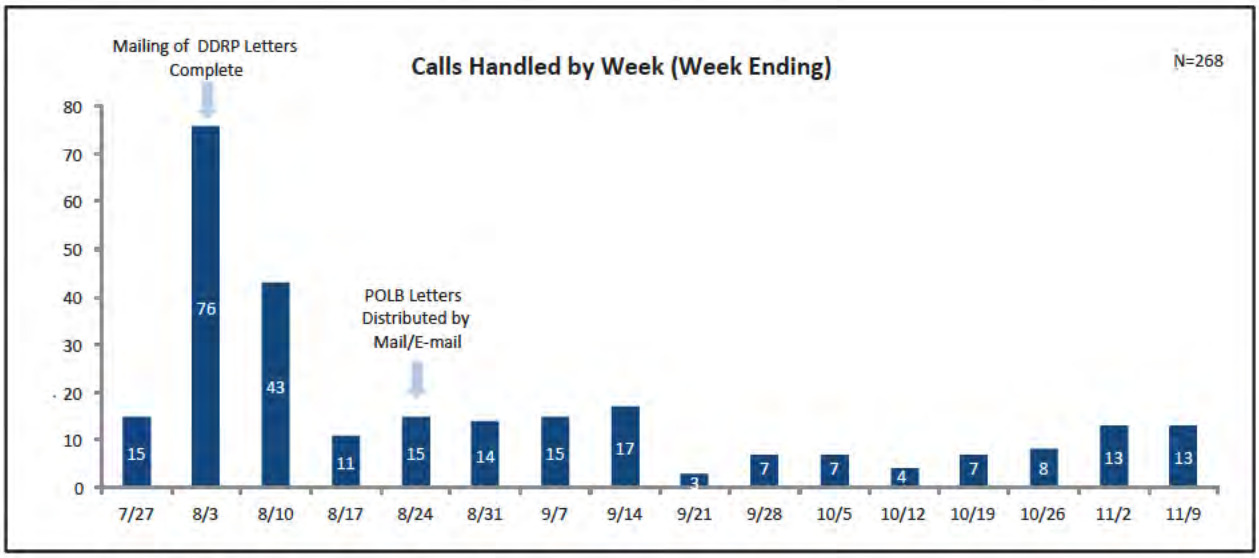
The ER/LA Opioid Analgesics REMS Program Call Center hours of operation are Monday – Friday, 8:00 a.m. to 8:00 p.m. Eastern Time (ET). Callers outside of these hours are instructed to leave a message that will be addressed by the Call Center or the appropriate company, if necessary.

Weekly Call Center reports are provided on Friday mornings. As such, the data provided for the Call Center include data one day past 60-day data lock. Data was collected through Thursday, November 8, 2012, and the final reports were provided to the Call Center Subteam on November 9, 2012.

Since go-live on July 23, 2012 the call center has received a total of 268 calls in this time period. The average length of a call is 3:44 minutes.

Figure 1 shows the Call Center weekly call volume. The Call Center volume was highest during the three weeks immediately following launch of the Call Center, July 23, 2012 through August 10, 2012, which also corresponds to the mailing of the DDRP Letter. Excluding this initial three-week period, the Call Center consistently averages approximately ten calls per week.

Figure 1: Call Center Weekly Call Volume (July 23, 2012 – November 8, 2012)



Source: REMS Call Center Summary Report

An assessment of abandoned calls was performed to ensure this was not the cause of the low call volume. There have been a total of seven abandoned calls from July 23, 2012 – November 8, 2012. The hold time for all abandoned calls is shown in Table 10 below.

Table 10: Assessment of Abandoned Calls (July 23, 2012 - November 8, 2012)

Abandoned Call Number	Date of Call	Hold Time Prior to Abandonment	Comments
1	July 30, 2012	8:17	Multiple calls received at same time, resulted in delay waiting for agent
2	September 24, 2012	2:00	
3	September 30, 2012	0:48	
4	October 12, 2012	1:16	
5	October 16, 2012	7:15	Multiple calls received at same time, resulted in delay waiting for agent
6	October 30, 2012	0:15	
7	October 30, 2012	0:15	

The primary focus of the shared Call Center is to answer REMS-related questions; however, the RPC instituted multiple processes to handle potential AE and product complaint reports that are

received by the Call Center. To date there has only been one potential AE report received through the Call Center, which was transferred to the appropriate member company.

2.5.4.1 Summary of Frequently Asked Questions (FAQs)

At Call Center go-live, a total of 98 unique FAQs were available to answer incoming inquiries. As of November 8, 2012, two FAQs have been revised to better address incoming inquiries, and 24 additional FAQs have been developed to address inquiries received, resulting in 122 FAQs in the Call Center library. The RPC Call Center team has been proactive in tracking and addressing inquiries in the form of additional FAQs and posting revisions and new FAQs on the website as needed. Table 11 below summarizes the top 25 most utilized FAQs and the corresponding number of utilizations for each of those FAQs. The two most utilized FAQs focused on mandatory components of the REMS Program and the definition of "prescribers" as defined by the ER/LA Opioid Analgesics REMS Program.

Table 11: Top 25 FAQs Utilized From July 23, 2012 -November 8, 2012

FAQ	Utilizations
Are there mandatory components associated with the REMS Program that I must complete (eg, program enrollment, training), to allow me to continue prescribing ER/LA opioid analgesics to my patients?	50
How are "Prescribers" defined in the ER/LA Opioid Analgesics REMS Program?	22
Will pharmacists be required to complete education/training, enrollment, or verification to dispense these opioid analgesic products?	15
When will this REMS Program education/training be available?	13
Is it really okay to flush my unused opioid pain medicine down the toilet?	13
Are there components of this REMS Program that impact outpatient or mail-order pharmacy practice?	12
How can I find out more about the REMS-compliant education/training and when it becomes available?	11
Is there someone specific to contact if I should have questions about the grant application/process?	10
When will the education/training be available?	8
What is a REMS Program and what is this REMS Program?	7
Who can submit a grant application to support independent, accredited ER/LA Opioid Analgesics REMS prescriber education/training?	7
Are there components of this REMS Program that impact inpatient or long-term care	7

Table 11: Top 25 FAQs Utilized From July 23, 2012 -November 8, 2012

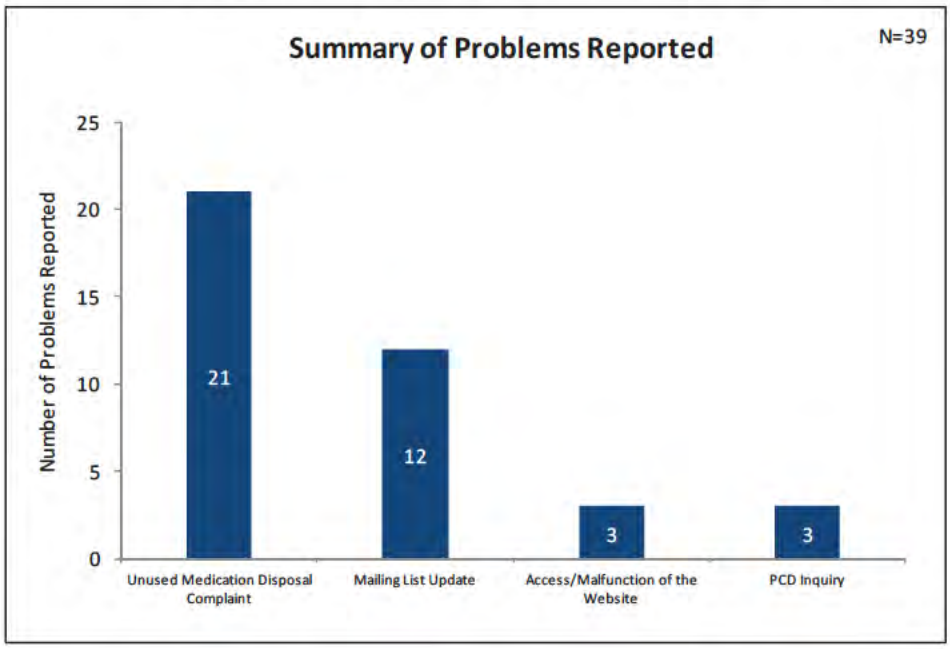
FAQ	Utilizations
pharmacy practice?	
Does this REMS Program require pharmacists to counsel patients on the safe use of ER/LA opioid analgesics?	7
If I am a CE provider, what is the process for applying for grant monies?	6
What pain medicines are included in this REMS Program?	5
Where can I go to access additional copies of the Patient Counseling Document (PCD)?	5
What happens if I do NOT participate in REMS-compliant education/training?	5
Who is funding the REMS-compliant, independent, accredited education/training?	5
How can pharmacists obtain the product-specific Medication Guides?	5
What extended-release/long-acting (ER/LA) opioid analgesics are involved in this REMS Program?	4
What if I have previously completed a/an [opioid, TIRF[1], Butrans, Embeda, Exalgo, Opana, OxyContin] REMS training, do I still need to complete additional education/training for the REMS Program?	4
Did this REMS Program impact the Medication Guides?	4
How do I find the Website/Access this/Troubleshoot that?	3
Can you tell me more about the safety education/training intended for prescribers, such as myself?	3
What areas of education are contained in the FDA's ER/LA Opioid Analgesics REMS 'Blueprint'?	3

[1] TIRF = Transmucosal Immediate Release Fentanyl

2.5.4.2 Problems Reported and Resolutions

The Call Center started receiving calls on July 23, 2012 and, as of November 8, 2012, there were 39 calls that could be classified as "reports of problems." These calls were focused on four main problems. These are: (1) 21 calls regarding questions related to disposal of unused medications, (2) 12 requests to update the mailing list for the DDRP Letters, (3) three problems accessing the website, or website malfunctions, and (4) three inquiries about the availability of alternative PCDs. Further details are provided below. Figure 2 depicts the four categories of calls related to reports of problems.

Figure 2: Summary of Problems Reported to Date (July 23, 2012 – November 8, 2012)



Source: REMS Assessment Problems Reported

Problem Reported #1

Issue: Disposal of unused medication down the toilet complaint: Complaints were received regarding the unused medication disposal information stated in the PCD. The statement currently reads: "Do flush unused medication down the toilet"

- Several HCPs alerted a local community water facilities director when they received the PCD. The director then notified the REMS communication vendor of these complaints.
- A prescriber suggested the PCD include other methods for disposing unused medications, in addition to flushing.

Resolution: The RPC continues to monitor any complaints of this nature and has modified the FAQ responding to this concern in the following manner:

Question: Is it really okay to flush my unused opioid pain medicine down the toilet?

Answer: According to FDA, flushing selected medicines down the sink or toilet is currently the safest way to immediately and permanently remove the risk of harm from the home. An alternative to flushing is to dispose of the expired/unwanted/unused medicines through a medicine take-back program. When a medicine take-back program isn't available, FDA believes that any potential risk to people and the environment from flushing ER/LA opioid analgesics is

outweighed by the real possibility of life-threatening risks from accidental ingestion of these medicines. You should contact your city or county government's household trash and recycling services to see if there is a medicine take-back program in your community and learn about any special rules regarding which medicines can be taken back. The FDA posts the dates for National-Take-Back Day at: http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/EnsuringSafeUseofMedicine/SafeDisposalofMedicines/ucm186187.htm. For additional information on the safe disposal of specific medications, please contact the FDA at 1-888-463-6332 and visit the FDA's website at: http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/EnsuringSafeUseofMedicine/SafeDisposalofMedicines/ucm186187.htm#MEDICINES.

Problem Reported #2

Issue: Mailing List Update: Caller requested that they be removed from the mailing list or would like to notify the REMS Program of a change in address. One caller reported that he received the DDRP Letter by accident, but refused to provide further information.

Resolution: All appropriate and possible changes to the mailing lists were made by the REMS communication vendor.

Problem Reported #3

Issue: Malfunction/Access of Website: One report was received that the website malfunctioned and two reports of a problem accessing the website were received.

Resolution: All website malfunctions and access issues were resolved with the website vendor, and enhancements were made to the FAQs used to respond to callers, giving better direction on how to access the website.

Problem Reported #4

Issue: PCD Inquiry: Two callers asked whether the PCD is available in different languages, specifically Spanish, and one caller asked for a PCD specific for veterinarians.

Resolution: At this time, the current process will remain unchanged. The RPC is currently translating the PCD document into Spanish.

2.5.4.3 ER/LA Opioid Analgesic REMS questions versus product-specific questions

From July 23, 2012 to November 8, 2012, the ER/LA Opioid Analgesic REMS Call Center received a total 268 calls of which there were seven product-specific questions and 270 general REMS-related questions. During the course of one call, multiple FAQs may have been utilized to address the caller’s inquiries. Any problems reported or inquiries that did not have an FAQ prepared were not included in the numbers in Table 12 below.

Table 12: Summary of General REMS Questions and Product-Specific Questions (July 23, 2012 – November 8, 2012)

Types of Questions	Frequency
General REMS Questions	270
Product Specific Questions	7
Total	**277**

Source: REMS Assessment REMS Questions versus Product-Specific Questions Report

Of the seven product-specific questions asked, one was a potential AE, which was transferred to the appropriate RPC member company. All other product-related inquiries were successfully transferred to the appropriate RPC member company.

Table 13 shows the number of REMS questions received by stakeholder type. Most calls were received from prescribers and from CE stakeholders.

Table 13: Summary of General REMS Questions and Product-Specific Questions by Stakeholders

Stakeholder	# General REMS Questions	# Product-Specific Questions
Prescriber	104	2
CE Stakeholders[1]	74	0
Pharmacist	44	3
Patient/Consumer/Caregiver	6	2
Distributor	0	0
All Other Stakeholders[2]	42	0
Total	**270**	**7**

[1] Refers to all Continuing Education stakeholders (eg, Accredited CE provider, Accreditor, Non-Accredited Medical Education Partner, etc.)

[2]Refers to all stakeholders that did not fall into the categories above (eg, veterinarian, animal control, pharmaceutical representative)

Source: REMS Questions versus Product-Specific Questions Report

2.5.4.4 Call Center Considerations for FDA

The RPC plans to request that FDA consider whether removal of the requirement for a centralized Call Center from the REMS Program may be appropriate after one year of operation and data collection. The rationale for requesting this consideration is as follows:

- The Call Center handled a total of 268 calls during the first four months of operation (July 23, 2012 – November 8, 2012).

- Call volume was highest during the first three weeks immediately following Call Center go-live (July 23, 2012 – August 10, 2012) which also corresponded to distribution of approximately 1.3 million DDRP and POLB letters. Call Center volume has been consistently low since that time, averaging 10 calls per week.
- The ER/LA Opioid Analgesics REMS website, which contains approved FAQs, is fully functional and available 24 hours a day, 7 days a week. To date, there has been no down-time.
- In addition to the FAQs that were anticipated prior to go-live, the RPC Call Center Team has developed new FAQs and enhanced existing FAQs in response to inquiries received from stakeholders. FAQs for all stakeholders are easily available on the website. The current list of FAQs presented on the website is a robust amount of information and responds to common (and not so common) inquiries. The RPC continues to assess and address stakeholder issues and concerns and, when possible, creates new, or revises current FAQs for the website.
- There were a total of seven abandoned calls, and the RPC does not consider this abandonment rate as an explanation for the consistently low call volume.
- Three requests to fulfill PCD orders have been received and no requests were made for DDRP and POLB letters, indicating this is not a primary route stakeholders are using to access these documents.

At this time, the RPC proposes that the centralized Call Center remain fully operational, Monday – Friday, 8:00 a.m. – 8:00 p.m. ET. The RPC will continue to monitor call volume, problems reported, and the need for additional FAQs. Within the One-Year FDA Assessment Report, the RPC may request that the Agency remove the requirement for a centralized Call Center from the REMS, if ongoing evaluation of the data supports discontinuation.

RPC understands that a request for discontinuation of the Call Center will require FDA approval, proper vendor notification and updates to the website. If a live representative is needed, the RPC member company product and contact information is also available on the website. Member companies are available to respond to REMS Program-related questions and/or their product-specific questions. If targeted or technical CE questions arise, stakeholders may contact the grants management vendor by e-mail via the website, and the grants management vendor will respond by e-mail or telephone.

2.5.4.5 Conclusion

The established performance goals regarding the Call Center were that an interim single toll-free number Call Center must be implemented no later than July 23, 2012, and a fully operational centralized Call Center must be implemented no later than 90 calendar days after the approval of the REMS (October 21, 2012). The RPC exceeded these goals by having a single multi-RPC member company fully functional Call Center available to all stakeholders as of July 23, 2012.

2.5.5 ER/LA Opioid Analgesics REMS Website

Another communication tool included in the ER/LA Opioid Analgesics REMS is a REMS website. The website, http://www.ER-LA-opioidREMS.com, was launched on July 23, 2012. The following items can be accessed through this website:

- REMS Overview
- Important Safety Material
- Medication Guides for each of the products included in the REMS
- US Prescriber Information for each of the products included in the REMS
- Materials for HCPs
  - ER/LA Opioid Analgesics REMS-Compliant Training
  - DDRP Letters
  - PCD
  - Medication Guides
  - Healthcare Professional FAQs
- Materials for Patients
  - Medication Guides
  - Patient FAQs
- A list of all REMS-compliant CE activities that are supported by independent educational grants from the ER/LA opioid analgesic companies to accredited CE providers (will be available when CE programs are available)

The RPC website is searchable and appears in search results, often on the first page of such results, when relevant search terms are used in major search engines.

2.5.5.1 Conclusion

The REMS website was launched concurrent with the launch of the Call Center and is accessible to all stakeholders for REMS information.

2.5.6 Patient Counseling Document

The PCD on Extended-Release/Long-Acting opioids is a tool to facilitate important discussions between prescribers and patients for whom an ER/LA opioid analgesic is being prescribed. The PCD contains important safety information about the drug products covered by the REMS. Key messages outlined in the PCD include the importance of taking ER/LA opioid analgesics exactly as prescribed, the need to store ER/LA opioid analgesics safely and securely—out of the reach of children, pets, and household acquaintances—to avoid risks from unintended exposure, the importance of not sharing these medications, even if someone has the same symptoms as the patient, and the proper methods of disposal of unneeded ER/LA opioid analgesics.

A PDF version of the PCD was posted on the website on July 23, 2012 (website launch), and has since been downloaded 1,822 times as of November 7, 2012. Since July 23, 2012 (Call Center go-live), three single PCD orders have been fulfilled by the ER/LA Opioid Analgesics REMS Call Center. The Call Center has received two inquiries thus far for Spanish versions of the PCD. The PCD is currently being translated into Spanish.

In addition, the PCD was included in DDRP Letter 1 and POLB Letter 1 communications (electronic and hardcopy) and is provided in Appendix B for reference.

2.5.6.1 Conclusion

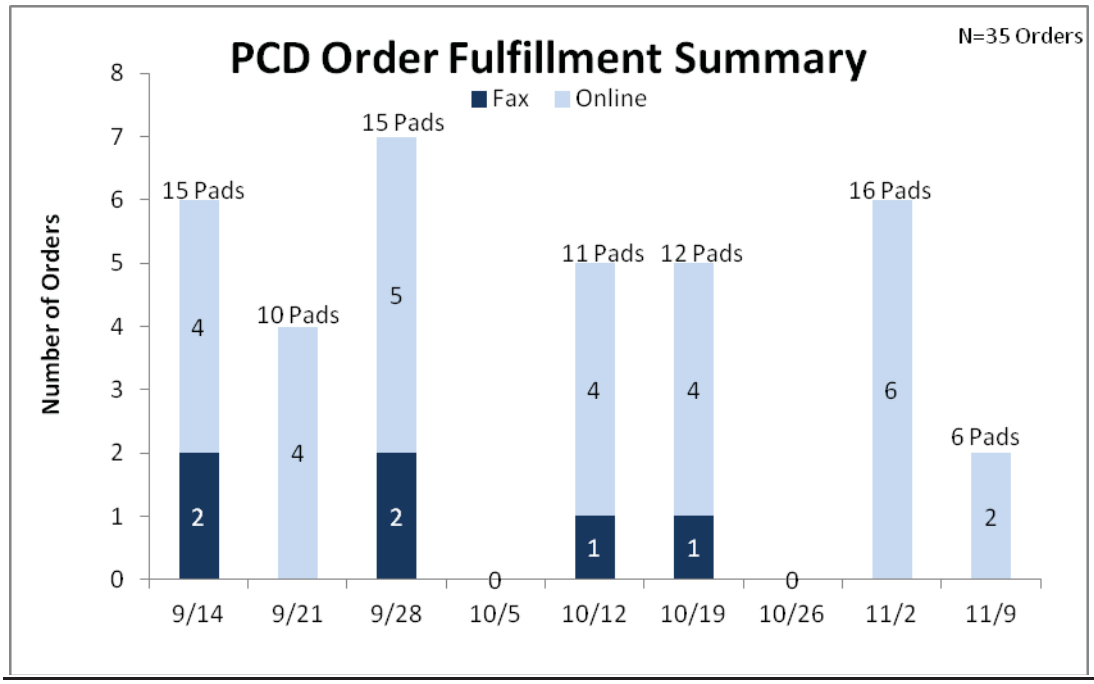
The PCD is a valuable reference tool for all stakeholders and is readily accessible to all stakeholders and has been downloaded from the REMS website more than 1,800 times. Few requests have been made to the Call Center for hardcopies of the PCD.

2.5.7 Patient Counseling Document Portal

As part of the REMS, a portal was designed for physicians to request (or 'order' free of charge) the PCD. The PCDs can be requested via an online order form or by fax. The fax order form is available on the portal. This feature became available on September 10, 2012.

As of November 7, 2012, 35 total orders (29 online, 6 fax), equating to 85 pads, have been fulfilled (no orders have been returned). The PCD portal vendor collects and batches orders for pick-up and packing from inventoried materials once per week on Fridays. Orders received prior to 5:00 p.m. (Central Time) on Thursday will ship on the following Friday of each week.

Figure 3: PCD Order Fulfillment Summary



2.5.7.1 Conclusion

The PCD is also available via the website portal. In the approximately two months since the portal ordering function has been available, 35 orders (85 pads) have been requested.

3. SUMMARY

All ER/LA Opioid Analgesic REMS requirements have been met or exceeded for the Six-Month FDA Assessment Report. Important milestones achieved for each are outlined below.

DDRP Letter 1 and POLB Letter

Distribution of the DDRP Letter 1 was initiated well in advance of the REMS performance goal with alternatives being sought to reach those prescribers who have not already received letters. The DDRP Letter 1 was successfully delivered to 98.4% (1,299,888/1,321,019) of the targeted DEA registrants. Additionally, two hundred sixty-five professional organizations and healthcare professional licensing boards were targeted to receive a version of the DDRP Letter 1, notifying these organizations of the REMS approval and its requirements. The goal for distribution of the POLB Letter was exceeded with 100% successful delivery of all letters.

REMS-compliant CE Training

The top-rated CE grant from the first round of RFA submissions has been awarded and program development is in process, with the first RPC-supported REMS-compliant CE expected to be available by March 1, 2013. At the time of data lock for this report, 49 additional grants were undergoing final evaluation to assure the most robust offering of REMS-compliant CE training.

Prescriber Survey and Qualitative Research

A prescriber knowledge survey and protocol were drafted and submitted to the FDA. The survey is also undergoing qualitative pre-testing with prescribers to confirm clarity of the questions and response options. The RPC is planning to conduct a baseline prescriber survey (BPS) to measure prescriber awareness and understanding, as well as self-reported behaviors and practices, prior to the availability of REMS-compliant training. The BPS will allow for a comparison of prescriber awareness and understanding, behavior and prescribing practices, and patient access associated with long-acting opioid analgesics prior to the start of the REMS with knowledge and understanding measured approximately two years after REMS training has started. The BPS is scheduled to be completed by March 1, 2013.

Call Center

The Call Center goals were exceeded by having a single, fully-functional Call Center for the ER/LA Opioid Analgesic REMS available to all stakeholders, as of July 23, 2012, sponsored by all RPC member companies. Calls are being received and answered following the established FAQs, with additional FAQs being developed as needed.

REMS Website

The ER/LA Opioid Analgesics REMS website was launched on July 23, 2012 with all FDA-approved REMS documents and information available to all stakeholders. The PCD is readily available for download from the ER/LA Opioid Analgesics REMS website, hardcopies can be ordered via the Call Center, and packs of 50 PCDs can be ordered on-line from the ER/LA Opioid Analgesics REMS website or by faxing the order form, which is also available on the website.

Table 14 shows the RPC's goals reached for the Six-Month FDA Assessment Report commitment, as well as progress towards future REMS requirements. The RPC will continue its efforts towards completing and exceeding the REMS performance goals for subsequent assessments.

Table 14: RPC Progress Made In Meeting REMS Requirements

FDA Assessment Report Requirements	Progress Made
Assessment 1 **Prescribers successfully completing training**	Two RFAs issued resulting in 81 CE grant submissions; one grant awarded. 45 applications still under review. On target to have first CE training started by March 1, 2013.
Assessment 2 **Independent audit of CE activities**	To be done by CE Accreditors; process to be described in One-Year FDA Assessment Report for the ER/LA Opioid Analgesics REMS
Assessment 3a **Prescriber survey**	BPS being conducted prior to availability of REMS-compliant CE activity.
Assessment 3b: Long Term Evaluation grants **Grants to CE orgs to assess prescribers' knowledge/practice changes 6-12 months after REMS-compliant training**	Details of Evaluation Grants process are in development. Will be provided in One-Year Assessment Report
Assessment 4 **Patient survey**	Process to be described in future FDA Assessment Reports
Assessment 5 **Surveillance monitoring for misuse, abuse, overdose, addiction, death and intervention taken**	Process to be described in future FDA Assessment Reports
Assessment 6 **Evaluation of drug utilization patterns (IMS data, claims data)**	Process to be described in future FDA Assessment Reports
Assessment 7 **Evaluation of changes in prescribing behavior**	Process to be described in future FDA Assessment Reports
Assessment 8 **Changes in Access to ER/LA opioid analgesics**	Process to be described in future FDA Assessment Reports

3.1 Status of Post-Approval Studies and Clinical Trials

FDA should refer to each sponsor's cover letter for information on the status of post-approval studies and/or clinical trials.

Appendix A: Glossary

Call Center Subteam:	The team responsible for selection and oversight of the vendor operating the centralized Call Center for the ER/LA Opioid Analgesics REMS, including development and ongoing operations.
Continuing Education Subteam:	The team responsible for design and implementation of CE activities for the REMS Program (eg, grant management system, review process).
Metrics Subteam:	The team responsible for designing and implementing the metrics Assessment Reports in accordance with FDA requirements.
Project Management Office:	The hub of the REMS Program execution including: 1) program management for ER/LA Opioid Analgesics REMS Program, 2) procurement of suppliers, and 3) implementation and ongoing operational support services for the approved REMS Program.
REMS Program Companies (RPC):	Companies with approved ANDAs/NDAs for ER/LA opioid analgesics. The RPC is the program's governing body with overall responsibility for supervision and direction of the program.
RPC Oversight Committee:	An appointed number of RPC member companies selected by the entire RPC responsible for day-to-day operations of the ER/LA Opioid Analgesics REMS.
Technology Subteam:	The team responsible for providing oversight and subject-matter expertise on the ER/LA Opioid Analgesics REMS Website and other technology related items, eg Call Center, metrics database,

Appendix B: Patient Counseling Document (PCD)

Patient Counseling Document on Extended-Release / Long-Acting Opioid Analgesics

Patient Name:

The DOs and DON'Ts of Extended-Release / Long - Acting Opioid Analgesics

DO:

- Read the **Medication Guide**
- Take your medicine exactly as prescribed
- Store your medicine away from children and in a safe place
- Flush unused medicine down the toilet
- Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Call 911 or your local emergency service right away if:

- You take too much medicine
- You have trouble breathing, or shortness of breath
- A child has taken this medicine

Talk to your healthcare provider:

- If the dose you are taking does not control your pain
- About any side effects you may be having
- About all the medicines you take, including over-the-counter medicines, vitamins, and dietary supplements

DON'T:

- **Do not** give your medicine to others
- **Do not** take medicine unless it was prescribed for you
- **Do not** stop taking your medicine without talking to your healthcare provider
- **Do not** break, chew, crush, dissolve, or inject your medicine. If you cannot swallow your medicine whole, talk to your healthcare provider.
- **Do not** drink alcohol while taking this medicine

For additional information on your medicine go to: **dailymed.nlm.nih.gov**

Patient Counseling Document on Extended-Release / Long-Acting Opioid Analgesics

Patient Name:

Patient Specific Information

Take this card with you every time you see your healthcare provider and tell him/her:

- Your complete medical and family history, including any history of substance abuse or mental illness
- The cause, severity, and nature of your pain
- Your treatment goals
- All the medicines you take, including over-the-counter (non-prescription) medicines, vitamins, and dietary supplements
- Any side effects you may be having

Take your opioid pain medicine exactly as prescribed by your healthcare provider.

Appendix C: Dear DEA-Registered Prescriber (DDRP) Letter

Subject:	**Announcement of a Risk Evaluation and Mitigation Strategy (REMS) for all extended-release/long-acting opioid analgesic drug products due to their risks of misuse, abuse,**

FDA-Required REMS Program for Serious Drug Risks

Dear **DEA**-Registered Prescriber:

Extended-release and long-acting (ER/LA) opioid analgesics are approved for the management of chronic moderate-to-severe pain in the U.S., and can be safe and effective in appropriately selected patients when used as directed. However, opioid analgesics are also associated with serious risks and are at the center of a major public health crisis of increased misuse, abuse, addiction, overdose, and death.

The U.S. ood and Drug Administration (FDA) has determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary for ER/LA opioid analgesics to ensure that the benefits continue to outweigh the risks of adverse outcomes (addiction, unintentional overdose, and death) resulting from inappropriate prescribing, abuse, and misuse. A REMS is a strategy to manage a known or potential serious risk associated with a drug product. In the interest of public health and to minimize the burden on the healthcare delivery system from having multiple unique REMS programs, pharmaceutical companies subject to this REMS have joined together to implement this REMS for all ER/LA opioid analgesic drug products.

The principal components of this REMS are:

a) Prescriber training on all ER/LA opioid analgesics,
b) the *Patient Counseling Document on Extended-Release and Long-Acting Opioid Analgesics* (PCD), and
c) a unique Medication ui de for each ER/LA opioid analgesic drug product.

The branded and generic drug products subject to this REMS include *all*:

- extended-release, oral-dosage forms containingG
  - hydromorphone,G
  - morphine,G
  - oxycodone,G
  - oxymorphone, orG
  - tapentadol;G
- fentanyl and buprenorphine-containing transdermal delivery systems; *and*
- methadone tablets and solutions that are indicated for use as analgesics.G

Prescriber Action

Under the REMS, you are **strongly encouraged** to do **all** of the following:

- **Train (Educate Yourself) -** Complete REMS-compliant training offered by an accredited provider of continuing education (CE) for your discipline. This training is being developed and will be offered early next year at no or nominal cost to prescribers. You will be notified when REMS-compliant training will become available. *REMS-compliant training* will: (a) be delivered by accredited CE

providers; (b) cover all elements of the DA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics ("FDA Blueprint"); (c) include a post-course knowledge assessment; and (d) be subject to independent audit of content and compliance with applicable accrediting standards.

- **Counsel Your Patients -** Discuss the safe use, serious risks, storage, and disposal of ER/LA opioid analgesics with patients and their caregivers every time you prescribe these medicines. The enclosed *Patient Counseling Document on Extended-Release/Long-Acting Opioid Analgesics* (PCD) should be used to facilitate these discussions.

- **Emphasize Patient and Caregiver Understanding of the Medication Guide -** Stress to patients and their caregivers the importance of reading the Medication uide that they will receive from their pharmacist every time an ER/LA opioid analgesic is dispensed to them, as the information in the Medication uide may have changed.

- **Consider Using Other Tools -** In addition to the PCD, there are other publicly-available tools to improve patient, household, and community safety when using ER/LA opioid analgesics, as well as compliance with conditions of treatment, including Patient-Prescriber Agreements (PPAs) and risk assessment instruments.

REMS-compliant Training Programs

A critical component of the ER/LA Opioid Analgesics REMS program is essential safety education for prescribers. REMS-compliant training for prescribers, as described previously, will be delivered by accredited CE providers and will include both general and product-specific drug information, as well as information on weighing the benefits and risks of opioid therapy, appropriate patient selection, managing and monitoring patients, and counseling patients on the safe use of these drugs. In addition, the education will include information on how to recognize evidence of, and the potential for, opioid misuse, abuse, addiction, and overdose.

It will be some time before the REMS-compliant training funded by educational grants from the pharmaceutical companies subject to this REMS becomes available. The DA developed core messages to be communicated to prescribers in the DA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics ("FDA Blueprint"), which will be used by accredited CE providers to develop REMS-compliant training courses. A follow-up letter notifying you of the availability of REMS-compliant training funded under this REMS will be sent not later than thirty (30) days before such training is offered. However, REMS-compliant education may also be offered by academic institutions or professional societies independent of REMS-related funding. We encourage you to successfully complete REMS-compliant training offered to improve your ability to prescribe these medications more safely.

The Patient Counseling Document on Extended-Release/Long-Acting Opioid Analgesics (PCD)

Enclosed with this letter is the Patient Counseling Document that was developed under the REMS for ER/LA opioid analgesics to assist you in having important conversations with patients for whom you select an ER/LA opioid analgesic. It contains important safety information common to the drug products subject to this REMS, and includes space for you to write additional information to help your patients use their specific ER/LA opioid analgesic safely. The PCD should be provided to the patient or their caregiver at the time of prescribing. Patients and their caregivers should be counseled on:

- the importance of taking these medicines exactly as you prescribe them,
- the need to store ER/LA opioid analgesics safely and securely – out of the reach of children, pets, and household members – to avoid risks from unintended exposure,

- the importance of not sharing these medications, even if someone has the same symptoms as the patient, *and*
- the proper methods of disposal of unneeded ER/LA opioid analgesics.

You can re-order or print additional copies of the PCD from www.ER-LA-opioidREMS.com.

Adverse Event Reporting

To report all suspected adverse reactions associated with the use of the ER/LA opioid analgesics, contact:

- the pharmaceutical company that markets the specific product, or
- the DA MedWatch program:
  - by phone at 1-800-FDA-1088 (1-800-332-1088) orG
  - online at www.fda.gov/medwatch/report.htmG

More information about this REMS can be obtained at: www.ER-LA-opioidREMS.com or by calling the ER/LA Opioid Analgesic REMS Call Center at 1-800-503-0784.

Sincerely,

The ER/LA Opioid Analgesic REMS Companies

Appendix D: Professional Organization/Licensing Board (POLB) Letter

Subject:	**Announcement of a Risk Evaluation and Mitigation Strategy (REMS) for all extended-release/long-acting opioid analgesic drug products due to their risks of misuse, abuse, addiction, and overdose**

FDA-Required REMS Program for Serious Drug Risks

Dear **<Professional Organization/Licensing Board>**:

We encourage you to share the following information with your <members/licensees>.

Extended-release and long-acting (ER/LA) opioid analgesics are approved for the management of chronic moderate-to-severe pain in the U.S., and can be safe and effective in appropriately selected patients when used as directed. However, opioid analgesics are also associated with serious risks and are at the center of a major public health crisis of increased misuse, abuse, addiction, overdose, and death.

The U.S. ood and Drug Administration (FDA) has determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary for ER/LA opioid analgesics to ensure that the benefits continue to outweigh the risks of adverse outcomes (addiction, unintentional overdose, and death) resulting from inappropriate prescribing, abuse, and misuse. A REMS is a strategy to manage a known or potential serious risk associated with a drug product. In the interest of public health and to minimize the burden on the healthcare delivery system from having multiple unique REMS programs, pharmaceutical companies subject to this REMS have joined together to implement this REMS for all ER/LA opioid analgesic drug products.

The principal components of this REMS are:

d) Prescriber training on all ER/LA opioid analgesics,
e) the *Patient Counseling Document on Extended-Release and Long-Acting Opioid Analgesics* (PCD), and
f) a unique Medication ui de for each ER/LA opioid analgesic drug product.

The branded and generic drug products subject to this REMS include *all*:

- extended-release, oral-dosage forms containing
  - hydromorphone,
  - morphine,
  - oxycodone,
  - oxymorphone, or
  - tapentadol;
- fentanyl and buprenorphine-containing transdermal delivery systems; *and*
- methadone tablets and solutions that are indicated for use as analgesics.

Prescriber Action

Under the REMS, prescribers are **strongly encouraged** to do **all** of the following:

- **Train (Educate Themselves) -** Complete REMS-compliant training offered by an accredited provider of continuing education (CE) for their discipline. This training is being developed and will be offered early next year at no or nominal cost to prescribers. You will be notified when REMS-compliant training will become available. *REMS-compliant training* will: (a) be delivered by accredited CE providers; (b) cover all elements of the DA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics ("FDA Blueprint"); (c) include a post-course knowledge assessment; and (d) be subject to independent audit of content and compliance with applicable accrediting standards.

- **Counsel Their Patients -** Discuss the safe use, storage, and disposal of ER/LA opioid analgesics with patients and their caregivers every time they prescribe these medicines. The enclosed *Patient Counseling Document (PCD) on Extended-Release/Long-Acting Opioid Analgesics* should be used to facilitate these discussions.

- **Emphasize Understanding the Medication Guide -** Stress to patients and their caregivers the importance of reading the Medication ui de that they will receive from their pharmacist every time an ER/LA opioid analgesic is dispensed to them, as information in the Medication uide may have changed.

- **Consider Using other Tools -** In addition to the PCD, there are other publicly-available tools to improve patient, household, and community safety when using ER/LA opioid analgesics, as well as compliance with conditions of treatment, including Patient-Prescriber Agreements (PPAs) and risk assessment instruments.

REMS-compliant Training Programs

A critical component of the ER/LA Opioid Analgesics REMS program is essential safety education for prescribers. REMS-compliant training for prescribers, as described previously, will include both general and product-specific drug information, as well as information on weighing the benefits and risks of opioid therapy, appropriate patient selection, managing and monitoring patients, and counseling patients on the safe use of these drugs. In addition, the education will include information on how to recognize evidence of, and the potential for, opioid misuse, abuse, addiction, and overdose.

It will be some time before the REMS-compliant training funded by educational grants from the pharmaceutical companies subject to this REMS becomes available. The DA developed core messages to be communicated to prescribers in the DA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics ("FDA Blueprint"), which will be used by accredited CE providers to develop REMS-compliant training courses. A follow-up letter notifying you of the availability of REMS-compliant training funded under this REMS will be sent not later than thirty (30) days before such training is offered. However, REMS-compliant education may also be offered by academic institutions or professional societies independent of REMS-related funding. We encourage you to successfully complete REMS-compliant training offered to improve your ability to prescribe these medications more safely.

The Patient Counseling Document on Extended-Release/Long-Acting Opioid Analgesics (PCD)

Enclosed with this letter is the Patient Counseling Document that was developed under the REMS for ER/LA opioid analgesics to assist you in having important conversations with patients for whom you select an ER/LA opioid analgesic. It contains important safety information common to the drug products subject to this REMS, and includes space for you to write additional information to help your patients use their specific ER/LA opioid analgesic safely. The PCD should be provided to the patient or their caregiver at the time of prescribing. Patients and their caregivers should be counseled on:

- the importance of taking these medicines exactly as you prescribe them,
- the need to store ER/LA opioid analgesics safely and securely – out of the reach of children, pets, and household members – to avoid risks from unintended exposure,
- the importance of not sharing these medications, even if someone has the same symptoms as the patient, *and*
- the proper methods of disposal of unneeded ER/LA opioid analgesics.

Prescribers can re-order or print additional copies of the PCD from www.ER-LA-opioidREMS.com.

Adverse Event Reporting

To report all suspected adverse reactions associated with the use of the ER/LA opioid analgesics, contact:

- the pharmaceutical company that markets the specific product, or
- the DA MedWatch program:
  - by phone at 1-800-FDA-1088 (1-800-332-1088) orG
  - online at www.fda.gov/medwatch/report.htmG

More information about this REMS can be obtained at: www.ER-LA-opioidREMS.com or by calling the ER/LA Opioid Analgesic REMS Call Center at 1-800-503-0784.

Sincerely,

The ER/LA Opioid Analgesic REMS Companies

Appendix E: Continuing Education Grant Requests for Applications (RFAs)

RFA010812:

REQUEST FOR (GRANT) APPLICATIONS (RFA)

Extended-Release and Long-Acting Opioid Analgesics

Risk Evaluation and Mitigation Strategy (REMS)

RFA CODE: ER/LA 010812

As a component of the Extended-Release (ER) and Long-Acting (LA) Opioid Analgesics REMS 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 FDA has required manufacturers of ER/LA opioid analgesics, known as the REMS Program Companies (RPC), to provide education for prescribers of these medications.

FDA has developed a Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics ("FDA Blueprint") 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 RPC is comprised of 15 companies[3] that have extended- release (ER) and/or /long-acting (LA) opioid products. RPC-supported REMS education will be provided through accredited continuing education (CE) activities supported by independent educational grants from these ER/LA opioid analgesic companies.[9]

The RPC would like to make your organization aware of grant funds available to support accredited independent continuing education (CE) for the ER / LA class-wide opioid analgesics REMS. The RPC is utilizing this Request for Grant Applications (RFA) process for this purpose. Accredited CE Providers must be engaged in or represent healthcare professionals who provide direct patient care (eg, Schools of Medicine, Pharmacy or Nursing, Hospitals, Medical Societies, Professional Associations, or governmental organizations) and may choose to collaborate with an Educational Planner(s) to assist in the development and/or execution of a proposed educational activity. For more information on grant application submission process, please see below.

[3] As of August 2012

Background:

This RFA is being provided on the RPC website at www.ER-LA-opioidREMS.com so that Accredited CE Providers can begin to develop grant applications prior to the go live date of the REMS Grant Management System (GMS) portal. This portal will allow for submission and processing of all RPC REMS grant requests and is projected to go live by late September 2012. When the GMS system is operational, you may access it by way of the RPC website at www.ER-LA-opioidREMS.com, via the right-hand-side link "If you are a Continuing Education Provider, click here for more information."

Timing for Applications:

There will be two cycles of grant submissions in 2012. For consideration in the initial round of grant reviews, which will occur approximately four to six weeks after posting of this RFA, grant applications must be submitted to the GMS within two weeks of the GMS site going live. A second round of grant reviews will occur approximately eight weeks after this initial RFA is posted. The exact submission deadline for the second cycle will be posted to the www.ER-LA-opioidREMS.com in early September, so please periodically visit the website to obtain future updates.

Grant Application Deadline for RFA 010812: September 24, 2012

Goal of RFA:	The goal of this RFA is to support high quality education using evidence-based methods intended to assist in ensuring 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). This will be accomplished by employing the elements of the approved "FDA Blueprint" for CE training.
Area of Interest:	ER/LA opioid analgesics prescribing best practices
Audience:	Healthcare professionals involved in the care of patients with chronic moderate-to-severe pain, licensed to practice in the USA and its territories, especially prescribers with a DEA registration to prescribe Schedule II and III drugs
Budget:	Preference will be given to Programs that demonstrate they are cost-effective, collaborative, and innovative educational activities. Budgets should be consistent with the reach and scope of the proposal. To optimize the learning opportunities,

the RPC intends to fund multiple activities dispersed across multiple providers. Therefore preference will be given to those grant requests that permit the RPC to support multiple high quality programs that will enable achievement of the prescriber education participation goals as described in the FDA-approved ER/LA Opioid REMS. Because of the intent to fund multiple diverse activities, there will need to be significant justification for consideration of single proposals in excess of $5M.

Parameters: **The successful grant application will include:**

1. Clear articulation of the elements of the approved FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics that are addressed by the proposal
2. Programming designed:
    a. Using evidence-based adult learning principles/preferences (see below):
        - Needs assessment of the target audience,
        - Instructional design appropriate to the target audience,
    b. To have the ability to provide learning opportunities to an interprofessional audience of prescribers
    c. To have a broad reach, with the ability to be scaled to meet needs of specific prescriber populations.
3. An assessment component that measures the effectiveness of programming that employs:
    a. ACCME PARS or other Accreditor database fields for data aggregation
    b. MedBiquitous ER/LA REMS standards in design to provide a uniform data set to FDA. ER/LA REMS standards are currently in development with MedBiquitous.
    c. AT MINIMUM includes evidence of program completion and assessment of change in prescriber knowledge and competence
4. Programming that adheres to standards for program planning and commercial support promulgated by the Accreditation Council for Continuing Medical Education® (ACCME®), or of another CE accrediting body

appropriate to the prescribers' medical specialty or healthcare profession.

Note: Co-sponsorships, partnerships, and or collaboration with other organizations engaged in education, including healthcare quality-focused organizations, medical societies, medical centers, and other Accredited CE Providers are encouraged.

Submission Link: Grant applications must be submitted via the GMS. When the GMS system is operational, you may access it by way of the RPC website at www.ER-LA-opioidREMS.com, via the right-hand-side link "If you are a Continuing Education Provider, click here for more information." For this specific RFA, the appropriate RFA code is 010812**.**

Applicant Eligibility Criteria

- Accredited CE Providers must be engaged in or represent healthcare professionals who provide direct patient care (eg, Schools of Medicine, Pharmacy or Nursing, Hospitals, Medical Societies, Professional Associations, or governmental organizations).
- Applicants must be accredited to provide CE by a national accrediting body*; or by an official state accrediting agency, and must demonstrate that their organization is in good standing at the time of application.
- Applicants must have demonstrated capabilities in the design and successful implementation of complex projects.
- Any educational activities proposed and implemented must be fully compliant with all applicable accrediting body standards, as well as other relevant standards, guidelines and requirements as they apply to the conduct of independent medical education.
- All grant applicants must describe their processes for: confirming that all elements of the "FDA Blueprint" are addressed, validating content for scientific and medical content accuracy, ensuring fair balance and controlling bias, as well as assuring that the education includes a post-activity knowledge assessment of all sections of the "FDA Blueprint."
- All grant applicants must be organizations in the United States and its territories.

* Eg ACCME, AAFP, AANP, AAPA, ACPE, ADA, ANCC, AOA, or equivalent accrediting body.

Required grant proposal elements:

1. Name of organization and person(s) responsible for this project
2. Name of any partner organizations involved with the proposed education, along with roles and responsibilities
3. Baseline summary of needs data, initial metrics, or project starting point
4. Description of project goal(s)
5. Description of educational methods to be utilized
6. Demonstration that the learning objectives address the needs assessment within the intended audience, instructional design, and architecture of the proposed activity
7. Narrative describing the proposed program in detail. Each activity component description must include the rationale and intended audience
8. Narrative describing quantitative/qualitative measures of success that must include audience reach and educational impact on healthcare professional's knowledge and competence, and may include attitudes, perceptions and skills
9. Description and qualifications of the members of the team that will be responsible for implementing this project
10. Explanation of rationale, efficiencies, and cost-effective approaches to both the live and enduring components
11. Detailed project timeline for each phase and milestone. This will serve as the basis of the milestone payments in the grant as described below
    a. Execution of Letter of Agreement: 35%
    b. Start of First Activity and Upon Acceptance of Update Report: 25%
    c. Mid-term of Grant Timeline and Upon Acceptance of Update Report: 30%
    d. Completion of Last Activity and Receipt/Acceptance of Required Grant-Related Documentation: 10%
12. Detailed budget provided using the template residing in the REMS Grant portal

SCOPE OF THE PROBLEM:

According to the 2011 Institute of Medicine 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 to $635 billion burden to the US (in 2010 dollars).[8]

Over the last decade:

- 257 million prescriptions for opioids were dispensed in 2009—a 48% increase compared with figures for 2000.
- There was a 111% increase in Emergency Department visits involving nonmedical use of prescription opioids, including hydrocodone, oxycodone, and methadone, between 2004 and 2008.
- From 1998 to 2008 there was a 400% increase in substance abuse treatment program admissions among people ages 12 and older who reported any pain reliever abuse.
- 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 10-25%.
- 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.

Source: Centers for Disease Control and Prevention

BACKGROUND INFORMATION ON THE ER/LA OPIOID ANALGESIC REMS:

The FDA held several meetings in 2010 and discussed at length with professional and patient organizations, industry, and at public meetings whether a risk evaluation and mitigation strategy (REMS) for the class of ER/LA opioid analgesic medications was required. The FDA analyzed the advice and comments provided during the meetings and determined that a class-wide REMS was necessary.

Section 505-1 of the Federal Food Drug and Cosmetic Act (FDCA) authorizes the FDA to require a REMS if the FDA determines that such strategy is necessary to ensure that the benefit of a drug outweighs the risks.

In accordance with section 505-1 of the FDCA, the FDA has determined that a REMS is necessary for all ER/LA opioid products. The FDA wants to ensure that the benefit of

ER/LA opioids products outweigh the risks of adverse outcomes (addiction, unintended overdose, and death) resulting from inappropriate prescribing, abuse, and misuse.

In the interest of public health and to minimize the burden on the healthcare delivery system of having multiple unique REMS programs, the FDA has determined that a single shared system should be used to implement the REMS for all members of the class.

Source: FDA REMS Letter to Manufacturers April 2011

In accordance with the statutory requirements for REMS, the RPC must ensure that "Training," which in this REMS will be accredited CE training, is made available to prescribers of ER/LA opioid products. The FDA has stated that "REMS-compliant training" must include all elements of the FDA Blueprint, a post-course knowledge assessment of all sections of the FDA Blueprint, and be subject to independent audit to confirm that conditions of the REMS training have been met. (FDA has agreed that Accrediting Bodies can serve as the independent auditors).

The RPC is utilizing the Request for Grant Applications (RFA) process. An RFA is a written notification which is being generated and distributed by the RPC describing appropriate areas of interest for which funding is available to support REMS CE. All grant applications received in response to the RFA will be thoroughly and critically reviewed by members of the RPC Grant Review Committee and the RPC Oversight Committee.

The Institute of Medicine report, "Health Professions Education: A Bridge to Quality," states, "… a new vision for clinical education in the health professions . . . is centered on a commitment to, first and foremost, meeting patients' needs."[7] The new vision reads: "***All health professionals should be educated to deliver patient centered care as members of an interdisciplinary team, emphasizing evidence based practice, quality improvement approaches, and informatics.***"

Perspectives on Educational Activity and Method of Education:

The most effective CE for health professionals is designed with a strong link to clinical practice.[1,2] The RPC is interested in supporting CE for HCPs that employs a variety of methods and educational vehicles that are designed based on adult learning preferences and strategies to reinforce educational interventions.[3,4,5]

Seven key attributes for effective education have been described by Robert Fox:[6]

1. Based on needs
2. Simulates application
3. Interactive with teachers, materials and colleagues
4. Provides anonymous, accurate feedback
5. Allows for reflection on practice
6. Allows learners some control over the experience
7. Leads to verifiable outcomes

These attributes will be among the considerations the RPC utilizes to evaluate grant applications received in response to this RFA.

---

1. Cauffman JG, et al (2003). Randomized controlled trials of continuing medical education: what makes them most effective? J Contin Educ Health Prof. Spring;23(2):67.

2. Bloom, B (2005). 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, 21:3, 380–385.

3. Davis DA, et. al. (1999). Impact of formal continuing medical education – Do conferences, workshops, rounds, and other traditional continuing education activities change physician behavior or health care outcomes? JAMA. 282: 867-874.

4. Marinopoulos SS, et al. (2007). Effectiveness in continuing medical education. Evid Rep Technol Assess (149):1-69.

5. Bordage, G et al. Continuing Medical Education Effect on Physician Knowledge. Effectiveness of Continuing Medical Education: American College of Chest Physicians Evidence-Based Educational Guidelines.CHEST.2009;135(suppl):29S-36S.

6. Fox R. presentation at the Pharmaceutical Alliance for CME (PACME) meeting, 2005.

7. IOM (Institute of Medicine). 2003. *Health Professions Education: A Bridge to Quality*. National Academies Press.

8. Committee on Advancing Pain Research, C.a.E. and M. Institute of, *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research:* The National Academies Press.

9. Adapted from FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.

RFA020912:

REQUEST FOR (GRANT) APPLICATIONS (RFA)

Extended-Release and Long-Acting Opioid Analgesics

Risk Evaluation and Mitigation Strategy (REMS)

RFA CODE: ER/LA 020912

The Extended-Release (ER) and Long-Acting (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 FDA has required manufacturers of ER/LA opioid analgesics, known as the REMS Program Companies (RPC), to provide education for prescribers of these medications.

FDA has developed a Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics ("FDA Blueprint") 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 RPC is comprised of 15 companies[4] that have extended- release (ER) and/or /long-acting (LA) opioid products. RPC-supported REMS education will be provided through accredited continuing education (CE) activities supported by independent educational grants from these ER/LA opioid analgesic companies.[9]

The RPC would like to make your organization aware of grant funds available to support accredited independent continuing education (CE) for the ER/LA class-wide opioid analgesics REMS. The RPC is utilizing this Request for Grant Applications (RFA) process for this purpose. Accredited CE Providers must be engaged in or represent healthcare professionals who provide direct patient care (eg, Schools of Medicine, Pharmacy or Nursing, Hospitals, Medical Societies, Professional Associations, or governmental organizations) and may choose to collaborate with an Educational Planner(s) to assist in the development and/or execution of a proposed educational activity. For more information on grant application submission process, please see below.

[4] As of August 2012

Background:

This RFA is being provided on the RPC website at www.ER-LA-opioidREMS.com, so that Accredited CE Providers can develop grant applications for submission through the REMS Grant Management System (GMS) portal, which is projected to go live by late September 2012. This portal allows for submission and processing of all RPC REMS grant requests and may be accessed by way of the RPC website at www.ER-LA-opioidREMS.com, via the right-hand-side link "If you are a Continuing Education Provider, click here for more information" and then clicking on the link "CE Grant Management System."

Timing for Applications:

This is the second of two RFAs in 2012. For consideration in the initial round of grant reviews, see RFA 010812 on the RPC website. **Due to the effects of Hurricane Sandy, the Grant Application Deadline for this RFA (RFA 020912) has been extended from November 5, 2012 at 11:59pm ET to November 12, 2012 at 8:00am ET.**

Goal of RFA:	The goal of this RFA is to support high quality education using evidence-based methods intended to assist in ensuring 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). This will be accomplished by employing the elements of the approved "FDA Blueprint" for CE training.
Area of Interest:	ER/LA opioid analgesics prescribing best practices
Audience:	Healthcare professionals involved in the care of patients with chronic moderate-to-severe pain, licensed to practice in the USA and its territories, especially prescribers with a DEA registration to prescribe Schedule II and III drugs
Budget:	Preference will be given to Programs that demonstrate they are cost-effective, collaborative, and innovative educational activities. Budgets should be consistent with the reach and scope of the proposal. To optimize the learning opportunities, the RPC intends to fund multiple activities dispersed across multiple providers. Therefore preference will be given to those grant requests that permit the RPC to support multiple high quality programs that will enable achievement of the prescriber education participation goals as described in the FDA-approved ER/LA Opioid REMS. Because of the intent to fund multiple diverse activities, there will need to be

significant justification for consideration of single proposals in excess of $5M.

Parameters: **The successful grant application will include:**

1. Clear articulation of the elements of the approved FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics that are addressed by the proposal
2. Programming designed:
    a. Using evidence-based adult learning principles/preferences (see below):
        - Needs assessment of the target audience,
        - Instructional design appropriate to the target audience,
    b. To have the ability to provide learning opportunities to an interprofessional audience of prescribers
    c. To have a broad reach, with the ability to be scaled to meet needs of specific prescriber populations.
3. An assessment component that measures the effectiveness of programming that employs:
    a. ACCME PARS or other Accreditor database fields for data aggregation
    b. MedBiquitous ER/LA REMS standards in design to provide a uniform data set to FDA. ER/LA REMS standards are currently in development with MedBiquitous.
    c. AT MINIMUM includes evidence of program completion and assessment of change in prescriber knowledge and competence
4. Programming that adheres to standards for program planning and commercial support promulgated by the Accreditation Council for Continuing Medical Education® (ACCME®), or of another CE accrediting body appropriate to the prescribers' medical specialty or healthcare profession.

    Note: Co-sponsorships, partnerships, and or collaboration with other organizations engaged in education, including healthcare quality-focused

organizations, medical societies, medical centers, and other Accredited CE Providers are encouraged.

Submission Link: Grant applications must be submitted via the GMS. When the GMS system is operational, you may access it by way of the RPC website at www.ER-LA-opioidREMS.com, via the right-hand-side link "If you are a Continuing Education Provider, click here for more information." For this specific RFA, the appropriate RFA code is 020912**.**

Applicant Eligibility Criteria

- Accredited CE Providers must be engaged in or represent healthcare professionals who provide direct patient care (eg, Schools of Medicine, Pharmacy or Nursing, Hospitals, Medical Societies, Professional Associations, or governmental organizations).
- Applicants must be accredited to provide CE by a national accrediting body*; or by an official state accrediting agency, and must demonstrate that their organization is in good standing at the time of application.
- Applicants must have demonstrated capabilities in the design and successful implementation of complex projects.
- Any educational activities proposed and implemented must be fully compliant with all applicable accrediting body standards, as well as other relevant standards, guidelines and requirements as they apply to the conduct of independent medical education.
- All grant applicants must describe their processes for: confirming that all elements of the "FDA Blueprint" are addressed, validating content for scientific and medical content accuracy, ensuring fair balance and controlling bias, as well as assuring that the education includes a post-activity knowledge assessment of all sections of the "FDA Blueprint."
- All grant applicants must be organizations in the United States and its territories.

* Eg ACCME, AAFP, AANP, AAPA, ACPE, ADA, ANCC, AOA, or equivalent accrediting body.

Required grant proposal elements:

1. Name of organization and person(s) responsible for this project
2. Name of any partner organizations involved with the proposed education, along with roles and responsibilities
3. Baseline summary of needs data, initial metrics, or project starting point

4. Description of project goal(s)
5. Description of educational methods to be utilized
6. Demonstration that the learning objectives address the needs assessment within the intended audience, instructional design, and architecture of the proposed activity
7. Narrative describing the proposed program in detail. Each activity component description must include the rationale and intended audience
8. Narrative describing quantitative/qualitative measures of success that must include audience reach and educational impact on healthcare professional's knowledge and competence, and may include attitudes, perceptions and skills
9. Description and qualifications of the members of the team that will be responsible for implementing this project
10. Explanation of rationale, efficiencies, and cost-effective approaches to both the live and enduring components
11. Detailed project timeline for each phase and milestone. This will serve as the basis of the milestone payments in the grant as described below
    a. Execution of Letter of Agreement: 35%
    b. Start of First Activity and Upon Acceptance of Update Report: 25%
    c. Mid-term of Grant Timeline and Upon Acceptance of Update Report: 30%
    d. Completion of Last Activity and Receipt/Acceptance of Required Grant-Related Documentation: 10%
12. Detailed budget provided using the template residing in the REMS Grant portal

SCOPE OF THE PROBLEM:

According to the 2011 Institute of Medicine 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 to $635 billion burden to the US (in 2010 dollars).[8]

Over the last decade:

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

- There was a 111% increase in Emergency Department visits involving nonmedical use of prescription opioids, including hydrocodone, oxycodone, and methadone, between 2004 and 2008.
- From 1998 to 2008 there was a 400% increase in substance abuse treatment program admissions among people ages 12 and older who reported any pain reliever abuse.
- 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 10-25%.
- 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.

Source: Centers for Disease Control and Prevention

BACKGROUND INFORMATION ON THE ER/LA OPIOID ANALGESIC REMS:

The FDA held several meetings in 2010 and discussed at length with professional and patient organizations, industry, and at public meetings whether a risk evaluation and mitigation strategy (REMS) for the class of ER/LA opioid analgesic medications was required. The FDA analyzed the advice and comments provided during the meetings and determined that a class-wide REMS was necessary.
Section 505-1 of the Federal Food Drug and Cosmetic Act (FDCA) authorizes the FDA to require a REMS if the FDA determines that such strategy is necessary to ensure that the benefit of a drug outweighs the risks.
In accordance with section 505-1 of the FDCA, the FDA has determined that a REMS is necessary for all ER/LA opioid products. The FDA wants to ensure that the benefit of ER/LA opioids products outweigh the risks of adverse outcomes (addiction, unintended overdose, and death) resulting from inappropriate prescribing, abuse, and misuse.
In the interest of public health and to minimize the burden on the healthcare delivery system of having multiple unique REMS programs, the FDA has determined that a single shared system should be used to implement the REMS for all members of the class.
Source: FDA REMS Letter to Manufacturers April 2011

In accordance with the statutory requirements for REMS, the RPC must ensure that “Training,” which in this REMS will be accredited CE training, is made available to prescribers of ER/LA opioid products. The FDA has stated that “REMS-compliant training” must include all elements of the FDA Blueprint, a post-course knowledge assessment of all sections of the FDA Blueprint, and be subject to independent audit to confirm that conditions of the REMS training have been met. (FDA has agreed that Accrediting Bodies can serve as the independent auditors).

The RPC is utilizing the Request for Grant Applications (RFA) process. An RFA is a written notification which is being generated and distributed by the RPC describing appropriate areas of interest for which funding is available to support REMS CE. All grant applications received in response to the RFA will be thoroughly and critically reviewed by members of the RPC Grant Review Committee and the RPC Oversight Committee.

The Institute of Medicine report, "Health Professions Education: A Bridge to Quality," states, "… a new vision for clinical education in the health professions . . . is centered on a commitment to, first and foremost, meeting patients' needs."[7] The new vision reads: "***All health professionals should be educated to deliver patient-centered care as members of an interdisciplinary team, emphasizing evidence-based practice, quality improvement approaches, and informatics.***"

Perspectives on Educational Activity and Method of Education:
The most effective CE for health professionals is designed with a strong link to clinical practice.[1,2] The RPC is interested in supporting CE for HCPs that employs a variety of methods and educational vehicles that are designed based on adult learning preferences and strategies to reinforce educational interventions.[3,4,5]
Seven key attributes for effective education have been described by Robert Fox:[6]

1. Based on needs
2. Simulates application
3. Interactive with teachers, materials and colleagues
4. Provides anonymous, accurate feedback
5. Allows for reflection on practice
6. Allows learners some control over the experience
7. Leads to verifiable outcomes

These attributes will be among the considerations the RPC utilizes to evaluate grant applications received in response to this RFA.

---

1. Cauffman JG, et al (2003). Randomized controlled trials of continuing medical education: what makes them most effective? J Contin Educ Health Prof. Spring;23(2):67.

2. Bloom, B (2005). 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, 21:3, 380–385.

3. Davis DA, et. al. (1999). Impact of formal continuing medical education – Do conferences, workshops, rounds, and other traditional continuing education activities change physician behavior or health care outcomes? JAMA. 282: 867-874.

4. Marinopoulos SS, et al. (2007). Effectiveness in continuing medical education. Evid Rep Technol Assess (149):1-69.

5. Bordage, G et al. Continuing Medical Education Effect on Physician Knowledge. Effectiveness of Continuing Medical Education: American College of Chest Physicians Evidence-Based Educational Guidelines.CHEST.2009;135(suppl):29S-36S.

6. Fox R. presentation at the Pharmaceutical Alliance for CME (PACME) meeting, 2005.

7. IOM (Institute of Medicine). 2003. *Health Professions Education: A Bridge to Quality*. National Academies Press.

8. Committee on Advancing Pain Research, C.a.E. and M. Institute of, *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research:* The National Academies Press.

9. Adapted from FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.

Appendix F: Grant Request Review Criteria

Criteria Name	Scale	Criteria Summary
1. Compliance	0 / 1	▪ Compliant with relevant laws, rules, guidelines, incl. ACCME SCS, Pharma Code, OIG ▪ If score 0: Disqualification
2. Alignment	0 / 1	▪ Elements of the approved FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics are clearly articulated ▪ Aligned to educational goals described in the RFA ▪ If score 0: Disqualification
3. Qualifications of Provider and Partners	0–3	▪ Reputation of CE provider organization (eg, accreditation standing, experience in the field of pain education, recognition/awards for educational activities, collaboration) ▪ Appropriateness of organization as a provider of REMS CE (eg, Schools of Medicine, Pharmacy or Nursing, Hospitals, Medical Societies, Professional Associations, or governmental organizations) ▪ Applicant must be the Provider of Record, and meet qualifications described in RFA (Applicant Eligibility Criteria: provides care/represents prescribers who provide care) ▪ If score 0: Disqualification
4. Needs Assessment (NA)	1–4	▪ Systematically describes knowledge gaps and practice gaps of target learners ▪ Employs quantitative/qualitative data describing educational needs (knowledge, competence, or performance) of target learners ▪ Links the use of education as a method to address those gaps
5. Purpose or Learning Objectives (LO)	0–3	▪ Stated learning objectives are specific, articulate, and appropriate for program ▪ Learning objectives address identified gaps in knowledge, competence, performance
6. Educational Design	0–5	▪ Clear explanation and rationale for the instructional design to be employed is provided ▪ Educational design is based on and relevant to needs, objectives, and style of target learners

Criteria Name	Scale	Criteria Summary
		▪ Evidence-based approach is employed
7. Program Design	0–3	▪ Focus of the program is education; majority of program time is devoted to learning ▪ Clear description of program and its component activities is provided ▪ Appropriate timeline is provided for all activities for which funding is requested ▪ Activities/educational interventions are appropriate for setting/desired activity results
8. Evaluation / Outcomes	0–7	▪ Includes clear description and rationale for outcomes level to be achieved ▪ Includes clear description of the evaluation methods both to determine whether the learning objectives of the program have been met and to assess the impact of the program based on an accepted outcomes scale (and, in the future, the outcomes from ER/LA Opioid REMS assessment)
9. Educational Innovation	0–3	▪ Creative and original concepts, innovative educational methodology are incorporated ▪ Evidence of inter-professional collaboration
10. Significance/ Impact	0–4	▪ Importance and likelihood of contributing to the improvement of patient care ▪ Importance and likelihood of advancing knowledge, skills, attitudes and performance relative to the objectives of the ER/LA Opioid REMS ▪ Likelihood of achieving significant HCP participation (REMS performance goals) ▪ Impact on broadening the participation of (and reach to) underrepresented groups (eg, gender, ethnicity, disability, geographic) relative to this REMS
11. RPC Budget	0–2	▪ Alignment and fit with RPC CE budget ▪ Congruence of budget with proposed program activities ▪ Cost-effective program design is provided ▪ Honoraria is itemized and appropriate for activity

Criteria Name	Scale	Criteria Summary
12. Operational Performance	0–2	▪ Veracity of proposal in meeting performance and outcome targets ▪ Detailed description of the process for tracking the financial, operational ,and attendance metrics outlined in the proposal, and providing status updates for milestone reporting ▪ Detailed description of the process to be deployed if provider is not meeting the committed metrics in the proposal ▪ Methods of audience recruitment are defined and independent