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ER/LA Opioid Analgesics REMS Overview – REMS Program Companies (RPC) Presentation

FDA Meeting

January 25, 2017

ER/LA Opioid Analgesics REMS Sponsors

- 3M Company
- Allergan Sales, LLC
- Apotex Inc.
- Aurolife Pharma, LLC
- Collegium Pharmaceutical, Inc.
- Daiichi Sankyo, Inc.
- Depomed, Inc.
- Endo Pharmaceuticals Inc.
- Impax Laboratories, Inc.
- Janssen Pharmaceuticals, Inc.
- Mallinckrodt, Inc.
- Mayne Pharma Inc.
- Mylan Inc.
- Nesher Pharmaceuticals (USA) LLC
- Novel Laboratories, Inc.
- Osmotica Pharmaceutical Corp.
- Pernix Therapeutics Holdings, Inc.
- Perrigo Company plc
- Pfizer, Inc.
- Purdue Pharma L.P.
- Ranbaxy Pharmaceuticals, Inc.
- Rhodes Pharmaceuticals L.P.
- Sandoz Inc.
- Teva Pharmaceuticals USA LLC
- The PharmaNetwork LLC
- Upsher-Smith Laboratories, Inc.
- VistaPharm, Inc.
- West-Ward Pharmaceuticals Corp.

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Current ER/LA Opioid Analgesics REMS Program History

April 2011: FDA notified manufacturers of ER/LA opioid analgesics of the requirement to submit a proposal for a class-wide, single, shared REMS.

January 2012: Approved ER/LA opioid analgesic NDA/ANDA holders executed a written agreement that created the RPC, which has overall responsibility for the program.

The ER/LA Opioid Analgesics REMS was approved on July 9, 2012.

- **The results of the REMS are now provided annually to FDA in July.**
- **As of February 29, 2016:**
  - **157,430 HCPs completed REMS-compliant accredited CE programs**
  - **Of those completers, 66,881 are ER/LA Opioid Prescribers**

May 2016: The RPC presented the results of the REMS Assessments at a Joint Advisory Committee Meeting. The committee voted unanimously to modify the REMS, with one of the recommendations being to include IR opioids in the program.

December 2016: FDA asked the RPC to provide an overview at this 1/25 meeting of the ER/LA Opioid Analgesics REMS and the RPC's current thinking on incorporating IR manufacturers into the program.

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Current Components of the ER/LA Opioid Analgesics REMS

Goal	**Reduce serious adverse outcomes resulting from inappropriate prescribing, misuse, and abuse of extended-release or long-acting (ER/LA) opioid analgesics while maintaining patient access to these medications. Adverse outcomes of concern include addiction, unintentional overdose and death.**
Central Component	**Accredited continuing education (CE) program for prescribers that is intended to enhance the safe and effective use of ER/LA opioid analgesics.**

Core Program Components

Accredited CE: Available to opioid prescribers and based on learning objectives established by the FDA Blueprint

Medication Guide: Dispensed with ER/LA opioid prescriptions and available through the website

Patient Counseling Document: One-page tool intended to facilitate important discussions between prescribers and patients

Website: Facilitates prescriber awareness of the availability of the REMS and REMS-compliant CE

Call Center: Single toll-free number that provides information and addresses questions from callers

Prescriber Communications: Provide information about the REMS and CE to DEA-registered prescribers of Schedule II/III drugs

Assessments: Submitted annually to the FDA

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Current RPC Organizational Structure

Participant Companies

- Holders of approved ER/LA opioid analgesic NDA(s)/ANDA(s)
- Overall responsibility for program development and implementation

RPC Subteams

- Specialized subteams focused on specific aspects / core workstreams of the REMS
- Examples: CE, Metrics, Regulatory, Drug Safety, External Communications

Non-Member Observer Companies

- Companies with filed/pending NDA(s)/ANDA(s) for ER/LA opioid analgesics, permitted to attend RPC and Subteam meetings

Current RPC Organizational Structure, cont'd.

Program Management Office (PMO)

- External project management vendor contracted by the RPC
- Provides overall REMS program management

REMS Vendors

- Contracted with and managed by the PMO on behalf of the RPC
- Provide specific REMS program services – e.g., surveillance monitoring, prescriber survey, website update and maintenance

CE Grantees

- CE providers that receive grants from the RPC
- Independently develop and provide REMS-compliant accredited CE programs

Current Process for Integrating New Participant Companies

1) FDA informs company of need to meet REMS requirements

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2) Company contacts RPC FDA Liaison, who informs PMO and RPC Legal

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3) Company executes a confidentiality agreement

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4) Company executes membership documentation

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5) Company initiates program participation

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6) Company offered orientation session

Comments

- Current contracting process for a single company takes 1-3 months
- Once a company initiates program participation, multiple process changes and updates to materials are required, for example:
  - REMS materials
  - Assessment protocols
  - Website listing of companies and products
  - Call center materials

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General Considerations for Integrating IR Opioid Manufacturers

Multiple steps are being discussed to update the governance and program processes to allow for expansion in the number of participating companies.

- **Revision of the membership agreements**
- **Updating of current administrative processes**

The RPC envisions that the process of revising, approving and having all 28 companies execute the updated membership agreements may take up to six months to complete.

The proposed onboarding process for IR companies applies only to companies that are not already participating in the ER/LA Opioid REMS.

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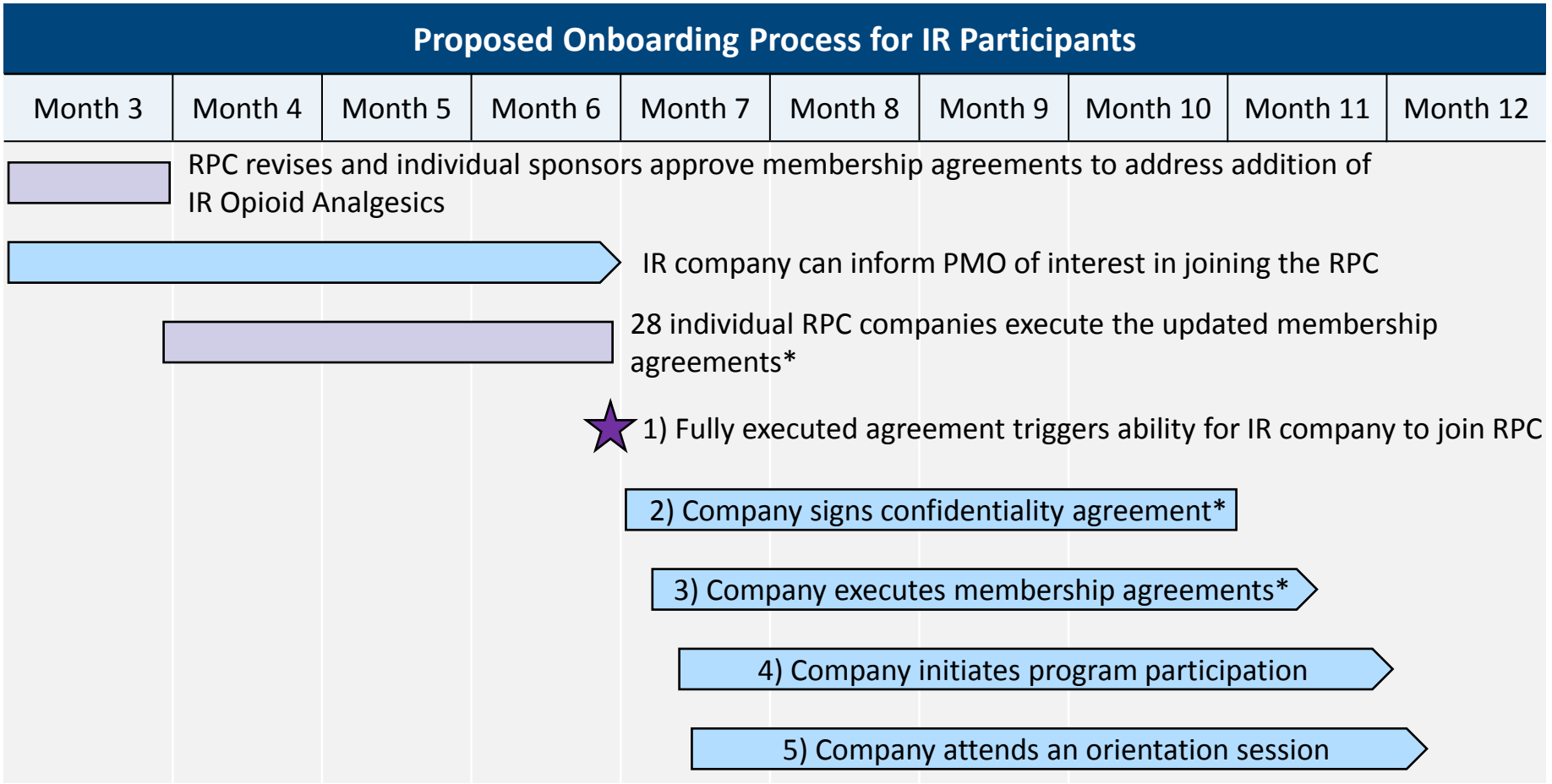
Proposed Timeline for Integrating 50+ Companies



*Timeline could be compressed if companies execute the relevant agreement(s) promptly.

Specific Considerations for Integrating IR Manufacturers

Updating RPC Documents

- Revise, approve, and execute membership agreements to address inclusion of IR manufacturers and ensure program structure can support 90+ companies

Updating REMS Materials

- Update/develop Medication Guide, Patient Counseling Document, and Healthcare Provider REMS communications
- Develop website for updated Opioid Analgesics REMS

Updating Program Processes

- Establish and implement Drug Master File for REMS document updates and assessment report submissions
- Incorporate and implement additional program changes required by the FDA resulting from Joint Advisory Committee recommendations

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Additional Challenges

Changes to the REMS program, once communicated by the FDA, may substantially impact existing REMS-compliant accredited CE activities and the current REMS Assessments, which may present challenges. The RPC asks the FDA to consider the following:

- Updating the Blueprint and Training Requirements must take into account the next steps for:
  - Previous completers of REMS-compliant accredited CE and other available courses
  - The length of the educational programs
  - Transition from current approved REMS-compliant accredited CE programs to those with updated content
  - Determining which additional prescriber groups should be included
- Changes must be clearly communicated to avoid confusion among various stakeholder groups
- A large number of competing educational programs will remain
- Other initiatives to address the opioid crisis will continue to confound REMS Assessments

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THANK YOU

The RPC looks forward to working with both the FDA and the IR opioid sponsors to help address this public health crisis

To begin the process of joining the RPC, please reach out to:

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