Industry Meeting to Discuss Opioid Analgesics REMS

MEETING DATE/TIME: January 25, 2017 @ 9:30 AM

LOCATION: White Oak Campus
10903 New Hampshire Avenue
Building 02, Room 2047 W
Silver Spring, MD 20903

MINUTES RECORDER: Wendy B. Brown, PharmD, BCACP

PANEL MEMBERS	TITLE
Douglas C. Throckmorton, MD	Deputy Director, Center for Drug Evaluation and Research (CDER)
Theresa Toigo, RPh, MBA	Associate Director for Drug Safety Operations, CDER
Claudia Manzo, PharmD	Director, Office of Medication Error Prevention and Risk Management (OMEPRM), Office of Surveillance and Epidemiology (OSE), CDER
Sharon Hertz, MD	Director, Division of Anesthesia, Analgesia and Addiction Products (DAAAP), Office of New Drugs (OND), CDER
Doris Auth, PharmD	Acting Associate Director, Division of Risk Management (DRISK), OSE, CDER
Elaine Lippmann, J.D.	Senior Regulatory Counsel, Office of Regulatory Policy (ORP), CDER

COMPANY NAME	ATTENDEE
Elite Pharma	Sophy Abraham (r)[1]
Vertice Pharma	Deepa Adiga (r)
AUROBINDO	Aysha Amman
PuraCap	Bernadette Attinger
Allergan	Carla Barrett
Sunrise Pharm	Deepak Bhalla
Inventive Health	Deborah Bingham
Inventive Health	Caitlin Briggs
NEOS	Willene Brondun (r)
Cipher	Lynne Bulger (r)
ANI Pharm	Ellen Camos (r)
Tris	Norma Cappetti (r)
Pernix Therapeutics	Elke Carter
Janssen	Soledad Cepeda
Apotex	Colin D'Cunha (r)

[1] *(r)* refers to meeting participant via remote access

Novel	Darshna Desai
AcelRx	Karen DiDonato
Amneal	Candis Edwards
Endo	Kal Elhoregy
Mallinckrodt	Lori Fiorentino
Mylan	Juliane Foley
Purdue	Enrique Garcia
West-Ward Eatontown, NJ	Nicole Garrity (r)
Lehigh Valley Technologies	Melissa Goodhead
Validus Pharm	Richard Guarino
Valeant	Mary Harrell (r)
Sun Pharma	Virginia Hogan (r)
Constantine Cannon	Mike Kayan
Inspirionrx	Eric Kinzler
Mallinckrodt	Karen Kapicko
Mallinckrodt	Nathan Kopper
Apotex	Kiran Krishnan (r)
Wockhardt	Poonam Kumar (r)
Sovereign Pharm.	Len Lawrence
Apotex	Kimberly Lovisek (r)
West-Ward Columbus	Suzanne McLeod
Apotex	Reshma Modi (r)
Janssen	Mary Mulligan
Oxford Pharmaceutical	Dave Murray (r)
Accord Healthcare	Sabita Nair
KVK Tech	Ranga Namburi (r)
KVK Tech	Shabari Nyalakonda (r)
KVK Tech (Avanthi)	Ashvin Panchal (r)
Dailchi Sankyo Pharma Dev	Ford Parker
Rhodes Pharma	Shiris Patel
Sunrise Pharm	Jayanti Patel (r)
Apotex	Victor Ramsaywak (r)
AbbVie	Cheryl Renz (r)
Wes Pharma Inc	Ganti Satya
Sentynl Therapeutics	Shawn Scranton
Pernix Therapeutics	Marsha Stanton
Lannett	Kristie Stephens
Egalet	Kurt Strittmatter (r)
RPC Vertical Pharm	Sharon Suarez (r)
Mikart	Jason Waldroup (r)
Perrigo	Keith Webber
Upsher-Smith Labs	Gregory Wedin
Collegium	John Weet
Inventive Health	John West
Pfizer	Gary Wilson (r)
Sandoz	John Peter Zak

BACKGROUND:

On July 9, 2012, FDA approved the risk evaluation and mitigation strategy (REMS) for extended-release (ER) / long-acting (LA) opioid analgesics. The goal is to reduce the serious adverse outcomes of overdose, addiction, and death that result from long-standing problems of inappropriate prescribing, misuse, and abuse of these products. The ER/LA opioid analgesics REMS is part of a multi-agency Federal effort to address the growing problem of prescription drug abuse and misuse. The central component of the ER/LA opioid analgesics REMS is an education program for prescribers (e.g., physicians, nurse practitioners, physician assistants). Under the REMS, application holders of ER/LA opioid analgesics are required to make educational programs available to health care providers (HCPs) who are prescribers of ER/LA opioid analgesics. The application holders are meeting this requirement by providing educational grants to accredited continuing education (CE) providers who offer training to prescribers at no or nominal cost. The ER/LA opioid analgesics REMS also includes a patient counseling document for prescribers to assist them in properly counseling patients on their responsibilities for using these medicines safely and to provide patients with additional written instructions as needed. The labeling for ER/LA opioid analgesics includes a product-specific, one-page Medication Guide to be given to patients each time they receive a prescription of their ER/LA opioid analgesic medicine.

In February 2016, FDA announced a multipart plan to address the opioid epidemic. As part of the plan, FDA stated its intent to update the REMS program requirements for opioids after considering advisory committee recommendations and review of existing requirements. On May 3 and 4, 2016, FDA held a joint meeting of the Drug Safety and Risk Management and Anesthesia and Analgesic Drug Products Advisory Committees. Results of a 36-month REMS assessment were presented at this meeting. The goal of the meeting was to seek comments from committee members as well as the public as to whether the ER/LA opioid analgesics REMS was meeting its goals: to assure safe use, without being unduly burdensome to patient access to the drugs and, to the extent practicable, minimize the burden to the health care delivery system. FDA also sought input from committee members on whether the REMS should be modified.

The committee members recommended that FDA (1) expand REMS requirements to include immediate-release (IR) opioid analgesics; (2) expand the FDA blueprint to incorporate pain management and education messages for other health care professionals involved in the management of patients with pain; and (3) require that education be mandatory, though options other than a REMS should be explored.

Because FDA recognized that developing a REMS for these widely prescribed products involving numerous application holders will present some challenges, FDA invited all affected application holders[2] to a January 2017 meeting to discuss the recommendations from the advisory committee members, the Agency's thinking regarding the recommendations, and potential strategies for developing an expanded REMS program.

[2] *Application holders* refers to all the manufacturers of new drug applications (NDAs) and abbreviated new drug applications (ANDAs) for ER/LA opioid analgesics that are subject to the REMS requirements. (ANDAs are commonly referred to as *generic drugs*.) The application holders have come together as a consortium and formed the REMS Program Companies (RPC). Throughout this background document, the manufacturers may be referred to as *application holders*, *applicants*, or *RPC*.

MEETING MINUTES:

AGENDA:

9:30 am – 9:35 am	Welcome	Douglas C. Throckmorton, MD Deputy Director for Regulatory Programs, CDER
9:35 am – 9:40 am	Introductions	Terry Toigo, RPh MBA Associate Director for Drug Safety Operations, CDER
9:40 am – 9:50 am	Development of the 2012 ER/LA Opioid Analgesic REMS	Terry Toigo, RPh, MBA Associate Director for Drug Safety Operations CDER
9:50 am – 10:00 am	Advice from Joint DSaRM and AADPAC Advisory Committees, May 3-4, 2016	Doris Auth, Pharm.D. Associate Director (Acting), Division of Risk Management, Office of Medication Error Prevention and Risk Management, CDER
10:00 am –10:10 am	FDA Plan: Opioid Analgesic Education	Sharon Hertz, MD Director, Division of Anesthesia, Analgesia and Addiction Products, Office of New Drugs, CDER
10:10 am – 10:25 am	Development of Shared System REMS	Elaine Lippmann, J.D. Senior Regulatory Counsel, Office of Regulatory Policy, CDER
10:25 am – 10:40 am	ER/LA Opioid Analgesics REMS Overview – REMS Program Companies (RPC) Presentation.	Greg Wedin Associate Director, Pharmacovigilance & Medical Information, Upsher-Smith Laboratories Nathan Kopper, Pharm.D., REMS Manager, Mallinckrodt
10:40 am – 11:30 am	Questions and Comments from Industry	FDA/Industry Panel

SUMMARY of MEETING DISCUSSION:

1. **Industry Question/Comment:** Grants for continuing education (CE) grantees for 2016-2017 do not include IR opioid analgesics. Incorporation of IR opioid analgesics into the REMS CE programs will involve a phased process. The RPC will work with Medbiquitous to define the new targeted prescribers. However, the process for awarding new [educational] grants for 2018 will begin within the next few months. To be able to appropriately plan the CE programs for 2018, we will need to see the final expanded FDA blueprint and a new patient counseling document by about May 2017.

Agency Response/Discussion: *The Agency asked how much flexibility there was with industry timelines associated with the expanded FDA blueprint. Industry indicated that there is not much flexibility; communication from the RPC to the potential 2018 CE grantees starts in April 2017. They clarified, though, that an outline of the expanded FDA blueprint (without all of the key messages) would be sufficient to begin the grant process, with specifics made available by the time grants are awarded —grants will be awarded in the summer of 2017 for the year of 2018. Industry indicated that it would be helpful to have the complete FDA blueprint later this year.*

2. **Industry Question/Comment:** Has the Agency made any other plans to measure how effective the modified REMS program will be? How long will it be before the public health outcomes of the REMS program are available?

   Agency Response: *The evaluation of the REMS has been challenging. The Agency is currently working with the RPC on changes to the assessments based on recommendations from the ER/LA REMS AC meeting in May 2016.*

3. **Industry Question/Comment:** Regarding the process of onboarding for IR application holders, has FDA or the RPC considered stepping back to an earlier REMS development phase to facilitate the incorporation of the new IR application holders? If not, there may be additional problems. Including IR application holders earlier in the process, rather than later, may help to smooth the onboarding process.

   Agency Response: *The Agency hopes that this expansion will not require going back to square one with REMS development because the current program has an existing industry infrastructure already in place.*

   RPC Response: *The proposed timeline includes 6-months for the RPC to revise current documents and agreements to include the IR opioid analgesics. New companies can begin to contact the RPC immediately following this meeting, which will also facilitate the process. The RPC will also continue working with legal input to facilitate the process.*

4. **Industry Question/Comment:** Will only Schedule II, IR opioid drug products be covered by REMS? For instance, Schedule III drug products would be excluded?

   Agency Response: *All scheduled opioid analgesics intended for outpatient use will be included in the REMS. However, it will not include transmucosal IR fentanyl (TIRF) products because they are covered under a separate REMS.*[3]

5. **Industry Question/Comment:** Prescriber behavior has been identified as part of the problem. How does this REMS program address changing prescriber behavior?

[3] The existing ER/LA opioid analgesics REMS includes a few Schedule III products.

Agency Response: *We are working on this because it is a very important aspect. The plan is to try and change prescriber behavior by educating prescribers more broadly on pain management. We are looking for ways to measure changes in prescriber behavior. Input is being sought from other relevant public agencies, and work continues.*

6. **Industry Question/Comment**: As addition of specialties or other HCPs are considered, will there be modification to the total number of prescribers to be trained?

   Agency Response: *The ultimate goal is to educate all prescribers registered with the DEA.*

7. **Industry Question/Comment:** Will other HCPs (e.g., institutional DEA prescribers, etc.) be included in the total, as completers? Data on physicians' assistants (PAs) and nurse practitioners (NPs) prescribers are already being collected, but not counted towards completer totals.

   Agency Response: *We anticipate that anyone that completes the training will be included in the total as a completer though we hope to identify the subset of the total completers that prescribe IR or ER/LA opioid analgesics. PAs and NPs should already be included in the totals if they are prescribing these products.*

8. **Industry Question/Comment:** A question was raised about other components of the REMS.

   Agency Response: *The Medication Guides have just been revised, and we do not anticipate further revisions at this point. However, we encourage the RPC to begin working on the additional materials (letters, patient counseling document, etc.). The Agency looks forward to reviewing those documents, especially because the RPC has access to the experts who can provide input on the content of those documents. The Agency encourages inclusion of IR application holders when working on updating/revising documents. Modifying the REMS documents and materials with input from IR application holders will help ensure that everyone is in agreement. The recent approval of changes to the IR opioid safety labeling is a perfect opportunity to begin using the new labeling and updating old product labeling.*

   Industry Response*: The RPC sub-workgroup has had some early discussions on the other components of the REMS, but has been waiting on further direction from the Agency.*

9. **Industry Question/Comment**: Does the Agency have plans to share this update with the EMA?

   Agency Response*: We have not yet shared this update with the EMA, but will discuss with Gerald Dal Pan (OSE Director) possible opportunities to share the information. (FDA provided an update to the EMA subsequent to this meeting)*

10. **Industry Question/Comment**: Why does FDA think expanding the prescriber population to include HCPs who may have very different behavior patterns (e.g., including PAs and NPs) would help with mitigation? We already are having problems assessing the current prescriber population?

Agency Response/Discussion*: There is overlap in the ER versus IR prescriber population, but not all prescribers for IR products prescribe ER products. It is critical that we broaden the REMS (e.g., dentists will be captured). This will help ensure appropriate use of these products by all along the pain management continuum.*

Commenter response*: In my experience, ancillary care providers do all of the counseling and provide the greatest contribution to safe use education.*

11. **Industry Question/Comment**: What's the current process for communication from the RPC to the Agency? How should feedback to the Agency be provided throughout this process?

    Agency Response*: There is a process in place by which the Agency communicates with the RPC. The Agency OSE Project Management staff is the point-of-contact for all communications with the RPC, which also has a single point-of-contact. This process will continue. For questions that relate to a specific application, applicants should use the usual communication process involving the product's project manager.*

12. **Industry Question/Comment**: Will the Agency provide notification letters?

    Agency Response*: Yes. However, the letter should not be the start of the process, or a required precursor. IR application holders should begin communication following this meeting, and the process for onboarding should occur as soon as possible. FDA may be able to assist if needed.*

    RPC Response*: We will have to take this issue back to our legal counsel because of the existing agreements.*

13. **Industry Question/Comment**: Is FDA thinking about collaborating with other agencies and having a summit on this public health crisis?

    Agency Response*: Yes. To the extent that interagency collaboration is possible, FDA will continue to do that.*

14. **Industry Question/Comment**: It was noted that cough and cold medications are out of scope for this REMS — can we refer to this meeting to respond to a General Advice letter that was received for such a medication regarding the opioid IR REMS?

    Agency Response*: The assigned project manager for that approved drug can be contacted for additional information.*