RADARS® SYSTEM News

Researched Abuse, Diversion, and Addiction-Related Surveillance (RADARS®) System

First Quarter 2010 Volume 5, Issue 1

In This Issue

Regulatory News

FDA Draft Guidance for Industry Assessment of Abuse Potential of Drugs - Please type the following into web browser.

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM198650.pdf

RADARS System Hosts Fourth Annual Scientific Meeting: *Risk Management of Scheduled Drugs- Evaluation of REMS for Opioids*

The Fourth Annual RADARS System Scientific Meeting, *Risk Management of Scheduled Drugs – Evaluation of REMS for Opioids* took place on April 14, 2010, in Bethesda, MD, marking the eighth anniversary of the RADARS System. Seventy-six attendees, including researchers and representatives from the pharmaceutical industry and regulatory agencies, participated.

"This meeting was an opportunity to stimulate discussion on some of the current challenges facing stakeholders including development of REMS for opioids and implications of REMS policy," said Richard C. Dart, M.D., Ph.D., RADARS System Executive Director. "Guest speakers presented various considerations for evaluating REMS for opioids, including an overview by FDA, options for measuring the impact of REMS for opioids on non-patients, measuring addiction in REMS for opioids pre-DSM V and the unintended consequences of past drug risk communications."

Dr. Dart provided an overview of 2009 RADARS System data as well as a presentation of baseline RADARS System data for opioid REMS evaluations.

Leading authorities in REMS and experts in public health interventions served as speakers at the meeting. The following describes the guest speakers and their presentation topics.

- Mary Willy, Ph.D., Deputy Director of the Division of Risk Management, Office of Surveillance and Epidemiology, FDA presented *Risk Evaluation and Mitigation Strategies (REMS): An Overview.* Dr. Willy's presentation summarized the elements of REMS and the requirements for assessment of REMS efforts.
- Nabarun Dasgupta, M.P.H., from the University of North Carolina – Chapel Hill and the RADARS System presented *Options for Measuring the Impact of Opioid REMS on Non-Patients.* Mr. Dasgupta discussed that societal expectations, FDAAA citation and foreseeable (unintended) consequences of opioid exposures are all reasons for measuring non-patients in REMS for opioids.
- Charles O'Brien, M.D., Ph.D., from the University of Pennsylvania presented *The DSM Approach to Diagnosis of Addiction.* Dr. O'Brien described current development of the Diagnostic and Statistical Manual of Mental Disorders (DSM) V and how the DSM V will address addiction and opioid use disorder.
- Robert Valuck, Ph.D., R.Ph., of the University of Colorado-Denver presented *Unintended Consequences of Drug Risk Communication: The Example of Antidepressants.* Dr. Valuck discussed an example of unintended consequences of drug risk communication relating to FDA warnings on antidepressants and risk of suicidality and how those consequences can be telling when applied to evaluation of REMS for opioids.

Mary Willy, PhD, Deputy Director of the Division of Risk Management, Office of Surveillance and Epidemiology, FDA, addresses the audience at the RADARS System Annual Meeting

A summary of the meeting is posted at www.RADARS.org.

RADARS System Responds to FDA *Draft Guidance for Industry Assessment of Abuse Potential of Drugs*

On January 26, 2010, the Food and Drug Administration (FDA) released *Draft Guidance for Industry Assessment of Abuse Potential of Drugs*. The draft guidance discusses a number of items of interest to the RADARS System and sponsors. Of particular interest, the draft guidance describes approaches and methods for abuse potential assessments.

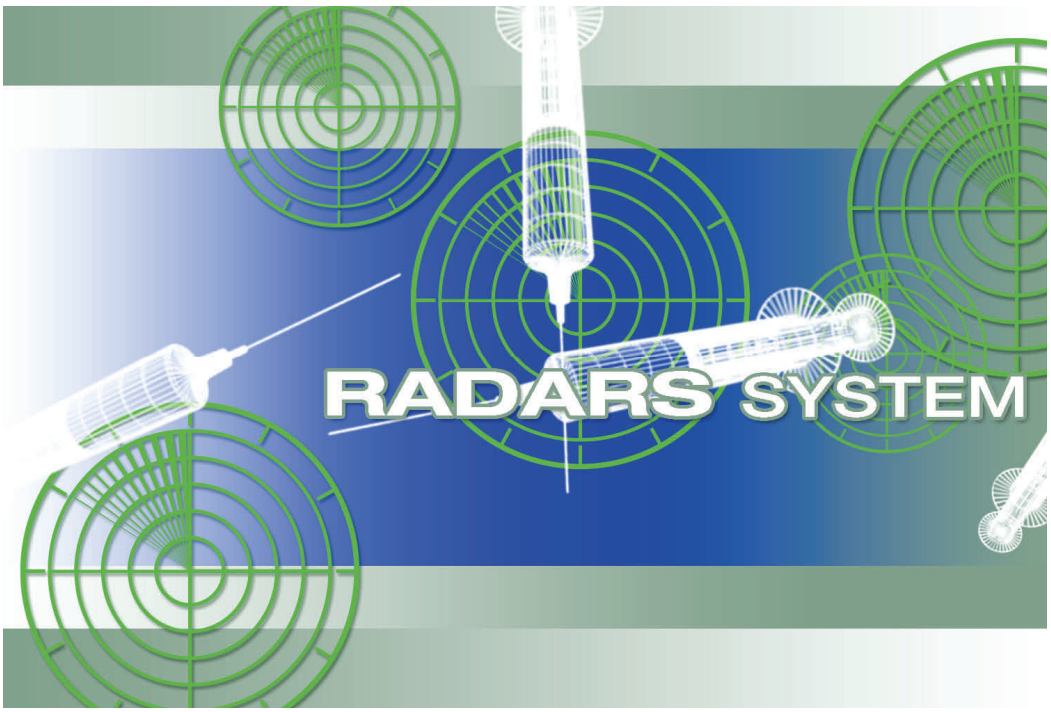
Among other things, the draft guidance states that sponsors should use publicly available data sources including but not limited to the Drug Abuse Warning Network (DAWN), the National Survey on Drug Use and Health (NSDUH), the Treatment Episode Data Set (TEDS), and Monitoring the Future (MTF) to monitor and assess risk potential of their products.

In the draft guidance, FDA further states, "Information from other sources that is neither systematically acquired nor statistically significant can provide only anecdotal information that a substance is being illicitly used, purchase, sold or diverted.

Richard Dart, M.D., Ph.D. commented. "In addition to the publicly available data listed by the FDA in the draft guidance, it is important to know that RADARS System data are systematically collected and go through robust quality assurance to ensure the end products are accurate data that meet applicable regulations." In addition, RADARS System data offer the following benefits:

- Product-specificity which is crucial for reporting differences observed due to the presence of abuse deterrent or extended release mechanisms, and between generic and branded products, among others.
- Research questions can be tailored according to the nature of a product's abuse deterrent properties since tracking overall coarse indicators is insufficient.
- Data collected and reported at regular, frequent time intervals (each quarter) with a short lag time (4 months after the end of the quarter of interest).

The RADARS System collects data in a systematic fashion and has a rigorous quality assurance program in place to assure that valid, accurate data are reported. Quality assurance programs are a crucial component of any surveillance system. A good quality assurance program consists of planned and systematic actions that ensure the project is performed and data are generated, documented and reported in accordance with Standard Operating Procedures (SOPs) and applicable regulations. The entire RADARS System quality assurance program ensures accurate data that meets regulatory requirements.



Edgar Adams, ScD (Member, RADARS System Advisory Board) & Jessica Brainerd, MPH: American Pharmacists Association Response to the Proposed Opioid Class-Wide REMS

In September, 2007, the passage of the Food and Drug Administration Amendments Act gave the FDA authority to require manufacturers of drug and biologic products to develop and implement Risk Evaluation and Mitigation Strategies (REMS) to ensure that the benefits of the drug outweigh the risks of the drug. The FDA can assert this authority during the review of an NDA or after a drug is approved if "new safety information" becomes available. Since the REMS provisions went into effect in March 2008 more than 100 REMS have been approved, including 5 for opioids. While 90 percent of the approved REMS have essentially only a Medication Guide, including 4 of the 5 opioid REMS, there is still an impact on pharmacists since CFR 208.24 requires that Medication Guides be dispensed at the pharmacy. The fifth opioid REMS, a fentanyl product, has been approved with a Medication Guide and full Elements to Assure Safe Use. In February 2009, the FDA proposed an opioid class REMS for extended release and long acting opioids due to concerns about inadvertent exposure and use by non-opioid tolerant individuals as well as abuse, misuse and diversion of these products.

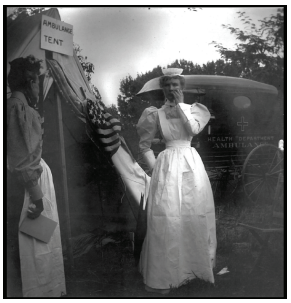
During 2009 and through October 2010, the FDA has provided an open-forum to the public to help assess the impact of the class-wide REMS on all stakeholders. To date a total of 1272 comments have been submitted to the docket, including comments from various pharmacy organizations. Additional perspective was provided in the November/December Journal of the American Pharmacists Association (APhA) in an article entitled "White Paper on designing a risk evaluation and mitigation strategies (REMS) system to optimize the balance of patient access, medication safety, and impact on the health care system." The white paper discusses a number of topic areas impacting REMS design and provides recommendations on balance, standardization, REMS levels, public education, individual patient education, provider education, pilot testing, data management, outcomes monitoring, and quality of care. This article summarizes a few key points from the white paper as well as comments from the National Council for Prescription Drug Programs (NCPDP) (FDA 2009-N-0143-0831.1).

The APhA reports that pharmacists are burdened by the increasing number of REMS programs, all with different systems and requirements thereby resulting in an increase in time spent working on prescription approvals that meet REMS requirements, delays in getting treatment to patients when problems with the REMS processes occur, and the potential for reduced provider participation. In a recent survey conducted by the APhA of 2,000 pharmacists, over 60% of the respondents indicated that risk management programs were confusing, carried excessive costs and have a negative impact on their practice. Even the distribution of Medication Guides provides challenges associated with increased administrative and financial burden, workflow inefficiencies, and supply challenges for pharmacists. They also note that the Medication Guide does not provide a balance of benefit and risk information. Furthermore, in the survey of pharmacists, only 26% correctly responded that a Medication Guide must be dispensed with both initial prescriptions and refills.

Key recommendations centered on standardization and data management including providing a seamless system that builds off of currently existing technologies routinely used by the vast majority of pharmacies such as integration into the systems for third party adjudication of pharmacy claims. This recommendation was echoed by the National Council for Prescription Drug Programs, the Standard Developments Organization for pharmacy. They noted that a transaction could be validated by a REMS database prior to submission to a third party payer. If the REMS criteria were not met, the prescription would not be forwarded for payment. A system meeting these criteria has already been piloted with physicians, pharmacists, and patients by a consortium including Analgesic Solutions, Covance, and eRx.

In summary, virtually all pharmacy groups have commented on the added burden of REMS programs, including those with only a Medication Guide, on their practice as well as the potential for reduced access to needed medications by patients. A number of recommendations have been presented including the need to integrate REMS programs into standard dispensing practice.

1860 – 2010 Denver Health Celebrates 150 Years



Since 1860, Denver Health has played a crucial role in sustaining a standard of health care that has resulted in Denver's reputation as one of our nation's healthiest cities. It has done so by its commitment to a mission that includes access to high quality health care for everyone, including the region's most vulnerable populations; superb emergency and trauma care; public health vigilance; education of the next generation of health care professionals; and research to advance the care of its patients. The RADARS System is proud to be an operation of the Rocky Mountain Poison and Drug Center, a division of Denver Health.

Please find more information at: http://www.denverhealth150.org/

Correction: In Volume 4 Issue 4 of the *RADARS System News*, we reported that in the article, *"RADARS® System Data for Evaluation of REMS"* that the Industry Working Group was part of The Pain Care Forum. This is incorrect; there is no formal affiliation between the groups. We apologize for any confusion this caused.

Recent RADARS System Publications and Presentations

Maxwell JC, McCance-Katz EF. Indicators of Buprenorphine and Methadone Use and Abuse: What Do We Know? *The American Journal on Addictions*, 19: 73–88, 2009.

Did You Know?

RADARS System Researcher Nabarun Dasgupta, MPH, presented RADARS System data at the SAMHSA/NIDA sponsored meeting *Buprenorphine in the Treatment of Opioid Addiction: Reassessment 2010* on May 10-11, 2010.

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Upcoming Meetings of Interest

- American Psychiatric Association, May 22-27, 2010. New Orleans, Louisiana
- Drug Information Association, June 13-17, 2010. Washington, District of Columbia
- College on Problems of Drug Dependence, June 12-17, 2010. Scottsdale, Arizona
- Council of State and Territorial Epidemiologists, June 6-10, 2010. Portland, Oregon
- Society American College Health Association, June 1-5, 2010. Philadelphia, Pennsylvania
- National for Academic Emergency Medicine, June 3-6, 2010. Phoenix, Arizona
- Association of State Alcohol and Drug Abuse Directors, June 1-6, 2010. Norfolk, Virginia
- American Society of Interventional Pain Physicians, June 26-30, 2010. Washington, District of Columbia

RADARS System Mission Statement

The RADARS System provides timely, product specific and geographically-precise data to the pharmaceutical industry, regulatory agencies, policymakers and medical/public health officials to aid in understanding trends in the abuse, misuse, and diversion of prescription drugs in the United States.

Rocky Mountain Poison and Drug Center and Denver Health and Hospital Authority

The RADARS System is a governmental nonprofit operation of the Rocky Mountain Poison and Drug Center (RMPDC), an agency of Denver Health (DH). The RMPDC has been in operation for more than 50 years, making it one of the oldest poison control centers in the nation. DH is the safety net hospital for the City and County of Denver and is the Rocky Mountain region's academic Level I trauma center and includes Denver Public Health, Denver's 911 emergency medical response system, nine family health centers, 12 school-based clinics, NurseLine, correctional care, Denver CARES, the Denver Health Medical Plan, and the Rocky Mountain Center for Medical Response to Terrorism, Mass Casualties and Epidemics.

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