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

Fourth Quarter 2008 Volume 3, Issue 4

In This Issue

Did You Know?

RADARS System data can be used to monitor specific products – both branded and generic.

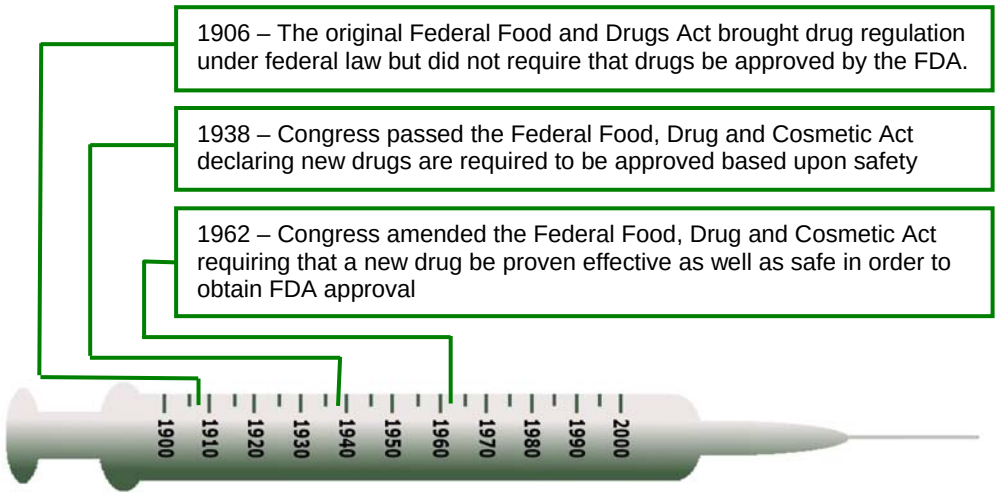
Newsletter Archive

To view all previous issues of The RADAR System News please visit our website at www.RADARS.org

Marketed Drugs That Have Not Received FDA Approval

For historical reasons, some drugs currently available in the United States lack required Food and Drug Administration (FDA) approval for marketing. Any drug product approved before 1962 lacks currently required approval based on safety or efficacy. The FDA estimates that as many as several thousand drug products are marketed illegally (without required approval).

Important Dates in Drug Marketing Approval Requirements:



Among the drugs that were "grandfathered" in and currently on the market are several opioids, including products monitored by the RADARS System. Specifically, several morphine products, methadone products, and certain hydrocodone combination products (hydrocodone/guaifenesin and hydrocodone/pseudoephedrine) have not been approved for safety or efficacy.

To address this concern, the FDA issued a compliance guidance policy (CPG) entitled, *Marketed Unapproved Drugs* in June 2006. According to Charles Lee MD., a medical officer at the Division of New Drugs and Labeling Compliance in the Center for Drug Evaluation and Research of the FDA, "the guidance outlined policies that are aimed at efficiently and rationally bringing all unapproved drugs into the approval process." Adding, "Since the publication of the CPG in June 2006, we have taken action against approximately 400 products and that is among seven different drug classes.[1]"

A number of enforcement actions can be taken against the unapproved products including: requesting voluntary compliance; providing notice of action in a *Federal Register* notice; issuing an untitled letter; issuing a Warning Letter; or initiation of a seizure or injunction.

For prescription opioid products, abuse, misuse and diversion are a significant safety concern. "For those unapproved narcotic drugs on the market, RADARS System data are a tool manufacturers can use to assist in addressing the safety concerns of their products with regard to abuse, misuse and diversion" according to Richard Dart MD, PhD.

[1] http://www.fda.gov/cder/drug/podcast/Unapproved_Drugs_ReachMD_DrLee.htm | FDA Drug Safety Podcasts FDA's Action Against Marketing Unapproved Drugs

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FDA Publishes List of Drugs with Potential Signals of Serious Risk

In September, the Food and Drug Administration published the first list of drugs that are being evaluated by the agency for potential safety risks. The list, called the *Potential Signals of Serious Risks/New Safety Information Identified by the Adverse Event Reporting System (AERS)*, will be published quarterly and evaluates marketed drugs based on a review of reports from AERS.

Of specific interest to manufactures of products with high abuse liability is the identification of extended-release oxycodone as a drug with a potential signal of serious risk for "drug misuse, abuse and overdose." Although the FDA was quick to state that, "the appearance of a drug on this list does not mean that FDA has concluded that the drug has the listed risk. It means that FDA has identified a *potential safety issue*, but does not mean that FDA has identified a causal relationship between the drug and the listed risk." Richard Dart MD, PhD, Executive Director of the RADARS System, stated that, "the appearance of a product on the list for the reason of drug misuse, abuse and overdose has broad and far-reaching implications in several areas including REMS requirements for drugs with high abuse liability." Adding, "we must watch this development closely."

The list was authorized by the passage of the Food and Drug Administration Amendments Act (FDAAA) of 2007. Title IX, section 921 of the FDAAA of 2007 directs FDA to "*conduct regular, bi-weekly screening of AERS database and post a quarterly report on the Adverse Event Reporting System Web site of any new safety information or potential signal of a serious risk identified by AERS within the last quarter."*

The *Potential Signals of Serious Risks/New Safety Information Identified by AERS* list provided twenty drugs identified through AERS for the period of time covering January through March 2008

Product Name: Active Ingredient (Trade) *or* Product Class	**Potential Signal of Serious Risk/New Safety Information**
Arginine Hydrochloride Injection (R-Gene 10)	Pediatric overdose due to labeling / packaging confusion
Desflurane (Suprane)	Cardiac arrest
Duloxetine (Cymbalta)	Urinary retention
Etravirine (Intelence)	Hemarthrosis
Fluorouracil Cream (Carac) and Ketoconazole Cream (Kuric)	Adverse events due to name confusion
Heparin	Anaphylactic-type reactions
Icodextrin (Extraneal)	Hypoglycemia
Insulin U-500 (Humulin R)	Dosing confusion
Ivermectin (Stromectol) and Warfarin	Drug interaction
Lapatinib (Tykerb)	Hepatotoxicity
Lenalidomide (Revlimid)	Stevens Johnson Syndrome
Natalizumab (Tysabri)	Skin melanomas
Nitroglycerin (Nitrostat)	Overdose due to labeling confusion
Octreotide Acetate Depot (Sandostatin LAR)	Ileus
Oxycodone Hydrochloride Controlled-Release (Oxycontin)	Drug misuse, abuse and overdose
Perflutren Lipid Microsphere (Definity)	Cardiopulmonary reactions
Phenytoin Injection (Dilantin)	Purple Glove Syndrome
Quetiapine (Seroquel)	Overdose due to sample pack labeling confusion
Telbivudine (Tyzeka)	Peripheral neuropathy
Tumor Necrosis Factor (TNF) Blockers	Cancers in children and young adults

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CEO of Denver Health and Hospital Authority Receives National Leadership Award

On November 21, 2008, Denver Health and Hospital Authority CEO Patricia A. Gabow, M.D. received the 2008 National Healthcare Leadership Award from the National Center for Healthcare Leadership (NCHL). The Award recognizes the healthcare leader whose commitment, values, and vision embody the primary mission of NCHL to identify and mentor future generations toward the goal of transforming organizational performance and improving healthcare in the United States. Dr. Gabow is the first woman to receive the award and Denver Health's the first safety net institution to receive the award.

The RADARS System is an operation of the Rocky Mountain Poison and Drug Center, an agency of Denver Health and Hospital Authority.

"In this time of financial instability in healthcare and all other industries, this award is a wonderful achievement for Dr. Gabow and for Denver Health" stated Richard Dart MD, PhD, Executive Director of the RADARS System and member of Denver Health Executive Staff. Adding, "our congratulations to Dr. Gabow on such an amazing achievement."

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RADARS System Third Annual Scientific Meeting – Save the Date!

Thursday, April 23, 2009 in Bethesda, Maryland

Additional details will be announced in the near future.

The RADARS System Annual Scientific Meeting encourages prescription drug abuse experts, representatives from the pharmaceutical industry, medical professionals, and federal regulatory agencies to discuss current trends in prescription drug abuse research and to develop strategies to ensure the safe and proper use of prescription medications.

Click here for additional RADARS System Annual Meeting information.

Did You Know?

The RADARS System consists of seven signal detection systems, each providing a unique perspective on prescription drug abuse, misuse and diversion.

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Recent RADARS System Publications and Presentations

- Bailey JE, Campagna E, Dart RC, Reporting for the RADARS System Poison Center Group. The Under Recognized Toll of Prescription Drug Abuse on Young Children. *Annals of Emergency Medicine*. In Press.
- Hays BD, Klein-Schwartz W, Doyon S. Toxicity of Buprenorphine Overdoses in Children. *Pediatrics*. 2008; 121: 782-786.
- Kirtland MN, Lemon S, Bailey JE, Dart RC. Effectiveness of a Poison Center Intervention on Product Coding. 2008 North American Congress of Clinical Toxicology. September, 2008.
- Kirtland MN, Bailey JE, Dart RC. Prescription Opioid Associated Death Rates Using RADARS System Data. American Academy of Addiction Psychiatry Conference. December, 2008.
- Montoya AM, Bailey JE, Dart RC. Current Nonmedical Prescription Drug Use Among College Students: Analysis of RADARS System Data. The American Academy of Addiction Psychiatry Conference. December, 2008.

Complete Publication List

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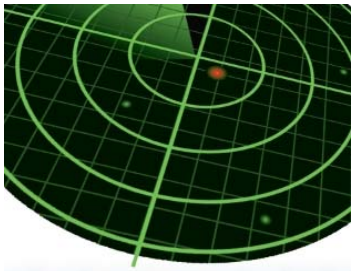

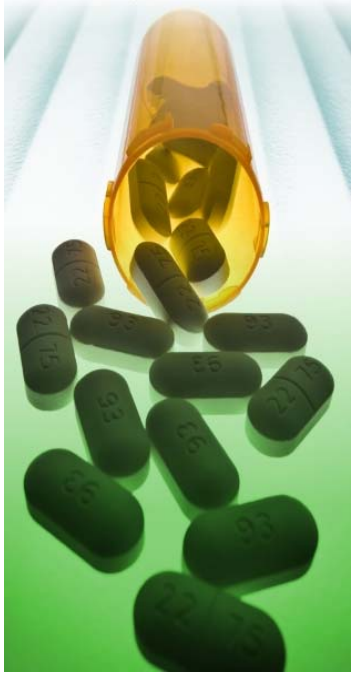

Upcoming Meetings of Interest

- American Academy of Pain Medicine, January 28-31, 2009. Honolulu, Hawaii
- American Society for Clinical Pharmacology and Therapeutics, March18-21, 2009. Washington, D.C.
- Drug Information Association, European Annual Meeting, March 23-25, 2009. Berlin, Germany
- Society of Toxicology, March 15-19, 2009. Baltimore, Maryland

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RADARS System Mission Statement

The RADARS System provides timely and geographically-specific 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.

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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.

DENVER HEALTH
Level One Care for ALL

RMPDC
ROCKY MOUNTAIN POISON & DRUG CENTER
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