

ADVERSE DRUG EVENT REPORTING AND MONITORING

- 1. REASON FOR ISSUE:** This Veterans Health Administration (VHA) Directive establishes national policy for the reporting, monitoring, and surveillance of adverse drug events (ADEs) entered into VHA's spontaneous ADE reporting system for observed and new ADEs at Department of Veterans Affairs (VA) medical facilities.
- 2. SUMMARY OF MAJOR CHANGES:** Changes include adverse events to vaccination/immunization products and the link to the Food and Drug Administration (FDA)/Centers for Disease Control (CDC) vaccine adverse event reporting system. Finally, cross-references to VHA Handbooks and standards were updated according to availability of more recent versions.
- 3. RELATED ISSUES:** VHA Handbooks 1050.01 and 1058.01.
- 4. RESPONSIBLE OFFICE:** The Chief Consultant for Pharmacy Benefits Management (PBM) Services (10P4P) is responsible for the contents of this Directive. Questions may be directed to 202-461-7326.
- 5. RESCISSIONS:** VHA Directives 2008-059, dated September 29, 2008, and 2008-072, dated October 30, 2008, are rescinded.
- 6. RECERTIFICATION:** This VHA Directive is scheduled for recertification on or before the last working day of September, 2019.

Carolyn M. Clancy, MD
Interim Under Secretary for Health

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ADVERSE DRUG EVENT REPORTING AND MONITORING

1. PURPOSE: This Veterans Health Administration (VHA) Directive establishes national policy for the reporting, monitoring, and surveillance of adverse drug events (ADE) entered into VHA's spontaneous ADE reporting system for observed and new ADEs at Department of Veterans Affairs (VA) medical facilities. **AUTHORITY:** 38 U.S.C. 7301(b). **NOTE:** *ADEs in this Directive include events related to medication (drug), vaccination, and immunization products.*

2. BACKGROUND: ADEs must be reported to the national VA Adverse Drug Event Reporting System (VA ADERS), and the Food and Drug Administration (FDA) MedWatch system at http://www.fda.gov/medwatch/safety/FDA-3500A_Fillable.pdf, or adverse events from vaccines to the Centers for Disease Control and Prevention (CDC) and the FDA Vaccine Adverse Event Reporting System (VAERS) at <https://vaers.hhs.gov/esub/index>. **NOTE:** *Disclosure of adverse events to patients is not addressed in this Directive. Consult current VHA policy for disclosure of adverse events to patients, VHA Handbook 1004.08, Disclosure of Adverse Events to Patients, at <http://www.ethics.va.gov/Handbook1004-08.pdf>. This is a related but separate policy.*

a. The VHA intranet spontaneous ADE reporting system, known as VA ADERS, standardizes reporting at the facility level, centralizes ADE data analysis, and improves the efficiency of ADE report coding used to categorize and classify symptoms associated with the event.

b. VA ADERS allows individuals to:

(1) Report, track, and electronically submit serious adverse drug events to the FDA's MedWatch system;

(2) Report, track, and electronically submit adverse events due to vaccine and immunization products to the CDC and FDA's VAERS program;

(3) Assess information on ADEs that are potentially preventable, and report to the personnel involved in ADE monitoring;

(4) Trend ADE data at local, regional, and national levels; and

(5) Track ADEs associated with newer drugs (i.e., drugs that have been on the market in the United States for 3 years or less).

c. The primary goal of VA ADERS is to improve ADE reporting as well as to provide ADE trending reports and an intranet portal for VA medical facilities to share process improvements as a result of ADE data analysis. VA ADERS achieves these objectives using a central database within VHA where all ADEs are reported uniformly, so that surveillance activities can identify safety concerns in Veterans promptly, and local VA medical facilities have data to track, trend, and compare information throughout the organization. This enhanced ADE reporting and tracking system enables VHA to take prompt action to ensure the safety of pharmaceutical drug product use.

d. Benchmarking ADE reporting by Veterans Integrated Service Networks (VISN) and VA medical facilities is conducted utilizing report totals and normalized reporting rates (expressed as reports per unique patient). Comparisons for benchmarking will utilize reporting trends from VA medical facilities of similar size and complexity and, where applicable, by drug, drug class, event of interest or ADE severity. Overall trends utilized for benchmarking are evaluated by the VA ADERS staff and the VA ADERS Advisory Committee. Benchmarking is communicated to the VISNs and VA medical facilities for review and sharing at the appropriate level.

3. POLICY: It is VHA policy that all ADEs that meet the definition of observed adverse drug reactions (ADR) (see paragraph 7b (1-3)) be reported into VA ADERS. ADRs observed in subjects participating in VA clinical trials research protocols should be reported as appropriate (see paragraph 5).

4. RESPONSIBILITIES:

a. **Pharmacy Benefits Management Services.** Pharmacy Benefits Management Services (PBM) is responsible for the administration and maintenance of VA ADERS.

b. **Chief Consultant, PBM.** The Chief Consultant, PBM, or designee, is responsible for ensuring that:

(1) VA MedSAFE and VA ADERS staff aggregate and analyze data nationally to identify potential signals of ADEs to support pharmacovigilance activities. **NOTE:** *All symptoms reported into VA ADERS that are associated with the ADE will be coded in accordance with terminology from the Medical Dictionary for Regulatory Activities (MedDRA).*

(2) VA ADERS staff generates a quarterly (or if feasible, monthly) trending report, which is shared with the VHA ADE Advisory Committee for review. **NOTE:** *VA medical facilities can also use VA ADERS reporting tools to build customized or ad hoc reports as needed.*

(3) A VA ADERS Advisory Committee is established with representative members appointed from the: PBM Clinical Pharmacy Section; Medical Advisory Panel (MAP); VA MedSAFE; VA ADERS and VA ADERS end users; National Center for Patient Safety (NCPS); Office of Research and Development (ORD); VISN Formulary Leaders; PBM Pharmacy Re-engineering staff; and PBM VA Central Office policy staff.

c. **VA ADERS Advisory Committee.** The VA ADERS Advisory Committee provides oversight of the VA ADERS system and is responsible for:

(1) Ensuring a mechanism is in place to communicate that further analysis is required by the VISNs to assess and intervene upon preventable ADE trends that have been identified by VA ADERS staff and confirmed by the committee.

(2) Reviewing process and system improvements reported by VISNs or VA medical facilities to evaluate and determine national applicability.

(3) Ensuring access to the VA ADERS Data Cube briefing books. **NOTE:** *The committee members define trending reports that will be contained in the VA ADERS Data Cube briefing*

books. Relevant committee members (e.g., representatives from NCPS and ORD committee members) communicate these reports from the briefing book, as needed.

(4) Meeting quarterly and reviewing the ADE data in VA ADERS. **NOTE:** *Ad hoc meetings and data requests are scheduled as needed by the VA ADERS Advisory Committee in response to significant ADE or an unusual cluster of ADEs reported by VISNs, VA medical facilities, and ORD or reported through the NCPS safety reports database.*

(5) Providing assistance, guidance, and education to VISNs when variation in reporting is identified as a trend by VA ADERS staff.

(6) Ensuring a mechanism is in place to communicate to VISNs preventable ADE trends analysis.

(7) Assisting in identifying quality assurance projects (such as medication use evaluations) for review and consideration by VA MedSAFE.

d. **VISN Director (or designee [i.e., VISN Pharmacist Executive]).**

(1) Requires that each VISN PBM or Formulary Committee review VA ADERS reports during their meetings.

(2) Requires that any process or system improvements made at the VISN level are shared with the VA ADERS Advisory Committee.

e. **Medical Facility Director.** The medical facility Director is responsible for ensuring that:

(1) The VA medical facility has a local ADE reporting policy that includes:

(a) Written procedures that describe the operation of the facility ADE reporting system through VA ADERS that meet or exceed requirements mandated by The Joint Commission in ADE reporting in accordance with the 2012 The Joint Commission standard MM.07.01.03. This standard requires analysis of serious ADEs and appropriate action based on the analysis.

(b) Instruction or education provided to all health care providers involved in direct patient care and researchers with clinical privileges conducting studies involving drugs on how to enter ADEs into the Computerized Patient Record System (CPRS).

(c) Procedures for reporting all ADEs meeting the definition of observed ADRs into VA ADERS.

(d) A description of the ADE that is associated with the suspect drug as determined by the clinical judgment of the staff or clinician reporting. Clinicians should not have to obtain approval by any other person or committee before submitting an ADE report and the causality does not have to be absolutely established before submitting a report.

(e) Training is provided to designated health care personnel on how to submit and retrieve reports from VA ADERS.

(f) A system is in place for sharing information from ADE reports and coordinating action from analysis of information with appropriate groups, such as: Associate Chief of Staff (ACOS) for Research and Development (R&D); Pharmacy & Therapeutics (P&T) Committee and Pharmacy Service; and, if applicable, Quality Management, Risk Managers, Patient Safety Managers or if the ADE was identified as preventable as a result of a medication error, the Safety Committee Officers.

(g) A procedure is in place for tracking, reviewing, and providing ADE reports monthly to the local VA medical facility P&T Committee. If the local P&T Committee only meets bi-monthly or quarterly, the reports must be submitted to a designated person who has the ability to call an ad hoc meeting, if the need arises.

(h) A procedure is established to communicate benchmarking data to the VA medical facility Directors, P&T Committees, and facility staff reporting ADEs. Action items approved to improve reporting or addressing benchmarking comparisons are to be reported to the local P&T Committee, the VISN PBM Formulary Committee, and the VA ADERS Advisory Committee.

(i) A system whereby ADEs identified as “preventable” are reviewed and analyzed is in place. Any action taken is to be reported to the local P&T Committee, the VISN PBM or Formulary Committee, and the VA ADERS Advisory Committee.

(j) A requirement is established that each local P&T Committee includes ADE report reviews as a standing agenda item at meetings.

(k) The requirement that any process or system improvements made at the medical facility level are shared with the VA ADERS Advisory Committee.

(2) Sufficient health care personnel are designated for ADE reporting into VA ADERS. A facility point of contact may be identified to coordinate and ensure the designated health care staff is reporting ADEs into VA ADERS.

5. VA APPROVED RESEARCH STUDIES:

a. This Directive is applicable to clinical trials if the research protocol requires the use of investigational drugs, comparator drugs or concurrent drugs, or any combination thereof (see VHA Handbook 1108.04, Investigational Drugs and Supplies, for definitions of these terms) if the drugs:

(1) Have been approved by the FDA,

(2) Are being used for an FDA approved indication, and

(3) Are being used at a dosage and in a patient population that is consistent with the official labeling of the drug.

b. When reporting is required, the investigator is responsible for:

(1) Reporting the ADR through the procedures set up by the medical facility and

(2) Notifying the IRB and other specified groups responsible for study oversight or management per the protocol and facility research policies if the ADR also meets the definition of an adverse event, serious adverse event, or an unanticipated adverse event.

c. Reporting in VA ADERS is not required if the investigational drugs, comparator drugs or concurrent drugs, or any combination thereof, are:

(1) Under an Investigational New Drug or

(2) Used in a clinical trial in which the investigator does not know participants' treatment assignment because of the use of a blinded methodology.

6. REFERENCES:

a. VHA Handbook 1058.01, Research Compliance Reporting Requirements.

b. VHA Handbook 1050.01, VHA National Patient Safety Improvement Handbook.

c. Nebeker JR, Barach P, Samore MH. "Clarifying adverse drug events: A clinical guide to terminology, documentation, and reporting," Annals of Internal Medicine. May 2004; 18; 140(10):795-801.

d. Safety of Medicines - A Guide to Detecting and Reporting Adverse Drug Reactions - Why Health Professionals Need to Take Action <http://apps.who.int/medicinedocs/en/d/Jh2992e/>.

e. The Importance of Pharmacovigilance - Safety Monitoring of Medicinal Products <http://apps.who.int/medicinedocs/pdf/s4893e/s4893e.pdf>.

f. Food and Drug Administration. "What Is A Serious Adverse Event?" Available at: <http://www.fda.gov/medwatch/report/DESK/advevnt.htm>. Updated January 10, 2014.

g. The Joint Commission Standard MM.07.01.03.

7. DEFINITIONS:

a. **Adverse Drug Event**. An Adverse Drug Event (ADE) is an injury resulting from the use of a drug. For the purposes of this Directive, this definition includes harm caused by the drug as a result of adverse drug reactions, drug-drug interactions, product quality problems, or drug overdoses (whether accidental or intentional). Severity levels are:

(1) **Mild ADE**. A mild ADE is an event that requires no intervention or minimal therapeutic intervention such as discontinuation of drug(s).

(2) **Moderate ADE**. A moderate ADE is an event that requires active treatment of adverse reaction, or further testing or evaluation to assess extent of non-serious outcome.

(3) **Serious ADE**. A serious ADE occurs when a patient's condition has one or more of the following outcomes (or requires medical intervention to prevent one of these outcomes): death,

a life-threatening experience, inpatient hospitalization (or a prolonged hospitalization), a persistent or significant disability, or a congenital anomaly or birth defect.

b. **Adverse Drug Reaction.** An Adverse Drug Reaction (ADR) is a response to a drug which is noxious and unintended and which occurs at doses normally used in individuals for prophylaxis, diagnosis, or therapy of disease or for the modification of physiologic function. *NOTE: There should be a causal or suspected link between a drug and adverse drug reaction. However, a causality assessment or association of the drug to the adverse drug reaction does not have to be established in order to report an adverse drug reaction or adverse drug event.*

(1) **Historical ADR.** A historical ADR is a past event or an event that reportedly occurred in the past at another health care setting. A historical ADR is defined in the CPRS system as “reported by the patient as occurring in the past; no longer requires intervention.”

(2) **Observed ADR.** An observed ADR is defined in CPRS as a reaction that is “directly observed or occurring while the patient was on the suspected causative agent.” *NOTE: Observed refers to a newly noted adverse outcome. Although the term implies that the provider of record made the diagnosis, the fact that a provider may not have visually “observed” an adverse drug reaction does not preclude reporting as “Observed.”*

(3) **Allergy.** An allergy is an ADR mediated by an immune response (e.g., rash, hives).

c. **Blinding.** A research methodology in which the investigators do not know a treatment assignment for any subject. Clinical trials are often *double-blind* (or *double-masked*), meaning that both subjects and investigators, as well as sponsor or investigator staff involved in the treatment or clinical evaluation of subjects, are unaware of each subject's assigned treatment. *NOTE: Blinding is intended to minimize the potential biases resulting from differences in management, treatment, or assessment of subjects, or interpretation of results that could arise as a result of subject or investigator knowledge of the assigned treatment.*

d. **Causality Assessment.** A causality assessment is a determination whether there is a reasonable possibility that the drug caused or contributed to an adverse event. It includes assessing temporal relationships, de-challenge or re-challenge information, association (or lack of association) with underlying disease and the presence (or absence) of a more likely cause.

e. **Medication Error.** A medication error is a mishap that occurs during prescribing, transcribing, dispensing, administering, adherence, or monitoring a drug. *NOTE: Not all medication errors lead to adverse outcomes.*

f. **VAMedSAFE.** VAMedSAFE is a PBM Center for Medication Safety with a mission to identify, track, and address preventable ADEs in the VA system with the primary focus on preventing ADRs. As a pharmacovigilance center, VAMedSAFE undertakes quality-improvement and safety initiatives that ultimately assess, monitor, and improve the safe and appropriate use of medications; promote risk reduction efforts; and enhance education and communication of ADEs as well as potential ADEs on a national level.

g. **Pharmacovigilance.** Pharmacovigilance is a clinical science whose objectives are the surveillance, evaluation, and signal detection of the undesirable effects of pharmaceutical products (drugs, biologics, medicines) used for medical therapy or diagnosis.

h. **Suspect Drug.** A suspect drug is a drug product administered before the ADE began and is believed by the reporter, manufacturer, or the health care agency to have contributed to its occurrence. It is “suspected” of being the cause of the ADE and this suspicion makes the ADE an ADR for reporting purposes. Types of suspect drugs include: drug products or products of biologic origin (vaccines, blood products); non-prescription drugs; replacement drugs (hormones, vitamins, minerals, electrolytes, and fluids); non-active ingredients (excipients); or medical, surgical, and dental devices and their interactions with drugs.

i. **VA ADERS Data Cube.** The VA ADERS Data Cube is a multidimensional database that stores the ADE data. The cube allows different views of the data to be quickly displayed.