

ASHP Guidelines on Adverse Drug Reaction Monitoring and Reporting

Pharmacists in organized health care systems should develop comprehensive, ongoing programs for monitoring and reporting adverse drug reactions (ADRs).¹ It is the pharmacist's responsibility and professional obligation to report any suspected ADRs. ADR-monitoring and reporting programs encourage ADR surveillance, facilitate ADR documentation, promote the reporting of ADRs, provide a mechanism for monitoring the safety of drug use in high-risk patient populations, and stimulate the education of health professionals regarding potential ADRs. A comprehensive, ongoing ADR program should include mechanisms for monitoring, detecting, evaluating, documenting, and reporting ADRs as well as intervening and providing educational feedback to prescribers, other health care professionals, and patients. Additionally, ADR programs should focus on identifying problems leading to ADRs, planning for positive changes, and measuring the results of these changes. Positive outcomes resulting from an ADR program should be emphasized to support program growth and development.

ASHP does not suggest that there is a predictable rate of incidence or severity of ADRs. The number and severity of ADRs reported in a given organization or setting would vary with the organization's size, type, patient mix, drugs used, and the ADR definition used.

Definitions

ASHP defines a significant ADR as any unexpected, unintended, undesired, or excessive response to a drug that

1. Requires discontinuing the drug (therapeutic or diagnostic),
2. Requires changing the drug therapy,
3. Requires modifying the dose (except for minor dosage adjustments),
4. Necessitates admission to a hospital,
5. Prolongs stay in a health care facility,
6. Necessitates supportive treatment,
7. Significantly complicates diagnosis,
8. Negatively affects prognosis, or
9. Results in temporary or permanent harm, disability, or death.

Consistent with this definition, an *allergic reaction* (an immunologic hypersensitivity, occurring as the result of unusual sensitivity to a drug) and an *idiosyncratic reaction* (an abnormal susceptibility to a drug that is peculiar to the individual) are also considered ADRs.

Several other definitions of ADRs exist, including those of the World Health Organization (WHO),² Karch and Lasagna,³ and the Food and Drug Administration (FDA).⁴

WHO: "Any response to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function."

Karch and Lasagna: "Any response to a drug that is noxious and unintended, and that occurs at doses

used in humans for prophylaxis, diagnosis, or therapy, excluding failure to accomplish the intended purpose."

FDA: For reporting purposes, FDA categorizes a *serious adverse event* (events relating to drugs or devices) as one in which "the patient outcome is death, life-threatening (real risk of dying), hospitalization (initial or prolonged), disability (significant, persistent, or permanent), congenital anomaly, or required intervention to prevent permanent impairment or damage."

For perspective, it may be helpful to note events that are not classified as ADRs. A *side effect* is defined by ASHP as an expected, well-known reaction resulting in little or no change in patient management (e.g., drowsiness or dry mouth due to administration of certain antihistamines or nausea associated with the use of antineoplastics). ASHP further defines a side effect as an effect with a predictable frequency and an effect whose intensity and occurrence are related to the size of the dose. Additionally, drug withdrawal, drug-abuse syndromes, accidental poisoning, and drug-overdose complications should not be defined as ADRs.

While individual health care organizations may need to apply ADR surveillance to different degrees for different groups of patients, ASHP believes it would be greatly beneficial if a common definition of ADRs were used in all settings to facilitate reporting, collective surveillance, and ADR-trend research.

Program Features

A comprehensive ADR-monitoring and reporting program should be an integral part of an organization's overall drug-use system. An ADR-monitoring and reporting program should include the following features:

1. The program should establish
 - a. An ongoing and concurrent (during drug therapy) surveillance system based on the reporting of suspected ADRs by pharmacists, physicians, nurses, or patients.⁵
 - b. A prospective (before drug therapy) surveillance system for high-risk drugs or patients with a high risk for ADRs.
 - c. A concurrent surveillance system for monitoring alerting orders. Alerting orders include the use of "tracer" drugs that are used to treat common ADRs (e.g., orders for immediate doses of antihistamines, epinephrine, and corticosteroids), abrupt discontinuation or decreases in dosage of a drug, or stat orders for laboratory assessment of therapeutic drug levels.^{6,7}
2. Prescribers, caregivers, and patients should be notified regarding suspected ADRs.
3. Information regarding suspected ADRs should be reported to the pharmacy for complete data collection

- and analysis, including the patient's name, the patient's medical and medication history, a description of the suspected ADR, the temporal sequence of the event, any remedial treatment required, and sequelae.
4. High-risk patients should be identified and monitored. High-risk patients include but are not limited to pediatric patients, geriatric patients, patients with organ failure (e.g., hepatic or renal failure), and patients receiving multiple drugs.⁶
 5. Drugs likely to cause ADRs ("high-risk" drugs) should be identified, and their use should be monitored. Examples of drugs that may be considered as high risk include aminoglycosides, amphotericin, antineoplastics, corticosteroids, digoxin, heparin, lidocaine, phenytoin, theophylline, thrombolytic agents, and warfarin.⁶
 6. The cause(s) of each suspected ADR should be evaluated on the basis of the patient's medical and medication history, the circumstances of the adverse event, the results of dechallenge and rechallenge (if any), alternative etiologies, and a literature review.
 7. A method for assigning the probability of a reported or suspected ADR (e.g., confirmed or definite, likely, possible, and unlikely) should be developed to categorize each ADR. Algorithms⁸⁻¹⁰ may be useful in establishing the causes of suspected ADRs. Subjective questions and the professional judgment of a pharmacist can be used as additional tools to determine the probability of an ADR. Questions might include the following:
 - a. Was there a temporal relationship between the onset of drug therapy and the adverse reaction?
 - b. Was there a dechallenge; i.e., did the signs and symptoms of the adverse reaction subside when the drug was withdrawn?
 - c. Can signs and symptoms of the adverse reaction be explained by the patient's disease state?
 - d. Were there any laboratory tests that provide evidence for the reaction being an ADR?
 - e. What was the patient's previous general experience with the drug?
 - f. Did symptoms return when the agent was readministered?
 8. A method for ranking ADRs by severity should be established.¹¹
 9. A description of each suspected ADR and the outcomes from the event should be documented in the patient's medical record.
 10. Serious or unexpected ADRs should be reported to the Food and Drug Administration (FDA) or the drug's manufacturer (or both).^a
 11. All ADR reports should be reviewed and evaluated by a designated multidisciplinary committee (e.g., a pharmacy and therapeutics committee).
 12. ADR-report information should be disseminated to health care professional staff members for educational purposes. Good topics for medical staff education include preventing ADRs and appropriate and effective care for patients who experience ADRs. Educational programs can be conducted as morning "report" discussions, newsletters, "grand rounds" presentations, algorithms for treatment, and multidisciplinary reviews of drug-use evaluations. Patient confidentiality should be preserved.
 13. In settings where it is possible, a pharmacy-coordinated ADR team or committee, consisting of a physician, nurse, quality improvement leader, an administrator, and a pharmacist is recommended.¹²⁻¹⁵ The team should be charged with adopting a definition for the organization, promoting awareness of the consequences of ADRs, establishing mechanisms for identifying and reporting ADRs, reviewing ADR patterns or trends, and developing preventive and corrective interventions.
 14. Continuous monitoring of patient outcomes and patterns of ADRs is imperative. Findings from an ADR-monitoring and reporting program should be incorporated into the organization's ongoing quality improvement activities. The process should include the following:
 - a. Feedback to all appropriate health care staff,
 - b. Continuous monitoring for trends, clusters, or significant individual ADRs,
 - c. Educational efforts for prevention of ADRs, and
 - d. Evaluation of prescribing patterns, patient monitoring practices, patient outcomes, and the ADR program's effect on overall and individual patient outcomes.

An overall goal of the ADR process should be the achievement of positive patient outcomes.

Benefits

An ongoing ADR-monitoring and reporting program can provide benefits to the organization, pharmacists, other health care professionals, and patients. These benefits include (but are not limited to) the following:

1. Providing an indirect measure of the quality of pharmaceutical care through identification of preventable ADRs and anticipatory surveillance for high-risk drugs or patients.
2. Complementing organizational risk-management activities and efforts to minimize liability.
3. Assessing the safety of drug therapies, especially recently approved drugs.
4. Measuring ADR incidence.
5. Educating health care professionals and patients about drug effects and increasing their level of awareness regarding ADRs.
6. Providing quality-assurance screening findings for use in drug-use evaluation programs.
7. Measuring the economic impact of ADR prevention as manifested through reduced hospitalization, optimal and economical drug use, and minimized organizational liability.

Role of the Pharmacist

Pharmacists should exert leadership in the development, maintenance, and ongoing evaluation of ADR programs. They should obtain formal endorsement or approval of such programs through appropriate committees (e.g., a pharmacy and therapeutics committee and the executive committee of the medical staff) and the organization's administration. In settings where applicable, input into the design of the pro-

gram should be obtained from the medical staff, nursing staff, quality improvement staff, medical records department, and risk managers.^{8,16–18} The pharmacist should facilitate

1. Analysis of each reported ADR,
2. Identification of drugs and patients at high risk for being involved in ADRs,
3. The development of policies and procedures for the ADR-monitoring and reporting program,
4. A description of the responsibilities and interactions of pharmacists, physicians, nurses, risk managers, and other health professionals in the ADR program,
5. Use of the ADR program for educational purposes,
6. Development, maintenance, and evaluation of ADR records within the organization,
7. The organizational dissemination and use of information obtained through the ADR program,
8. Reporting of serious ADRs to the FDA or the manufacturer (or both), and
9. Publication and presentation of important ADRs to the medical community.

Direct patient care roles for pharmacists should include patient counseling on ADRs, identification and documentation in the patient's medical record of high-risk patients, monitoring to ensure that serum drug concentrations remain within acceptable therapeutic ranges, and adjusting doses in appropriate patients (e.g., patients with impaired renal or hepatic function).

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^aTo report an adverse drug event to the FDA, use the MedWatch program. Reports can be mailed (MedWatch, 5600 Fishers Lane, Rockville, MD 20852–9787), faxed (800-FDA-0178), called in (800-FDA-1088), or reported by modem (800-FDA-7737). An easy-to-use FDA form 3500 can be used. This form should be available from a pharmacy.

Approved by the ASHP Board of Directors, November 16, 1994. Revised by the ASHP Council on Professional Affairs. Supersedes a previous version dated November 16, 1988.

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The bibliographic citation for this document is as follows: American Society of Health-System Pharmacists. ASHP guidelines on adverse drug reaction monitoring and reporting. *Am J Health-Syst Pharm.* 1995; 52:417–9.